

# DSABNS 2024

15th INTERNATIONAL CONFERENCE  
DYNAMICAL SYSTEMS APPLIED TO BIOLOGY  
AND NATURAL SCIENCES (DSABNS)

## **BOOK OF ABSTRACTS**

NOVA SCHOOL OF SCIENCE AND TECHNOLOGY  
(NOVA FCT)  
CAPARICA, PORTUGAL

15th INTERNATIONAL CONFERENCE  
DYNAMICAL SYSTEMS APPLIED TO BIOLOGY  
AND NATURAL SCIENCES  
**BOOK OF ABSTRACTS**

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## 15th INTERNATIONAL CONFERENCE DYNAMICAL SYSTEMS APPLIED TO BIOLOGY AND NATURAL SCIENCES (DSABNS)



The International Conference “Dynamical Systems Applied to Biology and Natural Sciences – DSABNS” has been a prestigious scientific event since 2010, held annually in February. The scientific programme includes Public Lectures for a broad audience, Plenary Talks to open and close the scientific sessions, Invited Talks providing context for parallel sessions filled with Contributed Talks by participants. A small number of Minisymposia, each consisting of 4-5 talks, was organized, offering the opportunity to explore complex or emerging topics in greater detail. Additionally, the conference hosted a Poster Session, creating opportunities for researchers to present their work visually and engage in discussions with their peers. The conference proceedings are documented in this Book of Abstracts.

The 15th Conference, DSABNS 2024, took place in Caparica, Portugal, hosted by the NOVA School of Science and Technology (NOVA FCT) and its Center for Mathematics and Applications (NOVAMath) from February 6-9, 2024. The program covered research in population dynamics, eco-epidemiology, infectious disease epidemiology, molecular and antigenic evolution, and methodological topics in the natural sciences and mathematics.

# DSABNS 2024

## 15th INTERNATIONAL CONFERENCE DYNAMICAL SYSTEMS APPLIED TO BIOLOGY AND NATURAL SCIENCES (DSABNS)



### Organizing Committee:

**FCT NOVA:** Fabio Chalub, Paulo Doutor, Paula Patrício, Maria do Céu Soares.

**The MTB group - BCAM:** Maíra Aguiar, Vizda Anam, Carlo Estadilla, Bruno V. Guerrero, Bechir Naffeti, Fernando Saldaña, Akhil Kumar Srivastav, Vanessa Steindorf, Nico Stollenwerk.

**FCUL:** Luis Mateus. **SSM:** Rubén Blasco. **UNIVAQ:** Chiara Cicolani.

### Scientific Committee:

Maíra Aguiar (BCAM); Carlos Braumann (UE); Fabio Chalub (FCT NOVA) Bob Kooi (VU); Andrea Pugliese (UNITN); Lucia Russo (UniNa); Costantinos Siettos (UNINA); Ezio Venturino (UNITO).

### Scientific Institutions:

BCAM: Basque Center for Applied Mathematics, Basque Country, Spain; UNITN: Università degli Studi di Trento, Italy; UE: Universidade de Évora, Portugal; FCT NOVA: NOVA School of Science and Technology, Lisbon, Portugal; VU: Vrije Universiteit Amsterdam, The Netherlands; UNITO: Università degli Studi di Torino, Italy; UNINA: Università degli Studi di Napoli Federico II, Italy; FCUL: Faculdade de Ciências da Universidade de Lisboa, Portugal; SSM: Scuola Superiore Meridionale, Napoli, Italy.

### Sponsors:

The organizers express gratitude for the sponsorship and support extended by the NOVA School of Science and Technology (NOVA FCT) and its Center for Mathematics and Applications (NOVAMath). They have played a key role in hosting and organizing the conference in collaboration with the Mathematical and Theoretical Biology Group (MTB BCAM).

Additionally, this event received support from the Basque Government through the BERC 2022-2025 program and the Spanish Ministry of Science, Innovation, and Universities (CEX2021- 001142-S/MICIN/AEI/10.13039/501100011033).

The European Society for Mathematical and Theoretical Biology (ESMTB), and the European Mathematical Society (EMS) have also contributed with financial support. Special thanks are extended to the Basque Foundation for Science (Ikerbasque).

15th conference on  
**DYNAMICAL SYSTEMS  
APPLIED TO BIOLOGY AND  
NATURAL SCIENCES**

6-9 of February 2024  
NOVA School of Science and  
Technology (NOVA FCT), Portugal

## PUBLIC LECTURES

Vincenzo Capasso - University of Milano, Italy  
Mirjam Kretzschmar - University of Utrecht, The Netherlands

## PLENARY SPEAKERS

Maíra Aguiar - BCAM Bilbao, ES  
Konstantin Blyuss - University of Sussex, UK  
Louise Dyson - University of Warwick, UK  
Isabel Gordo - IGC, PT  
Aaron King - University of Michigan, USA  
Yuliya Kyrychko - University of Sussex, UK  
Ruy M. Ribeiro - Los Alamos National Laboratory, USA  
Lucia Russo - CNR-STEMS, IT  
Ira Schwartz - University of Maryland, USA  
Nico Stollenwerk - BCAM Bilbao, ES

## SCIENTIFIC COMMITTEE

Maíra Aguiar - BCAM Bilbao, Spain  
Carlos Braumann - Évora University, Portugal  
Fabio Chalub - NOVA FCT, Portugal  
Bob Kooi - VU Amsterdam, The Netherlands  
Andrea Pugliese - UNITN, Italy  
Lucia Russo - CNR-STEMS, Italy  
Costantinos Siettos - UNINA, Italy  
Ezio Venturino - UNITO, Italy

## More info at:

<https://sites.google.com/view/dsabns2024>

## ORGANIZING COMMITTEE

Fabio Chalub - NOVA FCT  
Paulo Doutor - NOVA FCT  
Luis Mateus - FCUL  
Paula Patrício - NOVA FCT  
Maria do Céu Soares - NOVA FCT  
The MTB group - BCAM

## IMPORTANT INFORMATION

Registration opening:  
September 15, 2023  
Abstract submission deadline:  
November 3, 2023  
Notification of acceptance:  
November 30, 2023  
Registration deadline:  
January 12, 2024

## Contact:

[dsabns2024\\_novasst@bcamath.org](mailto:dsabns2024_novasst@bcamath.org)



15th conference on  
**DYNAMICAL SYSTEMS  
APPLIED TO BIOLOGY AND  
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6-9 of February 2024  
NOVA School of Science and  
Technology (NOVA FCT), Portugal

## INVITED SPEAKERS

Roberto Barrio - Univ. of Zaragoza, ES  
Carlos Braumann - Univ. of Évora, PT  
Fabio Chalub - NOVA FCT, PT  
Alberto D'Onofrio - Univ. of Trieste, IT  
Erida Gjini - IST, PT  
Maria Gutierrez - Univ. of Cambridge, UK  
Amira Kebir - Univ. of Tunis El Manar, TN  
Bob W. Kooi - VU Amsterdam, NL  
Marta Lopes - NOVA FCT, PT  
Giovanni Marini - FEM, IT  
Roderick Melnik - Univ. of Waterloo, CA  
Slimane ben Miled - Institut Pasteur de Tunis, TN  
Nicolás Moreno - BCAM, ES  
Gianni Pagnini - BCAM, ES  
Paula Patrício - NOVA FCT, PT  
Alberto Pinto - Univ. of Porto, PT  
Carla M. A. Pinto - Polytechnic Univ. of Porto, PT  
Andrea Pugliese - UNITN, IT  
Ganna Rozhnova - Univ. MCU, NL  
Christina Schenk - IMDEA Materials Institute, ES  
Cristiana Silva - ISCTE, PT  
Urszula Skwara - MCS Univ. Lublin, PL  
Lisete Sousa - FCUL, PT  
Uffe Thygesen - Technical Univ. of Denmark, DK  
Delfim Torres - Univ. of Aveiro, PT  
Abdessamad Tridane - Univ. of UAE, UAE  
Ezio Venturino - Univ. of Torino, IT

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# DSABNS 2024

15th INTERNATIONAL CONFERENCE  
DYNAMICAL SYSTEMS APPLIED TO BIOLOGY  
AND NATURAL SCIENCES (DSABNS)

## **SCIENTIFIC PROGRAM**

NOVA SCHOOL OF SCIENCE AND TECHNOLOGY  
(NOVA FCT)  
CAPARICA, PORTUGAL



**15th Conference DSABNS | Feb. 6 - 9, 2024 – Main schedule**  
**Tuesday - February 6, 2024 (Public and Plenary Lectures will take place at room “Grande Auditório”)**

|               |  |  |
|---------------|--|--|
| 8:00 - 9:15   | <b>Registration</b>  |  |
| 9:15 - 9:30   | <b>Opening</b>   |  |
| 9:30 - 10:15  | Public lecture I<br>Vincenzo Capasso   | Chair: Carlos Braumann<br>Controlling OQDS (olive quick decline syndrome) outbreaks caused by <i>Xylella fastidiosa</i>        |
| 10:20 - 11:05 | Plenary lecture I<br>Aaron A. King   | Chair: Carlos Braumann<br>Phylogenetic inference for Markov process models   |
| 11:05 - 11:30 | <b>Coffee break</b>  |  |
| 11:30 - 13:00 | 1 Mini-Symposium + 4 Parallel Sessions: (1 Invited talk + 3 Contributed talks) |  |
| 13:00 - 14:30 | <b>Lunch</b>   |  |
| 14:30 - 15:15 | Plenary lecture II<br>Maira Aguiar   | Chair: Yuliya Kyrychko<br>Complex dynamics in multi-strain dengue models and its impact on public health intervention measures |
| 15:20 - 16:50 | 4 Parallel Sessions: (1 Invited talk + 3 Contributed talks)                    |  |
| 16:50 - 17:20 | <b>Coffee break</b>  |  |
| 17:20 - 18:00 | Plenary lecture III<br>Isabel Gordo  | Chair: Fabio Chalub<br>Microbiome evolution in the mammalian gut   |
| 18:05 - 18:50 | Plenary lecture IV<br>Konstantin Blyuss  | Chair: Nico Stollenwerk<br>Mathematical modelling of replication-mutation dynamics of coronaviruses                            |
| 19:00         | <b>Closing</b>   |  |

|                       |                           |  |   |
|-----------------------|---------------------------|--|---|
| <b>Mini-Symposium</b> | <b>"Grande Auditório"</b> | <b>Theoretical models in sustainable agriculture: integrating ecology, evolution and economics</b> |   |
| 11:30 - 12:00         | MS talk I1                | Suzanne Touzeau  | Mathematical modelling for sustainable crop protection  |
| 12:00 - 12:20         | MS talk I2                | Àlex Giménez-Romero  | Modeling <i>Xylella fastidiosa</i> diseases: transmission dynamics, global spatiotemporal risk predictions and design of control strategies |
| 12:20 - 12:40         | MS talk I3                | Thomas Tunstall  | Tuning spatial distribution of pesticide to minimise the rate of resistance emergence   |
| 12:40 - 13:00         | MS organizer I            | Dana Lauenroth   | Multitype Galton-Watson processes for herbicide resistance evolution  |
|                       | MS co-organizer I         | Chaitanya S. Gokhale   |   |

|                |                      |                                |   |
|----------------|----------------------|--------------------------------|---|
| <b>Ecology</b> | <b>Room 201 - IV</b> | <b>Chair: Fernando Saldaña</b> |   |
| 11:30 - 12:00  | Invited talk 1       | Slimane Ben Miled              | Towards a generic agent based vector-host model   |
| 12:00 - 12:20  | Contributed talk 1   | Elizabeth Howell               | Immune interactions and heterogeneity in transmission drives the pathogen-mediated invasion of grey squirrels in the UK |
| 12:20 - 12:40  | Contributed talk 2   | Manon de la Tousche            | Modeling population dynamics and control strategies for a unique species evolving in heterogeneous landscape            |
| 12:40 - 13:00  | Contributed talk 3   | Ashvini Gupta                  | Chaos in a seasonal food-chain model with migration and variable carrying capacity                                      |

|                                      |                      |                           |   |
|--------------------------------------|----------------------|---------------------------|---|
| <b>Methodology in Biomathematics</b> | <b>Room 202 - IV</b> | <b>Chair: Luis Mateus</b> |   |
| 11:30 - 12:00                        | Invited talk 2       | Lisete Sousa              | The impact of multiple simultaneous testing in omics studies  |
| 12:00 - 12:20                        | Contributed talk 4   | Antonio Matas Gil         | Unraveling spatial patterns: Physics informed neural networks for solving the inverse problem in Turing systems |
| 12:20 - 12:40                        | Contributed talk 5   | canceled                  |   |
| 12:40 - 13:00                        | Contributed talk 6   | Andr as Telcs             | Causal discover for stochastic dynamic systems, a new Markov chain approach                                     |

| <b>Epidemiology</b> | <b>Room 203 - IV</b> | <b>Chair: Akhil Srivastav</b> |   |
|---------------------|----------------------|-------------------------------|---|
| 11:30 - 12:00       | Invited talk 3       | Andrea Pugliese               | Modelling releases of Wolbachia-infected male mosquitoes: when can this strategy be effective in reducing mosquito densities? |
| 12:00 - 12:20       | Contributed talk 7   | Bruno V. Guerrero             | Estimating the risk of arbovirus spreading in non-endemic areas: Basque Country as a case study                               |
| 12:20 - 12:40       | Contributed talk 8   | Jacob Roberts                 | Impact of targeted testing in early HIV infection on reducing transmission among men who have sex with men in The Netherlands |
| 12:40 - 13:00       | Contributed talk 9   | Eunha Shim                    | Assessing the transmission potential of mpox in East Asia during 2022-2023: a focus on Taiwan, China, Japan, and South Korea  |

| <b>Epidemiology</b> | <b>Room 204 - IV</b> | <b>Chair: Carlo Estadilla</b> |  |
|---------------------|----------------------|-------------------------------|--|
| 11:30 - 12:00       | Invited talk 4       | Abdessamad Tridane            | Modeling the impact of mobility suppression and vaccinations in containing epidemics in cities network   |
| 12:00 - 12:20       | Contributed talk 10  | Tatiana Sannikova             | SEIR model in contact network of urban population  |
| 12:20 - 12:40       | Contributed talk 11  | Bárbara Rodrigues             | Integro-differential SIR model with Lagrangian approach  |
| 12:40 - 13:00       | Contributed talk 12  | Mennatallah Gouda             | Characterization of the long-distance dispersal kernel of white-tailed deer and evaluating its impact on chronic wasting disease spread in Wisconsin, US |

| <b>Miscellaneous</b> | <b>Room 201 - IV</b> | <b>Chair: Paulo Doutor</b> |  |
|----------------------|----------------------|----------------------------|--|
| 15:20 - 15:50        | Invited talk 5       | Cristiana J. Silva         | Modeling the impact of individual behaviors on epidemic spreading through hybrid models  |
| 15:50 - 16:10        | Contributed talk 13  | Abhyudai Singh             | Hybrid systems modeling of ecological population dynamics                                |
| 16:10 - 16:30        | Contributed talk 14  | Aurelien Youmbi            | Biological control of diamondback moth: a mathematical approach                          |
| 16:30 - 16:50        | Contributed talk 15  | Burcu Gürbüz               | An extensive numerical approach to model the dynamics of the acute inflammatory response |

| <b>Neurosciences</b> | <b>Room 202 - IV</b> | <b>Chair: Fabio Chalub</b> |  |
|----------------------|----------------------|----------------------------|--|
| 15:20 - 15:50        | Invited talk 6       | Roberto Barrio             | Patterns of movement on insects: small CPGs, bifurcations and ubiquitous tripod gait |
| 15:50 - 16:10        | Contributed talk 16  | Robert Allen               | Insights into neural oscillator network dynamics using a phase-isostable framework   |
| 16:10 - 16:30        | Contributed talk 17  | Joana Cabral               | Superposition of stationary waves in brain activity vary with anesthesia             |

| <b>Methodology in Biomathematics</b> | <b>Room 203 - IV</b> | <b>Chair: Nico Stollenwerk</b> |   |
|--------------------------------------|----------------------|--------------------------------|---|
| 15:20 - 15:50                        | Invited talk 7       | Uffe Thygesen                  | Estimation in nonlinear stochastic differential equations using the Laplace approximation             |
| 15:50 - 16:10                        | Contributed talk 18  | Fearghus Downes                | Modelling bovine hormone dynamics: a compartmental approach   |
| 16:10 - 16:30                        | Contributed talk 19  | Ana Niño-López                 | UMAP dimensionality reduction to analyse B Acute Lymphoblastic Leukemia patients data                 |
| 16:30 - 16:50                        | Contributed talk 20  | Gustavo Carrero                | A mathematical model for the formation of patterns on tulip petals caused by the tulip-breaking virus |

| <b>Epidemiology</b> | <b>Room 204 - IV</b> | <b>Chair: Vanessa Steindorf</b> |   |
|---------------------|----------------------|---------------------------------|---|
| 15:20 - 15:50       | Invited talk 8       | Urszula Skwara                  | Some applications of fractional calculus to mathematical modelling of vector-borne diseases   |
| 15:50 - 16:10       | Contributed talk 21  | Martim Geraldes                 | The historical ecological background of West Nile virus in Portugal provides one health knowledge and opportunities into the future |
| 16:10 - 16:30       | Contributed talk 22  | Marta Pardo-Araujo              | Colonization dynamics of the invasive vector <i>Aedes albopictus</i> in Spain: thermal biology and human mobility                   |
| 16:30 - 16:50       | Contributed talk 23  | Luís Mateus                     | Time-scale separation and center manifold analysis in a vector-host model   |

**15th Conference DSABNS | Feb. 6 - 9, 2024 – Main schedule**  
**Wednesday - February 7, 2024 (Public and Plenary Lectures will take place at room “Grande Auditório”)**

|               |   |   |
|---------------|---|---|
| 8:30 - 9:15   | <b>Registration</b>   |   |
| 9:30 - 10:15  | Plenary lecture V<br>Ira B. Schwartz  | Chair: Konstantin Blyuss<br>Predicting extreme outbreaks due to demographic and parametric noise in epidemics   |
| 10:20 - 11:05 | Plenary lecture VI<br>Nico Stollenwerk  | Chair: Paula Patrício<br>The role of import in subcritical epidemiological systems leading to large fluctuations, case studies: COVID-19 after lockdown lifting and vector-borne disease invasion scenarios |
| 11:05 - 11:30 | <b>Coffee break</b>   |   |
| 11:30 - 13:00 | <b>1 Mini-Symposium + 4 Parallel Sessions: (1 Invited talk + 3 Contributed talks)</b> |   |
| 13:00 - 14:30 | <b>Lunch</b>  |   |
| 14:30 - 15:15 | Public lecture II<br>Mirjam Kretzschmar   | Chair: Andrea Pugliese<br>Mathematical models for public health interventions in aging populations  |
| 15:20 - 16:50 | <b>4 Parallel Sessions: (1 Invited talk + 3 Contributed talks)</b>                    |   |
| 17:00 - 18:30 | <b>Poster Session<br/>Coffee Break and Cocktail</b>                                   |   |

|                       |                           |   |  |
|-----------------------|---------------------------|---|--|
| <b>Mini-Symposium</b> | <b>“Grande Auditório”</b> | <b>Statistical physics tools applied to stochastic models in population dynamics and epidemic spreading</b> |  |
| 11:30 - 12:00         | MS organizer II           | Uwe C. Täuber   | Fluctuations and spatial correlations in chemical reaction kinetics, population dynamics, and epidemic spreading |
| 12:00 - 12:20         | MS talk II1               | Uwe C. Täuber   | Computing macroscopic reaction rates in reaction-diffusion systems using Monte Carlo simulations                 |
| 12:20 - 12:40         | MS talk II2               | Ruslan Mukhamadiarov  | Effects of lattice dilution on the nonequilibrium phase transition in the stochastic SIR model                   |
| 12:40 - 13:00         | MS talk II3               | Géza Ódor   | Super-spreader hot-spots, mobility and lock-down effects on the dynamics of SIR epidemic models                  |
| 13:00 - 13:20         | MS talk II4               | Lluís Hernández-Navarro   | Coupled environmental and demographic fluctuations shape the evolution of cooperative antimicrobial resistance   |

|                  |                      |                                |  |
|------------------|----------------------|--------------------------------|--|
| <b>Evolution</b> | <b>Room 201 - IV</b> | <b>Chair: Fernando Saldaña</b> |  |
| 11:30 - 12:00    | Invited talk 9       | Fabio Chalub                   | An overview of finite and infinite population models in evolutionary dynamics      |
| 12:00 - 12:20    | Contributed talk 24  | Megan Oliver                   | Host manipulation by parasites to facilitate transmission                          |
| 12:20 - 12:40    | Contributed talk 25  | Chiara Cicolani                | Exponential synchronization of Kuramoto oscillators with time-delayed interactions |
| 12:40 - 13:00    | Contributed talk 26  | Jonathan Hamley                | Parasite infection and the evolution of host senescence                            |

|                      |                      |                           |  |
|----------------------|----------------------|---------------------------|--|
| <b>Cell Dynamics</b> | <b>Room 202 - IV</b> | <b>Chair: Bob W. Kooi</b> |  |
| 11:30 - 12:00        | Invited talk 10      | Gianni Pagnini            | Generalized Fokker–Planck equations for superstatistical systems   |
| 12:00 - 12:20        | Contributed talk 27  | Juan Magalang             | Modelling optimal therapy switching strategies to mitigate drug resistance development                                     |
| 12:20 - 12:40        | Contributed talk 28  | Mahmoud A. Ibrahim        | Dynamics of chronic myelogenous leukemia with logistic growth and cell division delay                                      |
| 12:40 - 13:00        | Contributed talk 29  | Peter Boldog              | Modeling cell cycle dynamics in cell cultures: implications for cancer therapy in well mixed and spatial structured models |

| Ecology       | Room 203 - IV       | Chair: Roberto Barrio |  |
|---------------|---------------------|-----------------------|--|
| 11:30 - 12:00 | Invited talk 11     | Carlos Braumann       | Are populations in random environments following Itô or Stratonovich calculus? Does it matter? |
| 12:00 - 12:20 | Contributed talk 30 | Andy White            | A temporal refuge from predation can change the outcome of prey species competition            |
| 12:20 - 12:40 | Contributed talk 31 | Paul Georgescu        | Global stability of coexistence equilibria for n-species models of facultative mutualism       |
| 12:40 - 13:00 | Contributed talk 32 | Soumitra Pal          | Impact of fear and group defense on the dynamics of a predator-prey system                     |

| Epidemiology  | Room 204- IV        | Chair: Paula Patrício |  |
|---------------|---------------------|-----------------------|--|
| 11:30 - 12:00 | Invited talk 12     | Ganna Rozhnova        | COVID-19 and chronic illness interactions in transmission dynamics   |
| 12:00 - 12:20 | Contributed talk 33 | Rubén Blasco-Aguado   | A study of COVID-19 dynamics in Basque Country and Italy   |
| 12:20 - 12:40 | Contributed talk 34 | Carlo Estadilla       | Cost-effectiveness of COVID-19 vaccination by modeling a counterfactual scenario: a case study of the Basque Country                               |
| 12:40 - 13:00 | Contributed talk 35 | Bechir Naffeti        | The dynamic of the COVID-19 in the Basque Country: a mathematical model considering losing and boosting immunity, vaccination and control measures |

| Methodology in Biomathematics | Room 201 - IV       | Chair: Fernando Saldaña |  |
|-------------------------------|---------------------|-------------------------|--|
| 15:20 - 15:50                 | Invited talk 13     | Delfim Torres           | Dynamic SIR models with exact solution   |
| 15:50 - 16:10                 | Contributed talk 36 | Sten Madec              | From a co-infection SIS model to the replicator equation   |
| 16:10 - 16:30                 | Contributed talk 37 | Ricardo Castelhano      | Behavior of a SIR model with vaccination ruled by an imitation game: from equilibrium stability to positive Lyapunov exponents |
| 16:30 - 16:50                 | Contributed talk 38 | canceled                | canceled   |

| Miscellaneous | Room 202 - IV       | Chair: Ezio Venturino |  |
|---------------|---------------------|-----------------------|--|
| 15:20 - 15:50 | Invited talk 14     | Erida Gjini           | Dynamical underpinnings of multi-strain colonization systems using the replicator equation   |
| 15:50 - 16:10 | Contributed talk 39 | Suman Chakraborty     | Modelling and optimizing resource allocation to defence chemicals and counter-counter defence by enzyme inhibitors in parasitic and trophic interactions |
| 16:10 - 16:30 | Contributed talk 40 | Jacques Hermes        | The rise of the mini-models  |
| 16:30 - 16:50 | Contributed talk 41 | canceled              | canceled   |

| Ecology       | Room 203 - IV       | Chair: Paulo Doutor |  |
|---------------|---------------------|---------------------|--|
| 15:20 - 15:50 | Invited talk 15     | Roderick Melnik     | Complex biosocial dynamics: nonlocal cooperative behavior, psychological effects, and collective decision-making               |
| 15:50 - 16:10 | Contributed talk 42 | Subrata Dey         | Analytical detection of stationary and dynamic patterns in a prey-predator model with reproductive Allee effect in prey growth |
| 16:10 - 16:30 | Contributed talk 43 | Jyotirmoy Roy       | Local and global dynamics of a predator-prey model with maturation delay in generalist predator                                |
| 16:30 - 16:50 | Contributed talk 44 | Masoom Bhargava     | Spatiotemporal dynamics in trade-off prey predator model with doomed function response   |

| Epidemiology  | Room 204 - IV       | Chair: Andrea Pugliese |  |
|---------------|---------------------|------------------------|--|
| 15:20 - 15:50 | Invited talk 16     | Christina Schenk       | Mathematical modeling and control of thermal and disease transmission dynamics   |
| 15:50 - 16:10 | Contributed talk 45 | Torsten Lindström      | On the stochastic engine of contagious diseases in exponentially growing populations   |
| 16:10 - 16:30 | Contributed talk 46 | Marian Petrica         | Identification of the parameters in a modified SIRD epidemic model using ensemble neural networks                            |
| 16:30 - 16:50 | Contributed talk 47 | Diana Taipe            | Extreme values and related hitting probabilities in epidemic models analyzed via level-dependent quasi-birth-death processes |

| 17:00 - 18:30                 |           | Poster Session        |  |   |
|-------------------------------|-----------|-----------------------|--|---|
| Cancer                        | Poster 1  | Yuri Garcia Vilela    | Existence of cyclic treatment routines on cancer adaptive therapies  |   |
|                               | Poster 2  | Rocío Picón-González  | Topological analysis on leukaemia data: predictions for all relapse  |   |
| Epidemiology                  | Poster 3  | Akhil Kumar Srivastav | Analyzing the influence of explicit vector dynamics on dengue transmission models  |   |
|                               | Poster 4  | Bechir Naffeti        | The dynamic of the COVID-19 in the Basque Country - a mathematical model considering losing and boosting immunity, vaccination and control measures                                |   |
|                               | Poster 5  | Bruno V. Guerrero     | Estimating the risk of arbovirus spreading in non-endemic areas: Basque Country as a case study  |   |
|                               | Poster 6  | Carlo Estadilla       | Cost-effectiveness of COVID-19 vaccination by modeling a counterfactual scenario: a case study of the Basque Country   |   |
|                               | Poster 7  | Cristina Januário     | Controlling infectious diseases: the decisive phase effect on a seasonal vaccination strategy  |   |
|                               | Poster 8  | Enrique Gabrick       | Modelling two vaccination doses in SEIR model  |   |
|                               | Poster 9  | Jacob Roberts         | Prospects of HIV elimination among men who have sex with men: a systematic review of mathematical models   |   |
|                               | Poster 10 | Luis Mateus           | Time-scale separation and center manifold analysis in a vector-host model  |   |
|                               | Poster 11 | Maarten De Jong       | Modelling infection dynamics in the host to design optimal treatment   |   |
|                               | Poster 12 | Marcos Amaku          | Modelling the effect of vaccination strategies against bovine brucellosis  |   |
|                               | Poster 13 | Martim Gerales        | The historical ecological background of west nile virus in Portugal provides one health knowledge and opportunities into the future  |   |
|                               | Poster 14 | Nico Stollenwerk      | The role of import in subcritical epidemiological systems leading to large fluctuations, case studies: COVID-19 after lockdown lifting and vector-borne disease invasion scenarios |   |
|                               | Poster 15 | canceled              | canceled   |   |
|                               | Poster 16 | Sara Sottile          | A geometric analysis of the impact of large but finite switching rates on vaccination evolutionary games   |   |
|                               | Poster 17 | Tomás Freire          | Fitness cost in context: decomposition using the replicator equation with invasion fitnesses for multispecies systems  |   |
|                               | Poster 18 | Ilse Westerhof        | Risk classifications for severe COVID-19; the European, Dutch, and Norwegian approaches  |   |
|                               | Evolution | Poster 19             | Blair Matarlo  | How genetic trade-offs affect the evolution of pesticide resistance: a model approach |
|                               |           | Poster 20             | Chiara Cicolani  | Exponential synchronization of Kuramoto oscillators with time-delayed interactions    |
| Immunology                    | Poster 21 | Artur Fassoni         | Modeling CART-T cell immunotherapy: insights with differential equations   |   |
|                               | Poster 22 | Kamilia Azib          | Optimal control model of immunotherapy for recurrent autoimmune disease  |   |
| Methodology in biomathematics | Poster 23 | Cristina Dias         | Procedure for analyzing networks of randomized block designs   |   |
|                               | Poster 24 | Mariana Ramos         | Organism motion in three dimensions: symbolic dynamics approach  |   |
|                               | Poster 25 | canceled              | canceled   |   |
|                               | Poster 26 | Nelson Jamba          | Stochastic differential equations mixed model with inclusion of genetic values   |   |
|                               | Poster 27 | Patrícia Antunes      | Analyzing higher-order moments and statistical distributions in modeling natural phenomena   |   |
|                               | Poster 28 | Paula Simões          | Analysing the weight carried by a soldier, according to his function, for the development of exoskeletons  |   |
|                               | Poster 29 | Vanda M. Lourenço     | A hybrid robust-weighted AMMI modeling approach with generalized weighting schemes   |   |
|                               | Poster 30 | Nataliya Stankevich   | Specific oscillatory activity in the simplest neuron model with discrete time  |   |
| Miscellaneous                 | Poster 31 | Miguel Braga          | On the robustness of random forests for genomic prediction and selection in breeding studies   |   |
|                               | Poster 32 | Ruddy Urbina          | Condensation patterns on substrates with different density of nucleation sites   |   |
|                               | Poster 33 | Sabrina Spigno        | Digestion or decomposition: a system dynamics approach   |   |
|                               | Poster 34 | Preeti                | Tackling malaria in India: an epidemic model with Beddington-Deangelis incidence rate and saturated treatment  |   |
|                               | Poster 35 | Om Yadav              | A higher order finite element method for coupled reaction diffusion models arising in biology  |   |
|                               | Poster 36 | Subit Jain            | Deformable dynamical system applied to medical image analysis  |   |
|                               | Poster 37 | Frank Kemayou         | Mathematical modeling and control of nematode impact on banana production  |   |

**15th Conference DSABNS | Feb. 6 - 9, 2024 – Main schedule**  
**Thursday - February 8, 2024 (Plenary Lecture will take place at room “Grande Auditório”)**

|               |  |                     |   |
|---------------|--|---------------------|---|
| 8:30 - 9:15   | <b>Registration</b>  |                     |   |
| 9:30 - 10:15  | Plenary lecture VII<br>Ruy M. Ribeiro  | Chair: Maira Aguiar | Modeling the dynamics of SARS-CoV-2 within the host |
| 10:20 - 12:10 | 1 Mini-Symposium + 4 Parallel Sessions: (1 Invited talk + 4 Contributed talks) |                     |   |
| 12:10         | <b>Lunch</b>   |                     |   |
|               | <b>FREE AFTERNOON</b>  |                     |   |
|               | <b>Social Program – excursion</b>  |                     |   |
| 20:00         | <b>CONFERENCE DINNER at "Pezinhos no Tejo" Restaurant</b>                      |                     |   |

|                       |                           |   |  |
|-----------------------|---------------------------|---|--|
| <b>Mini-Symposium</b> | <b>“Grande Auditório”</b> | <b>Slow-fast systems in biology: geometric singular perturbation theory applications and new perspectives</b> |  |
| 10:20 - 10:50         | MS organizer III          | Sara Sottile  | Slow-fast systems in biology: geometric singular perturbation theory applications and new perspectives |
| 10:50 - 11:10         | MS talk III1              | Nikola Popovic  | Front propagation in two-component reaction-diffusion systems with a cut-off                           |
| 11:10 - 11:30         | MS talk III2              | Iulia Martina Bulai   | Modeling fast information and slow(er) disease spreading: a geometric analysis                         |
| 11:30 - 11:50         | MS talk III3              | Panagiotis Kaklamanos   | Multiple-timescale dynamics in sleep-wake regulation and REM-nREM alternations                         |
| 11:50 - 12:10         | MS talk III4              | Annalisa Iuorio   | Far-from-threshold dynamics in sloped semi-arid environments driven by autotoxicity effects            |

|                                      |                      |                                  |   |
|--------------------------------------|----------------------|----------------------------------|---|
| <b>Methodology in Biomathematics</b> | <b>Room 201 - IV</b> | <b>Chair: Abdessamad Tridane</b> |   |
| 10:20 - 10:50                        | Invited talk 17      | Amira Kebir                      | Optimal control theory: a mathematical approach to public health strategies                     |
| 10:50 - 11:10                        | Contributed talk 48  | Grzegorz Graff                   | Discriminating time series via entropy-based indices, with an application to cardiological data |
| 11:10 - 11:30                        | Contributed talk 49  | Armando Bazzani                  | The multilayer interaction structure of an ecological network and the Lotka-Volterra models     |
| 11:30 - 11:50                        | Contributed talk 50  | Carlos Correia Ramos             | Behavior in a dynamical model   |
| 11:50 - 12:10                        | Contributed talk 51  | canceled                         | canceled  |



|                      |                      |                                 |   |
|----------------------|----------------------|---------------------------------|---|
| <b>Miscellaneous</b> | <b>Room 202 - IV</b> | <b>Chair: Paula Patrício</b>    |   |
| 10:20 - 10:50        | Invited talk 18      | Nicolas Moreno                  | How hydrodynamics interactions and reactivity of surface proteins on enveloped viruses can determine an optimal protein density |
| 10:50 - 11:10        | Contributed talk 52  | Blake McGrane-Corrigan          | Stability for a discrete-time nonlinear dispersal model   |
| 11:10 - 11:30        | Contributed talk 53  | Laid Boudjellal                 | Modelling of tumor-immune system interactions   |
| 11:30 - 11:50        | Contributed talk 54  | Ghilmana Sarmad                 | Modelling the fear factor as delay spatiotemporal epidemic model  |
| 11:50 - 12:10        | Contributed talk 55  | Charlotte Manser                | A mathematical framework for measuring and tuning tempo in developmental gene regulatory networks                               |
| <b>Ecology</b>       | <b>Room 203 - IV</b> | <b>Chair: Andrea Pugliese</b>   |   |
| 10:20 - 10:50        | Invited talk 19      | Giovanni Marini                 | Modeling the West Nile virus incidence and seroprevalence in the avian host population in Northern Italy                        |
| 10:50 - 11:10        | Contributed talk 56  | Cinzia Soresina                 | The effect of auto-toxicity in plant-growth dynamics: a cross-diffusion model   |
| 11:10 - 11:30        | Contributed talk 57  | Maarten de Jong                 | Optimal scheduling for relay intercropping  |
| 11:30 - 11:50        | Contributed talk 58  | Marine Courtois                 | Re-mating consequences on the efficiency of the sterile insect technique  |
| 11:50 - 12:10        | Contributed talk 59  | canceled                        | canceled  |
| <b>Epidemiology</b>  | <b>Room 204- IV</b>  | <b>Chair: Vanessa Steindorf</b> |   |
| 10:20 - 10:50        | Invited talk 20      | Bob W. Kooi                     | Periodically forced epidemiological models for dengue fever   |
| 10:50 - 11:10        | Contributed talk 60  | Hee-Dae Kwon                    | Optimal control problem of epidemic models based on deep reinforcement learning   |
| 11:10 - 11:30        | Contributed talk 61  | Ryosuke Omori                   | Modelling an infectious disease transmitted via cannibalism - White Spot Syndrome virus outbreak in Kuruma shrimp               |
| 11:30 - 11:50        | Contributed talk 62  | Fernando Saldaña                | On the role of the objective functional on optimal control outcomes for a SIR-type model with vaccination                       |
| 11:50 - 12:10        | Contributed talk 63  | canceled                        | canceled  |

**15th Conference DSABNS | Feb. 6 - 9, 2024 – Main schedule**  
**Friday - February 9, 2024 (Plenary Lectures will take place at room “Grande Auditório”)**

|               |  |   |
|---------------|--|---|
| 8:30 - 9:15   | <b>Registration</b>  |   |
| 9:30 - 10:15  | Plenary lecture VIII<br>Yuliya Kyrychko  | Chair: Ganna Rozhnova<br>Mathematical modelling of time-delayed systems with distributed delays |
| 10:20 - 11:05 | Plenary lecture IX<br>Louise Dyson   | Chair: Nico Stollenwerk<br>Modelling the transmission of SARS-CoV2 in the UK                    |
| 11:05 - 11:30 | <b>Coffee break</b>  |   |
| 11:30 - 13:00 | 1 Mini-Symposium + 3 Parallel Sessions: (1 Invited talk + 3 Contributed talks) |   |
| 13:00 - 14:30 | <b>Lunch</b>   |   |
| 14:30 - 16:00 | 4 Parallel Sessions: (1 Invited talk + 3 Contributed talks)                    |   |
| 16:00 - 16:30 | <b>Coffee break</b>  |   |
| 16:30 - 17:10 | Plenary lecture X<br>Lucia Russo   | Chair: Bob W. Kooi<br>Slow manifolds in complex dynamical systems                               |
| 17:10 - 17:45 | <b>Prizes and Closing</b>  |   |

| Mini-Symposium | Room 201 - IV    | Recent advances in mathematical modeling of infections diseases at the individual and population levels |  |
|----------------|------------------|---|--|
| 11:30 - 12:00  | MS organizer IV1 | Gergely Röst  | Waiting for the perfect vaccine  |
| 12:00 - 12:20  | MS organizer IV2 | Stanca Ciupe  | Understanding short and long-term dynamics of hepatitis B viral kinetics following therapy |
| 12:20 - 12:40  | MS talk IV1      | Peter Rashkov   | Repellent-based mitigation measures for vector-borne diseases: a control theory approach   |
| 12:40 - 13:00  | MS talk IV2      | Jonathan E Forde  | A mathematical model of chronic infection and immune exhaustion                            |

| Cancer        | Room 202 - IV       | Chair: Bruno V. Guerrero |  |
|---------------|---------------------|--------------------------|--|
| 11:30 - 12:00 | Invited talk 21     | Marta Lopes              | Sparsity-inducing network inference and classification for the identification of gene expression signatures in gliomas |
| 12:00 - 12:20 | Contributed talk 64 | Diego Rodrigues          | Ordinary differential equation modeling for contact inhibition and the proliferation of melanoma <i>in situ</i>        |
| 12:20 - 12:40 | Contributed talk 65 | Artur Fassoni            | Limit cycles in periodic Lotka-Volterra systems modeling cancer adaptive therapy                                       |
| 12:40 - 13:00 | Contributed talk 66 | Monica Salvioli          | Improving mathematical models of cancer through game-theoretic modelling: a study in non-small cell lung cancer        |

| Ecology       | Room 203 - IV       | Chair: Carlos Braumann |   |
|---------------|---------------------|------------------------|---|
| 11:30 - 12:00 | Invited talk 22     | Carla Pinto            | On a new population model for urban infestations  |
| 12:00 - 12:20 | Contributed talk 67 | Laura Mansier          | Population-dynamical model to optimise agricultural landscape management for natural pest control |
| 12:20 - 12:40 | Contributed talk 68 | Jesús Arnau            | Larvicide treatment optimization at a botanical garden  |
| 12:40 - 13:00 | Contributed talk 69 | canceled               | canceled  |

| <b>Epidemiology</b> | <b>Room 204 - IV</b> | <b>Chair: Carlo Estadilla</b> |  |
|---------------------|----------------------|-------------------------------|--|
| 11:30 - 12:00       | Invited talk 23      | Maria A. Gutierrez            | Evolution towards immune escape in an epidemic with vaccination: a mathematical approach                                       |
| 12:00 - 12:20       | Contributed talk 70  | Nir Gavish                    | Dynamics of a two-strain epidemic model with waning immunity - a perturbative approach   |
| 12:20 - 12:40       | Contributed talk 71  | Marcel Fang                   | A two-stage SEIRS reinfection model with multiple endemic equilibria   |
| 12:40 - 13:00       | Contributed talk 72  | Akhil Srivastav               | Bifurcation and chaos in biological phenomena with secondary homologous and heterologous infection for two strain dengue model |

| <b>Ecology</b> | <b>Room 201 - IV</b> | <b>Chair: Luis Mateus</b> |   |
|----------------|----------------------|---------------------------|---|
| 14:30 - 15:00  | Invited talk 24      | Ezio Venturino            | The role of bacteria in an anaerobic digester   |
| 15:00 - 15:20  | Contributed talk 73  | Francesca Acotto          | Mitigating the negative effects of eastern cottontail invasion in Italy using z-type control techniques |
| 15:20 - 15:40  | Contributed talk 74  | Thibault Malou            | Pest detection from a biology-informed inverse problem and pheromone sensors                            |
| 15:40 - 16:00  | Contributed talk 75  | canceled                  | canceled  |

| <b>Miscellaneous</b> | <b>Room 202 - IV</b> | <b>Chair: Bob W. Kooi</b> |   |
|----------------------|----------------------|---------------------------|---|
| 14:30 - 15:00        | Invited talk 25      | Vanessa Steindorf         | Insights into multi-strain dengue fever dynamics: an integro-differential equation approach |
| 15:00 - 15:20        | Contributed talk 76  | Elena Luengo              | Interdependence of tests in statistical tests suites. Case of study                         |
| 15:20 - 15:40        | Contributed talk 77  | canceled                  | canceled  |
| 15:40 - 16:00        | Contributed talk 78  | canceled                  | canceled  |

| <b>Epidemiology</b> | <b>Room 203 - IV</b> | <b>Chair: Paulo Doutor</b> |   |
|---------------------|----------------------|----------------------------|---|
| 14:30 - 15:00       | Invited talk 26      | Alberto Pinto              | Evolutionary vaccination strategies for the reinfection SIRS model  |
| 15:00 - 15:20       | Contributed talk 79  | Philipp Städter            | Individual-based modeling of day care centers predicts optimal surveillance strategies against SARS-CoV-2 |
| 15:20 - 15:40       | Contributed talk 80  | Alex Best                  | The effects of spatial structure on the ecology and evolution of infectious disease                       |
| 15:40 - 16:00       | Contributed talk 81  | André Brito                | Influenza model with temperature-incidence association  |

| <b>Epidemiology</b> | <b>Room 204 - IV</b> | <b>Chair: Maria do Céu Soares</b> |  |
|---------------------|----------------------|-----------------------------------|--|
| 14:30 - 15:00       | Invited talk 27      | Paula Patrício                    | Social vs. individual age-dependent costs of imperfect vaccination   |
| 15:00 - 15:20       | Contributed talk 82  | Giulio Pisaneschi                 | Pandemic preparedness, suppression and mitigation: how does individual behavior perturb optimal social distancing? |
| 15:20 - 15:40       | Contributed talk 83  | Vizda Anam                        | Within-host models unravelling the dynamics of dengue reinfections   |
| 15:40 - 16:00       | Contributed talk 84  | Fernando Córdova-Lepe             | The $\beta$ -SEIR approach for modeling infectious pandemics, when human behavior is an inevitable factor          |



# DSABNS 2024

15th INTERNATIONAL CONFERENCE  
DYNAMICAL SYSTEMS APPLIED TO BIOLOGY  
AND NATURAL SCIENCES (DSABNS)

## **PUBLIC LECTURES**

NOVA SCHOOL OF SCIENCE AND TECHNOLOGY  
(NOVA FCT)  
CAPARICA, PORTUGAL



# CONTROLLING OQDS (OLIVE QUICK DECLINE SINDROME) OUTBREAKS CAUSED BY *XYLELLA FASTIDIOSA*.

Vincenzo Capasso<sup>1</sup>

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The motivation of our research has arisen by the outbreak of an epidemic caused by the pathogen *Xylella fastidiosa* and known as olive quick decline syndrome (OQDS), which has been seriously affecting olive production of the Apulia region (Italy) since 2013, leading to dramatic socio-economic losses.

Current agronomic practices are mainly based on uprooting the sick olive trees and their surrounding ones, with later installment of more resistant olive cultivars. Unfortunately, both of these practices are having an undesirable impact on the environment (most of these trees were several hundred years old), and on the economy (e.g., costs of the new installments, the loss of production for some years and, the last but not less important, the oil quality produced by more resistant cultivars may not match the high standards of the previous ones).

Based on a mathematical model expressed in terms of a reaction diffusion-system, it has emerged that the best cost-effective practice consists of the removal of a suitable amount of weed biomass (reservoir of the juvenile stages of the insect vector *P. Spumarius* of *X. fastidiosa*) from olive orchards and surrounding areas, without requiring neither the removal nor the substitution of the existing olive trees [1, 3, 4].

It has to be evidenced that the same kind of disease has been affecting most of the Mediterranean regions, wherever there is a large population of olive trees, in association with the fact that the pathogen *X. fastidiosa* can infect a large number of productive plants of relevant socio-economic importance (e.g., grapevines, almond trees, citrus plants).

In recent papers *Zelus renardii* (Hemiptera, Reduviidae) has been identified as a predator of *P. Spumarius* for a possible control of a *Xylella* epidemic.

Here, by generalizing the above mentioned models, a spatially structured mathematical model has been proposed to include the predator *Zelus renardii* in the dynamics of a *Xylella* epidemic.

The fact that *Z. renardii* has been reported to be a generalist predator implies the choice of an Holling type III functional response of predation in the mathematical model. As a consequence, it has been shown that the introduction of *Z. renardii* as a predator of *P. Spumarius* is not an efficient control strategy to eradicate a *Xylella* epidemic. Instead, the introduction of a specialist predator or of a parasitoid, whenever identified, would lead to the eventual eradication of a *Xylella* epidemic; as a matter of fact, in this case the appropriate choice for the predation functional response would be an Holling type II.

In either cases it has been confirmed, as from our previous results, that a significant

reduction of the weed biomass can lead to the eradication of the vector population, hence of a *Xylella* epidemic, independently of the presence of predators [2].

A relevant contribution of our approach consists of a suitable restriction of measures of intervention (control) only to a subregion of the whole habitat of interest (in accordance to the *motto* "Think globally, act locally").

All of the above has been illustrated by a set of computational experiments, within a variety of different possible parameter scenarios.

**Acknowledgements** This work has been performed in collaboration with Sebastian Anița, Edoardo Beretta, Matteo Brunetti, Matteo Montagna, Simone Scacchi, Ezio Venturino.

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- [2] Anița, S., Capasso, V., Montagna, M., Scacchi, S. (2022). Predators as a possible strategy for controlling a *Xylella* epidemic? *Mathematical Modelling of Natural Phenomena* 7: 279–305. <https://doi.org/10.1051/mmnp/2022043>
- [3] Beretta, E., Capasso, V., Scacchi, S., Brunetti, M., Montagna, M. (2022). Prevention and control of OQDS (olive quick decline syndrome) outbreaks caused by *Xylella fastidiosa*. *Journal of Theoretical Biology* 542: 111118. <https://doi.org/10.1016/j.jtbi.2022.111118>
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# MATHEMATICAL MODELS FOR PUBLIC HEALTH INTERVENTIONS IN AGING POPULATIONS

Mirjam Kretzschmar<sup>\*1,2,3</sup>, Michiel van Boven<sup>1,3</sup>, Jurjen van der Schans<sup>4</sup>, Christiaan van Dorp<sup>5</sup> and Debbie van Baarle<sup>3,4</sup>

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Recent experience with the SARS-CoV2 pandemic has shown that public health policy makers dealing with infectious disease control face increasingly complex questions and need to evaluate an increasing quantity of data and information. To make effective use of scientific evidence for informed decisions, and to assess available intervention options, mathematical modeling of infectious diseases has proven to be an indispensable tool. In this presentation I will discuss important concepts that are at the basis of epidemic models, and how these concepts are used to evaluate interventions. Then, focussing on vaccination, I will present an age-structured model formulated as a system of partial differential equations, and scenarios for various vaccination strategies. I investigate how targeting vaccination to specific age groups, in particular to older adults, influences the effectiveness of these strategies in reducing transmission and mortality. I also discuss how aging of populations interacts with disease dynamics and vaccination effectiveness. In the medical field, the concept of frailty is used to describe health states of older individuals, and various indices have been proposed to quantify frailty [1]. There is large variation between individuals in frailty, and it is known that immune responses and vaccine efficacy generally decrease with age. Moreover, frailty correlates strongly with mortality rates. We present first attempts to include frailty into infectious disease models to assess its impact on vaccination effectiveness on the populations level.

## References

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# DSABNS 2024

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## PLENARY TALKS

NOVA SCHOOL OF SCIENCE AND TECHNOLOGY  
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# COMPLEX DYNAMICS IN MULTI-STRAIN DENGUE MODELS AND ITS IMPACT ON PUBLIC HEALTH INTERVENTION MEASURES

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Dengue fever epidemiological dynamics shows large fluctuations in disease incidence, and several mathematical models describing the transmission of dengue viruses have been proposed to explain the irregular behavior of dengue epidemics. Multi-strain dengue models are often modeled with SIR-type models where the SIR classes are labeled for the hosts that have seen the individual strains. The extended models show complex dynamics and qualitatively a very good result when comparing empirical data and model simulations. However, modeling insights for epidemiological scenarios characterized by chaotic dynamics, such as for dengue fever epidemiology, have been largely unexplored. The problem is mathematically difficult and to make the urgently needed progress in our understanding of such dynamics, concepts from various fields of mathematics as well the availability of good data for model evaluation are needed.

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# MATHEMATICAL MODELLING OF REPLICATION-MUTATION DYNAMICS OF CORONAVIRUSES

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RNA viruses in general, and coronaviruses in particular, are fascinating in terms of living “on the edge”: they have very fast replication rates associated with high mutation rates, thus forming the so-called *quasi-species*, i.e. swarms of closely related genetic mutants all related to and dominated by the viral master sequence. The advantage of this evolutionary strategy lies in creating a heterogeneous pool of phenotypes better able to adjust and respond to environmental change and selection pressure from their hosts. In most RNA viruses, high mutation rate is associated with RNA-dependent RNA polymerase (RdRp) that lacks proofreading capabilities and hence, cannot maintain fidelity during viral replication. In contrast, coronaviruses that have the largest genomes among all RNA viruses infecting humans, do have a special enzyme, exoribonuclease (ExoN) that is able to correct errors during viral replication. In this talk I will discuss a model of coronavirus replication with account for mutations and the effects of ExoN. I will consider different modes of viral replication, as well as the conditions for viral persistence and “error catastrophe”, where mutations lead to viral extinction due to the loss of genetic information. We will also consider the effects of different classes of antiviral drugs acting through the inhibition of RdRp, an enzyme that is essential for replication of coronaviruses, inhibition of ExoN responsible for maintaining fidelity during viral replication, or through the mechanism of lethal mutagenesis.

# MODELLING THE TRANSMISSION OF SARS-CoV2 IN THE UK

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During the height of the COVID-19 pandemic it was often necessary to develop situational understanding in the context of limited, but evolving, data. I will discuss two such strands of work in a UK context. Firstly, using the wide range of UK data to estimate the extent of school transmission of SARS-CoV2 and the potential impact of school-based testing strategies and interventions. Secondly, during the emergence of the UK Delta wave assessing the growth rate of the invading variant of concern, and using the characteristics of positive cases to determine whether the wave had reached the general population. The work discussed is taken from references [1–4].

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## MICROBIOME EVOLUTION IN THE MAMMALIAN GUT

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The tempo and mode of bacteria evolution in the mammalian gut is still poorly understood. By performing in vivo experimental evolution for thousands of generations in the mouse gut, we show that the successful colonization of a commensal invader strain of *Escherichia coli* depends on the species diversity of the existing gut microbiota. Following *E. coli* colonization, we found that two modes of selection are responsible for its evolutionary dynamics: one in which diversifying selection leads to long-term coexistence of ecotypes and a second in which directional selection propels selective sweeps intertwined with events of horizontal gene transfer. Two summary statistics of mutation trajectories are proposed, which allow to quantitatively determine the dominant modes of selection from time series sequencing data. In our experiments, diversifying selection was marked by the emergence of metabolic mutations, and directional selection by acquisition of prophages, which bring their own benefits and costs. In both modes, we observed parallel evolution, indicative of rapid adaptation, and rates of mutation accumulation similar to those observed in vitro, where *E. coli* adapts to a much simpler environment. The experiments show how rapid ecotype formation and phage domestication can be in the mammalian gut. They further suggest that massive amounts of intra-species horizontal gene transfer can occur when strains stably co-exist in the same host.



# PHYLODYNAMIC INFERENCE FOR MARKOV PROCESS MODELS

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The project of phylodynamics is the extraction of information on the nature of a stochastic population process from data on the relationships among genomic samples taken from individuals in the evolving population. In its purest form, its core problem may be factored into two subproblems: the identification of genealogical trees expressing the relationships between genomic samples and the probabilistic linkage of these genealogies to the generating stochastic process. In this work, we focus on the latter. Specifically, we view the genealogy as data and aim to compute the likelihood of the genealogy under a given Markovian population process. For example, this process might be a model for the transmission of an infectious disease.

Two distinct approaches to this problem already exist. The older builds on the Kingman coalescent [2–4] and variations thereon; the younger, on generalized linear birth-death processes [5–7]. The key element in the tractability of both approaches has been the computability of certain approximate reverse-time transition probabilities, but these approximations are only accurate in the limit of large population size and/or small sample fraction. In this work, we eliminate the need for such approximations.

To accomplish this, we construct a novel class of genealogy-valued Markov processes, each uniquely induced by any given discretely-structured Markovian population process. The latter class is sufficiently rich as to encompass most infectious-disease transmission models of practical interest. Preliminary results for the unstructured case were given in Ref. [1]. We present a theorem giving the exact probability distribution of genealogies conditional on the history of the population process. We then show how integration over the space of population histories yields a nonlinear filtering equation with continuous and discrete portions. This equation may be integrated via well understood Feynman-Kac approaches, which can be cast as sequential Monte Carlo algorithms.

The results are a strict generalization and unification of existing approaches. The proofs rely on several constructions which are both novel and more natural than the reverse-time constructions used in the more limited coalescent- and birth-death-process theories. Importantly for applications, the implied algorithms can be carried out entirely in forward time, which greatly expands the class of models that can be treated exactly.

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# MATHEMATICAL MODELLING OF TIME-DELAYED SYSTEMS WITH DISTRIBUTED DELAYS

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Time delays can arise in various physical, biological, physiological and engineering fields, such as chemical reactions, control systems, and biological systems, among others. Since in many realistic settings, the delays are not constant, it is more applicable to use some distribution of time delays to describe the system's dynamics.

In this talk I will review the effects of distributed time delays on the dynamics of coupled systems with applications to modelling of neural networks and epidemic modelling. In particular, I will discuss the effects of two different types of distributed-delay coupling in the system of two mutually coupled Kuramoto oscillators [3]: one where the delay distribution is considered inside the coupling function, and the other where the distribution enters outside the coupling function. I will also consider a globally coupled network of active and inactive oscillators with distributed-delay coupling and show the conditions for aging transition [2], associated with suppression of oscillations, for several different distributions of time delays. Furthermore, I will look into the effects of various time delay distributions on the stability of the endemic steady state in a mathematical model with vaccination and perceived side effects of vaccine and the disease itself [1].

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# MODELING THE DYNAMICS OF SARS-CoV-2 WITHIN THE HOST

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Modeling the within host dynamics of viral infection has provided insight into the biology of different viral infections. SARS-CoV-2 is not an exception. We and others have developed models to describe the dynamics of SARS-CoV-2 viral load within an infected person. These models described the viral load extremely well and allow quantification of key dynamical characteristics of the virus, including duration of viral shedding, possibility of viral rebound and the effect of treatment. Moreover, they shed light on the effects of innate and acquired immune responses in controlling the virus. We also studied the relationship between a person's viral load over time, to its infectious profile and the probability of testing positive. Based on empirical data and models of the probability of detection for different tests, we define the profile of positivity for typical infected persons. These models link viral load dynamics with epidemiological transmission and interventions to better define control strategies.

# SLOW MANIFOLDS IN COMPLEX DYNAMICAL SYSTEMS

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Since Newton's era, mathematical models for dynamical systems have been constructed from first principles. However, complex systems in biology and ecology (like the brain, the climate) or other ecological and social systems (like epidemic disease), remain challenging problems in order to derive accurate, computationally efficient, interpretable models. To address this problem, different approaches have been proposed to the construct reduced-order models (ROMs) for the study and analysis of complex and multiscale mathematical models. Due to the inherent multiscale character of the system (introduced as stiffness to the model), the effective/slow dynamics frequently evolves on low-dimensional invariant topological spaces, usually called slow invariant manifolds (SIMs).

Traditionally, the identification of SIM approximations is obtained by methods of Geometric Singular Perturbation Theory (GSPT), originally developed to deal with singularly perturbed dynamical systems characterized by an explicit timescale splitting.

In this talk, I will illustrate how the interplay of numerical analysis, machine learning and manifold learning techniques can be useful for the bifurcation analysis and the control of multi- and large-scale complex dynamical systems. The variables used to construct these dynamical systems will be obtained in a data-driven manner through the manifold learning scheme, Diffusion Maps. I will discuss two different ways to face the problem: 1) the "Equation Free" approach which bypasses the need of construction of ROMs; and 2) a physics-informed machine learning (PIML) approach, based on the concept of GSPT, for deriving SIMs of singularly perturbed dynamical systems of ODEs. Both approaches are based on the idea that the large scale complex dynamical system under study is characterized by slow dynamics which can be embedded in a low-dimensional invariant manifold.

# PREDICTING EXTREME OUTBREAKS DUE TO DEMOGRAPHIC AND PARAMETERIC NOISE IN EPIDEMICS

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One of the main obstructions to epidemic simulations and control based on models is noise and uncertainty that stems from demographics, fluctuating parameters and social adaptation [1, 2, 4, 5]. Within stochastic models, outbreak sizes are described by probability distributions of occurrence, which one would like to understand and analyze based on various noise characteristics. Here we solve the canonical problem of calculating the dynamics and likelihood of extensive outbreaks in a population within a large class of stochastic epidemic models with demographic and parametric noise, including the susceptible-infected-recovered (SIR) model and its general extensions [1, 3]. In the limit of large populations, for demographic noise we compute the probability distribution for all extensive outbreaks, including those that entail unusually large or small (extreme) proportions of the population infected. Our approach reveals that, unlike other well-known examples of rare events occurring in discrete-state stochastic systems, the statistics of extreme outbreaks emanate from a full continuum of most probable paths, each parameterized by an effective force of infection due to noise.

In addition to demographic noise, we can extend our analysis techniques to noisy infection (contact) and recovery rates on the distribution of outbreak sizes in the stochastic SIR model [3]. The rates are modeled as Ornstein-Uhlenbeck processes with finite correlation time and variance, which we illustrate using outbreak data from the RSV 2019-2020 season in the US. In the limit of large populations, we find analytical solutions for the outbreak-size distribution in the long-correlated (adiabatic) and short-correlated (white) noise regimes, and demonstrate that the distribution can be highly skewed with significant probabilities for large fluctuations away from mean-field theory. Furthermore, we assess the relative contribution of demographic and reaction-rate noise on the outbreak-size variance, and show that demographic noise becomes irrelevant in the presence of slowly varying reaction-rate noise but persists for large system sizes if the noise is fast.

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# THE ROLE OF IMPORT IN SUBCRITICAL EPIDEMIOLOGICAL SYSTEMS LEADING TO LARGE FLUCTUATIONS, CASE STUDIES: COVID-19 AFTER LOCKDOWN LIFTING AND VECTOR-BORNE DISEASE INVASION SCENARIOS

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The epidemiological threshold between exponential growth and exponential decline has to be redefined in systems with import which originates from external reservoirs. Here still we have supercritically an exponential increase, but subcritically a stationary state can be reached via imported infected disease cases in abundance of susceptibles.

During the COVID-19 pandemic many countries experienced a harsh lockdown which could not be sustained for long time. However, the lifting of the lockdown should avoid a new exponential explosion of cases, such that we approached from below the above described epidemic threshold including import. Close to the threshold, as in many critical phenomena and especially in percolation known for long time, large fluctuations occur. Hence the system was regulated close to such a state with large fluctuations and power law scaling. We investigate in the example of the Basque Country with very good data on COVID-19 cases, hospitalizations and ICU admissions this scenario in the second half of 2020, which also gives a good basis for the analysis of the subsequent introduction of vaccines and its impact in 2021.

In another case study, well in line with the recent climatic changes, in areas where vector-borne diseases like dengue fever, chikungunya and Zika e.g. are not established but tropical mosquito invasion started to be observed in recent years, we are again in a sub-critical regime approaching from below the epidemic threshold, where now in the Basque Country we have good data on imported cases, returning travelers from endemic countries infected, and proxy data for mosquito abundance, in this case egg counts, modulating the infectivity to eventual autochthonous cases. Hence risk maps are desired, again in an epidemiological scenario of approaching an epidemiological threshold from below.

In both case studies concepts from dynamical isotropic percolation come to place, with import as a conjugated external field in technical terms of phase transitions. Data analysis and stochastic process analytics and simulations give insight into the role of import causing eventual large isolated outbreaks, far from the usually considered mean field approximation of simple ODE epidemic models [1–4].

**This work was also presented as a poster.**



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# PATTERNS OF MOVEMENT ON INSECTS: SMALL CPGS, BIFURCATIONS AND UBIQUITOUS TRIPOD GAIT

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Global and local synchronization patterns in biological processes is key to understanding the dynamics of biological networks. In this talk we present some results we have obtained on global synchronization of small networks of neurons. We are interested in the dynamics of Central Patterns Generators (CPG), small groups of interconnected neurons that produce rhythmic patterns even in the absence of rhythmic input. These groups of neurons control the production of rhythmic patterns like those appearing in the heart beat, chewing, respiration and movement. Here, we explore a Hodgkin-Huxley like model neuron, introduced by Ghigliazza and Holmes [3], by computing its spike-counting diagrams and the main bifurcations. These techniques give us a ‘roadmap’ for its dynamics. With this we can explore a 6-neuron CPG introduced to model the movement of insects to understand the possible gaits the model can produce. To do so we perform a quasi-Monte-Carlo sweep followed with automatic detection techniques [2]. As a result, we get a complete picture of the patterns and their evolution while changing a parameter [1]. This study reveals the complete dominance of the tripod gait in the region of fast movement regime, like in the real case of insects in Nature [4]. Using continuation techniques we explain the transitions of different gaits in the current CPG. Finally, we explore a family of synthetic CPGs to show that all of them behave similarly and we generalize the study for different topologies showing the ubiquity of the tripod gait.

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# TOWARDS A GENERIC VECTOR-HOST MODEL

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The aim of our work is to develop a conceptual generic agent-based model to formalize the interaction of vector and host given climate change. The model consists in creating a hypothetical example of a vector-host system. It simulates the vector's life cycle while considering interactions with hosts and the temperature. It is presented following the ODD protocol [1, 2] and based on parameters and processes to conceptualize the vector-host complexity [3, 4]. It could accommodate a broad spectrum of vector species and different biogeographic regions. Our model can be extended to more ecologically complex systems with multiple species and real-world landscape complexity to test different host- and/or vector-targeted control strategies and identify practical approaches to managing vector population and movement patterns.

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# ARE POPULATIONS IN RANDOM ENVIRONMENTS FOLLOWING ITÔ OR STRATONOVICH CALCULUS? DOES IT MATTER?

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Let  $X(t)$  be the size at time  $t \geq 0$  of a population with growth affected by environmental random fluctuations. A suitable model is the stochastic differential equation (SDE)  $\frac{dX(t)}{X(t)} = f(X(t))dt + \sigma dW(t)$ , where the deterministic rate (satisfying some mild assumptions)  $f(x)$  is the “average” growth rate when the population size is  $x$ . The cumulative environmentally induced deviations from average up to time  $t$  are approximated by  $\sigma W(t)$ , where  $\sigma$  is a noise intensity parameter and  $W(t)$  is a standard Wiener process.

There are several stochastic calculi to handle the SDE, Itô and Stratonovich being the most commonly used. Unfortunately, they give rise to apparently different solutions and qualitative behaviors. Even in the simplest Malthusian growth case  $f(x) \equiv r$ , when the “average” growth rate  $r \in ]0, \sigma^2/2]$ , Itô calculus predicts population extinction and Stratonovich calculus predicts unbounded growth. This led to a controversy on which stochastic calculus is more appropriate to describe the population dynamics. One can see in [1] a discussion and references on this issue, as well as the solution to the controversy. It lies on users wrongly assuming that the “average” growth rate  $f(x)$  means exactly the same under the two calculi, while it indeed represents two different “averages”, the arithmetic average for Itô calculus and the geometric average for Stratonovich calculus. Taking into account the difference between the two averages, both calculi give exactly the same qualitative and quantitative results. So, it does not matter which calculus one chooses, as long as one uses the corresponding correct average and associated  $f(x)$  expression.

We will also prove a similar result for general SDE population growth models having density-dependent noise intensities  $\sigma(x)$ ; however, the geometric average is replaced by the  $\phi$ -average, where  $\phi(x)$  depends on the shape of the noise intensity  $\sigma(x)$ . What about stochastic calculi that are not Itô nor Stratonovich?

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# AN OVERVIEW OF FINITE AND INFINITE POPULATION MODELS IN EVOLUTIONARY DYNAMICS

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We consider three classical models of biological evolution: (i) the Moran process, an example of a reducible Markov Chain; (ii) the Kimura Equation, a particular case of a degenerated Fokker-Planck Diffusion; (iii) the Replicator Equation, a paradigm in Evolutionary Game Theory.

In this talk, we will revise all these models, and show their interconnections in two distinct levels. Firstly, we will show using a direct approach that (ii) is the diffusion approximation of (i), and (iii) is obtained from (ii) in an appropriate limit. Secondly, we will reformulate all models as gradient flows (i.e., as time step minimizations of certain functionals) and show that the same limits apply [1, 2].

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# DYNAMICAL UNDERPINNINGS OF MULTI-STRAIN COLONIZATION SYSTEMS USING THE REPLICATOR EQUATION

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Understanding the interplay of different polymorphisms in co-colonization systems with multiple interacting strains remains difficult. High dimensionality and complex non-linear feedbacks make the analytical study of such systems very challenging. When strains are similar (quasi-neutrality assumption), we can model trait variation as perturbations in parameters, which simplifies analysis. In a series of studies [1–4], we have applied singular perturbation theory to such multi-strain system and advanced analytically to obtain their explicit collective dynamics in terms of a *fast* (neutral) dynamics and a *slow* (non-neutral) dynamics. The slow dynamics are given by the replicator equation for  $N$  strain frequencies. The coefficients of this replicator system are pairwise invasion fitnesses between strains, which, in our model, are an explicit sum of pairwise asymmetries along all trait dimensions, weighted by parameters of the neutral system. Here I will highlight some key features of this derivation, the uses of the replicator equation to better understand such multi-strain system, and links with data to verify theoretical model predictions. Applications may range from epidemiology (e.g. *S. pneumoniae* dynamics) to microbiota or social evolution.

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# EVOLUTION TOWARDS IMMUNE ESCAPE IN AN EPIDEMIC WITH VACCINATION: A MATHEMATICAL APPROACH

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At the population level, immunity helps control the spread of infectious diseases. At the host level, however, immunity may contribute to the evolution of pathogens towards immune escape: the pathogen may mutate to evade the existing immunity. Therefore, infections in hosts with prior immunity might have an increased risk of antigenic escape, relative to infections in naïve individuals. We study the overall population-level consequences of this heterogeneity.

We use deterministic SIR-type compartmental models with imperfect vaccination. We find analytically the final epidemic size, which allows us to define an escape pressure function at the population level. We discuss how the vaccination coverage changes the escape pressure, and the evolutionary implications of this result for vaccination campaigns.

Part of this work is published in [1], but with modifications to allow for reinfections. The compartmental model now has 'SIRI' structure (with vaccination), but we can still find its final size to obtain the escape pressure analytically. If the immunity acquired from past infections is weak, including reinfections as potential drivers of evolution qualitatively changes our past results and implications for the escape pressure.

**Acknowledgements** This work was done in collaboration with my PhD supervisor, Professor Julia R. Gog.

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# OPTIMAL CONTROL THEORY: A MATHEMATICAL APPROACH TO PUBLIC HEALTH STRATEGIES

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Public health strategies are vital for addressing diverse challenges, from infectious disease outbreaks to chronic conditions. This work explores the intersection of mathematics and public health, focusing on the application of Optimal Control Theory. We discuss its broader applications and its specific role in controlling cancer stem cells in cancer treatment and optimizing strategies for managing the COVID-19 pandemic.

We begin with an introduction highlighting the significance of public health challenges and the indispensable role of mathematical models in addressing them. Core concepts of Optimal Control Theory, such as control variables, state variables, cost functions, and constraints, are presented.

To demonstrate practical applications, we introduce the Susceptible-Infectious-Recovered (SIR) model and its adaptation for optimizing control strategies in epidemiology. Optimization aims to meet public health objectives, such as minimizing infections, mortality, and economic costs while enhancing healthcare system efficiency, especially crucial in the context of COVID-19.

We further extend Optimal Control Theory to the domain of cancer treatment, emphasizing the control of cancer stem cells. Mathematical models guide strategies targeting these cells, addressing their role in treatment resistance, and improving therapeutic outcomes, offering potential breakthroughs in cancer therapy.

In summary, this work sheds light on the invaluable role of mathematics, specifically Optimal Control Theory, in shaping effective public health strategies. It serves as a call to action for public health professionals, policymakers, and researchers to leverage mathematical tools to enhance disease management, resource allocation, and, ultimately, the well-being of society.

# PERIODICALLY FORCED EPIDEMIOLOGICAL MODELS FOR DENGUE FEVER

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We compare the dynamic behaviour two compartmental models for vector-borne Dengue fever disease. One is a two-strain [1] model (where a secondary infection occurs by the other strain) and the other a one-strain multi-group model (where a secondary infection is an re-infection) [2, 3]. Besides infection and recovery two epidemiological mechanisms, temporary immunity and disease enhancement or neutralization, are taken into account. The parameter values are realistic for Dengue fever epidemics. The focus is on the modelling of seasonality. In both type of models, in addition to stable epidemiological limit cycles, quasi-periodic and chaos dynamics occurs in a wide range of parameter values. Especially the two-parametric tor infection rate versus enhancement factor in the host population will be consider.

The following types of codimension-one bifurcations occur in the studied region of the parameter space: transcritical, tangent, Hopf as well a torus bifurcation for limit cycles. Further the organizing centers the cusp and Bogdanov-Takens codimension-two bifurcations and, as a consequence, also a codimension-one global bifurcation for the endemic equilibrium. In [1] it is shown that in addition a torus bifurcation destruction leads to chaos and.

In the autonomous version of the one-strain version no chaos is found [4]. However, by periodical (yearly) oscillations of the number of vector individuals as forcing, chaos exists in a substantial part of the parameter space. A codimension-one curve of resonance 1:1 bifurcation of the disease-free limit cycle forms also the transcritical bifurcation of the limit cycle. A torus bifurcation is the onset of a chaos. An endemic limit cycle undergoes also a tangent bifurcation, further there is a codimension-two resonance 1:1 bifurcation point, which forms boundary of the chaotic region in the parameter space is the disease-free saddle limit cycle.

In conclusion: in the autonomous two-strain model a torus bifurcation gives chaos which does not exist in the one-strain model. In both non-autonomous model with periodic forcing by seasonal periodicity in the vector population, also chaos exists where the region of existence in the two-parameter diagram for the nonautonomous two-strain model is

shaped by a saddle disease-free limit cycle.

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# SPARSITY-INDUCING NETWORK INFERENCE AND CLASSIFICATION FOR THE IDENTIFICATION OF GENE EXPRESSION SIGNATURES IN GLIOMAS

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Gliomas are brain tumors characterized by generally low survival rates among patients. To identify new targets for more personalized therapies, a deeper understanding of the molecular drivers of glioma heterogeneity is required. Not only detecting changes in individual molecular entities may reveal crucial knowledge about disease development and progression, but also understanding their role within the broader molecular network may help uncover their impact in the disease. Achieving this understanding can be accomplished through the application of statistical and network inference methods to the high-dimensional omics datasets (e.g., transcriptomics) that are now being generated.

We propose a methodology based on regularization to infer glioma transcriptomic subnetworks from data obtained from The Cancer Genome Atlas and classify patients into different glioma types. The unique features associated with the three main glioma types (astrocytoma, oligodendroglioma, and glioblastoma) as well as the shared features between them are first identified using the joint graphical lasso (JGL) method [1]. Robust sparse multinomial regression [2] is then performed to assess the relevance of accounting for prior network-based information in the separation between glioma types.

The application of JGL to the glioma transcriptomic data enabled the identification of sparse networks highlighting shared gene connections across the glioma types and exclusive connections to each type. The following classification task considered both i) the full set of variables and ii) the set of variables involved in the subnetworks identified. A comparable high predictive performance was obtained for both approaches, highlighting the diagnostic value of the set of selected variables. Moreover, the sparse networks identified allowed not only the identification of genes that are relevant for diagnosis, but also the estimation of the underlying relations, which is extremely useful for disease understanding. The natural and crucial next step for considering the molecular players identified as biomarkers might encompass further biological validation.

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# MODELING THE WEST NILE VIRUS INCIDENCE AND SEROPREVALENCE IN THE AVIAN HOST POPULATION IN NORTHERN ITALY

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West Nile virus (WNV) is one of the most threatening mosquito-borne pathogens in Italy where hundreds of human cases were recorded during the last decade. In the Emilia-Romagna region, WNV has been present since 2008, leading to the establishment of an integrated surveillance network. Here, we aimed at estimating the WNV incidence in the avian population through a modeling framework which enabled us to eventually assess the fraction of birds that present anti-WNV antibodies at the end of each epidemiological season.

We fitted a deterministic SIR model to ornithological data, consisting of 25,930 specimens collected between 2013 and 2022: every year from May to November birds belonging to resident Corvidae species are captured or shot and tested for WNV genome presence. We found that the incidence peaks between mid-July and late August and that infected birds seem on average 31% more likely to be captured. Predicted seroprevalence is spatially and temporally heterogeneous, and for 2018 we estimated the largest outbreak (up to about 60% of the birds were infected), consistently with the anomalous number of recorded human infections.

Thanks to our modeling study we quantified WNV infection dynamics in the avian community, which is still poorly investigated despite its importance for virus persistence.

To the best of our knowledge, this is among the first studies providing quantitative information on infection and immunity in the bird population, yielding new important insights on WNV transmission dynamics. Specifically, assessing avian immunity will help predictive models to estimate the risk of WNV spillover to the human population.

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# COMPLEX BIOSOCIAL DYNAMICS: NONLOCAL COOPERATIVE BEHAVIOR, PSYCHOLOGICAL EFFECTS, AND COLLECTIVE DECISION-MAKING

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Nonlocal models are essential in the description of many biosocial processes and phenomena. One such example is pertinent to collective decision-making, whose studies at a deeper level are intrinsically connected to brain network models [4]. In the animal kingdom, we can already find rich and complex dynamics produced by collective decision-making. In performing various tasks, cooperative behaviours benefit the group in a way that is impossible to achieve by an individual alone. As hunting is one of the most common types of collaboration seen in nature, our representative example here will be based on a nonlocal cooperative hunting model of integro-differential coupled equations. We analyze this and associated models mathematically to study the influence of nonlocal interactions, amplified by psychological effects such as multiple emotions, e.g. fear or affiliation towards teammates [2].

Human collective biosocial dynamics and decision-making exhibit even more complex biosocial interactions and psychological behaviours. Considering a hierarchy of statistical-mechanics-based models and focusing on nonlocal kinetic models, we also emphasize the special role of drift-diffusion decision-making models in life sciences [3]. Motivated by the fact that life itself is an ultimate nonequilibrium process, we connect our analysis with nonequilibrium brain network models. Specifically, we discuss nonequilibrium landscapes of human brain networks in the context of neurodegenerative diseases. The link to the above considerations is established via working memory, a key function in decision-making, which is affected early during the onset of neurodegenerative diseases and can serve as a key to better understanding the course of such diseases and developing treatments [1]. Our analysis here is based on brain connectome data. Finally, given recent results on studying out-of-equilibrium systems with AI methodology, we provide further insight into these results in our particular context for their potential usage in facilitating collective human decision-making derived from complex biosocial dynamics.

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# HOW HYDRODYNAMICS INTERACTIONS AND REACTIVITY OF SURFACE PROTEINS ON ENVELOPED VIRUSES CAN DETERMINE AN OPTIMAL PROTEIN DENSITY

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Enveloped viruses like SARS-CoV-2 and Influenza exhibit diverse surface proteins, or spikes, which play a crucial but poorly understood role in their infectivity. These spikes vary greatly in number, morphology, and reactivity across different viruses. As virus transmissibility is not solely determined by genetic sequences, we need new tools to unravel the effects of spike functionality, interactions, and morphology. Here, we postulate hydrodynamic interactions as a significant factor influencing the viral infectivity of enveloped viruses and propose micro-rheological characterization as a means to differentiate between virus types [1]. To gain insights into how spikes impact virion mobility and infectivity, we employ mesoscopic hydrodynamic simulations to investigate the diffusivity of spike-decorated structures. Additionally, we explore the interplay between spike affinity and passive viral transport. Our findings unveil a strong influence of spike size and distribution on the diffusional mechanism of SARS-CoV-2. We propose and validate a universal mechanism that elucidates the connection between optimal virion structure and maximal infectivity for a broad spectrum of virus families, shedding light on this complex and essential aspect of viral behavior.

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# GENERALIZED FOKKER–PLANCK EQUATIONS FOR SUPERSTATISTICAL SYSTEMS

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Superstatistical systems are nonequilibrium systems in stationary states with large fluctuations of intensive quantities. Different effective statistical processes can be obtained according to the statistical properties of those fluctuations. We derive the generalized Fokker–Planck equation for such systems where the distribution of the fluctuations is reflected into the involved operators. Application to recent findings in biological systems and to fractional diffusion are discussed. In particular, by collecting from literature data the experimental evidence of anomalous diffusion of passive tracers inside cytoplasm, and in particular of subdiffusion of mRNA molecules inside live *Escherichia coli* cells, we obtain the probability density function of molecules' displacement and we derive the corresponding Fokker–Planck equation [1]. Molecules' distribution emerges to be related to the Krätzel function and its Fokker–Planck equation to be a fractional diffusion equation in the Erdélyi–Kober sense. The irreducibility of the derived Fokker–Planck equation to those of other literature models is also discussed.

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# SOCIAL VS. INDIVIDUAL AGE-DEPENDENT COSTS OF IMPERFECT VACCINATION

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In diseases with long-term immunity, vaccination is known to increase the average age at infection as a result of the decrease in the pathogen circulation. This implies that a vaccination campaign can have negative effects when a disease is more costly (financial or health related costs) for higher ages. This work considers an age-structured population transmission model with imperfect vaccination. Our aim is to compare the social and individual costs of vaccination, assuming that disease costs are age-dependent. A model coupling pathogen deterministic dynamics for a population consisting of juveniles and adults, both assumed to be rational agents, is introduced [1]. The parameter region for which vaccination has a positive social impact is fully characterized and the Nash equilibrium of the vaccination game is obtained. Finally, collective strategies designed to promote voluntary vaccination, without compromising social welfare, are discussed.

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# EVOLUTIONARY VACCINATION STRATEGIES FOR THE REINFECTION SIRI MODEL

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In this work, we study the evolution of vaccination decisions in a homogeneous population depending on the morbidity risks of the vaccine, the morbidity risks of the disease, and also depending on the decisions of all other individuals. In 2017, Martins and Pinto introduced the evolutionary vaccination dynamics of the population vaccination strategy for the basic reinfection SIRI model. We analyze the changes provoked in the vaccination dynamics when the morbidity risks also evolve with the course of the disease.

# ON A NEW POPULATION MODEL FOR URBAN INFESTATIONS

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In this talk we describe mathematical models to analyze the threats posed to health, economic, social and environmental aspects, by the spread of rodents and insects in cities. We study incidence, and seasonal and weather influence to improve the design of proper intervention strategies. The models are adequately fitted to data from Madrid, Spain, between 2010 and 2013 [1].

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# MODELLING RELEASES OF WOLBACHIA-INFECTED MALE MOSQUITOES: WHEN CAN THIS STRATEGY BE EFFECTIVE IN REDUCING MOSQUITO DENSITIES?

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Releases of Wolbachia infected females of *Aedes aegypti* mosquitoes have been tried with the aim of replacing the original population, since Wolbachia infected *Aedes aegypti* mosquitoes are much less susceptible to dengue infections [5]. Several mathematical models have been developed to analyse this strategy [4], and understanding potential population dynamics, including spread in space. Cytoplasmic incompatibility (CI), i.e. the loss in fertility of wild-type females mated with Wolbachia-infected males ensures, in principle, that, if the density of Wolbachia-infected mosquitoes is above a critical value, population replacement will occur, even if Wolbachia-infected mosquitoes have lower fitness.

CI has been employed also in a different control strategy, i.e. the continuous release of Wolbachia infected males. In principle, this may reduce the population density or even eradicate it, because of mating competition between wild-type and Wolbachia infected males, as described in [6].

Two experimental releases of Wolbachia infected males of a new line (ARwP), with complete CI, have been performed in Rome in 2018 and 2019 to test the effectiveness of the method for controlling the population density of *Aedes albopictus* mosquitoes [1, 2]. The data obtained from the case-control experiments have been fitted to a model, with temperature-dependent parameters, of mosquito population dynamics [3]. The results allow to establish the potential reductions in population density that could be obtained with a given frequency and size of releases, and potentially to optimize them.

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# COVID-19 AND CHRONIC ILLNESS INTERACTIONS IN TRANSMISSION DYNAMICS

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SARS-CoV-2 infection currently causes common cold- or flu-like illness in most individuals, but patients with chronic conditions still experience a higher chance of COVID-19 hospitalization and death. It is crucial to estimate and project COVID-19 burden in chronic patients of different ages and to determine how best to protect them from severe COVID-19. In this talk, I will present mathematical modeling results on projecting COVID-19 dynamics and evaluating the impact of vaccination strategies in chronic patients of different ages. In the model, the population is stratified by age, risk due to chronic conditions, and immunity level before the start of a seasonal post-pandemic outbreak. For risk classification due to pre-existing chronic conditions, different guidelines are compared that stratify the population into three risk groups (low-, moderate-, and high-risk), i.e., the European classification by the European Centre for Disease Prevention and Control and national classifications by the public health institutes in individual European countries. A variety of strategies is considered such as vaccination of high-risk individuals, high- and moderate-risk individuals, individuals above 65 years old, individuals above 80 years old, and combinations of these strategies. I will discuss how best vaccination strategies differ depending on the metrics used for their evaluation: 1) maximum vaccination impact as quantified by the reduction in the number of hospitalizations due to vaccination; 2) maximum vaccination effectiveness as quantified by the number needed to vaccinate to prevent one hospitalization.

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# MATHEMATICAL MODELING AND CONTROL OF THERMAL AND DISEASE TRANSMISSION DYNAMICS

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The SARS-CoV-2 pandemic has underscored the indispensable role of mathematical tools in addressing global health crises. Effective modeling of spatial dynamics and the impact of associated political measures has proven crucial in this context, necessitating the consideration of high-diffusive connections such as airways and highways. In response to this need, we present a novel approach that addresses the challenges of linking models of mixed dimensionality. We couple a discrete (network) model with a continuum model. The resulting problem of mixed dimensionality consists of a problem where the low dimensional problem is embedded in the high-dimensional one.

Our method integrates mixed-dimensional diffusive models with a SIR-type (susceptible, infected, recovered) compartment model. We delve into the investigation of the mixed formulation's well-posedness and derive stable finite element discretizations, laying the groundwork for accurate and efficient simulations [1]. Subsequently, we employ some of these diffusive models for modeling the environment in reinforcement learning-based control based on stochastic policy gradient methods for thermal and disease transmission dynamics problems. We elucidate our findings through a combination of theoretical insights and numerical results. By offering this comprehensive perspective, we aim to demonstrate the potential of our approach in advancing our understanding of these types of phenomena and enhancing our ability to develop effective control strategies in the face of global health crises.

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# MODELING THE IMPACT OF INDIVIDUAL BEHAVIORS ON EPIDEMIC SPREADING THROUGH HYBRID MODELS

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We consider a class of hybrid problems constructed to model the complex features of population dynamics, in which the microscopic individual behaviors and the macroscopic collective dynamics are closely intertwined. The macroscopic dynamics are modeled by a system of differential equations, embedded in a geographical network structure, whereas the microscopic dynamic is modeled by an agent-based process, which can integrate various individual behaviors. The transition between the macroscopic and the microscopic scales involves the generation of a social network, which reproduces the social interactions occurring in the population. The hybrid model is studied in an abstract and theoretical framework, by establishing the existence and uniqueness of relevant solutions, their continuous dependence with respect to a variation of its parameters and the possible emergence of pseudo-periodic solutions. The way the model is designed allows its application to a large number of evolution problems arising, for example, in sociology, economics, geography and epidemiology [1].

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# SOME APPLICATIONS OF FRACTIONAL CALCULUS TO MATHEMATICAL MODELLING OF VECTOR-BORNE DISEASES

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Vector-borne diseases account for approximately 17% of all infectious diseases in the world and they cause about 700 000 deaths each year [4]. Vector-borne diseases are transmitted by vectors, which are blood-sucking insects e.g. mosquitoes, ticks, and fleas. Our work mainly focuses on mosquito-borne diseases such as dengue, zika and chikungunya. We extend a classical SISUV model [3] to a fractional-order system given by fractional-order differential equations [1]. This type of model better characterizes the virus transmission process as it involves memory and hereditary properties. We also consider a fractional version of SIRUV model [2]. We investigate asymptotic stability for both models and perform numerical simulations.

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# THE IMPACT OF MULTIPLE SIMULTANEOUS TESTING IN OMICS STUDIES

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Nowadays, in molecular biology research, a single scientist conducts a huge number of hypothesis tests in a short timeframe, surpassing the combined efforts of past generations. The phenomenon of performing multiple tests, in which the probability of a difference being significant by chance increases, is commonly known as the problem of multiplicity or multiple comparisons in statistical tests. The nature of omics studies (genomics, proteomics, metabolomics, transcriptomics, etc) set them apart from traditional multiple testing issues in other fields, often presenting an immense scale of multiple hypothesis testing challenges, with the number of tests reaching thousands. This has shifted the focus of methodological discussions from whether to correct for multiple testing to determining the most effective correction methods.

To address the complexities associated with multiple comparisons, researchers often adjust the p-values or the significance level threshold. This adjustment controls for FWER (Family-Wise Error Rate) corresponding to uphold a consistent 0.05 probability of committing a Type-I error. The key advantage of employing such adjustments lies in the prevention of pursuing misleading positive findings or expending resources unnecessarily. However, since the statistical power is limited as the number of hypotheses tested increases, the problem of multiple testing in omics studies is commonly addressed by controlling FDR (False Discovery Rate), which is less stringent than controlling FWER. The extensive adoption of FDR is thought to be driven by and rooted in modern technologies generating large datasets, characterized by vast numbers of measurements on a relatively limited set of experimental units [1].

Over the past three decades, numerous innovative multiple testing methods have been developed, prompting a re-evaluation of conventional approaches. This talk aims to present some of these methods and to discuss the impact of applying them in large datasets.

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# INSIGHTS INTO MULTI-STRAIN DENGUE FEVER DYNAMICS: AN INTEGRO-DIFFERENTIAL EQUATION APPROACH

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Motivated by dengue fever epidemiology, we propose a system of integro-differential equations (IDE) to study the disease transmission dynamics at the population level. We aim to incorporate and analyze the effect of a general time delay term describing acquired cross-immunity protection after the first infection, and also the effect of antibody-dependent enhancement (ADE), both characteristics of dengue fever. A detailed qualitative analysis of the model is performed, and a method that reduces a class of IDE to the corresponding ODE system, manifold symmetry, and perturbation theory are used to show the instability of the coexistence steady state. Numerical simulations identify other bifurcation structures, and the solutions of the system indicate oscillatory dynamics and even chaotic behavior for a specific value of the parameter representing the ADE. Furthermore, we observed that the choice of the distributed function for the cross-immunity period had no effect on the qualitative behavior of the system when compared with the particular case (ODE case). However, the invasion reproduction number depends on the average cross-protection time, which can affect whether the infection could coexist or not. Lastly, the scenarios present here help us to understand the dynamics of multi-strains at the population level, and we conclude that mechanisms and intrinsic characteristics of dengue fever, such as ADE and cross-protection, play a significant role and may hinder the prediction of the next outbreaks of the disease.

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# ESTIMATION IN NONLINEAR STOCHASTIC DIFFERENTIAL EQUATIONS USING THE LAPLACE APPROXIMATION

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Stochastic differential equations are highly useful for modelling dynamic systems in biology and other natural sciences, because domain knowledge can provide the structure of the equations while the driving noise represents the partial unpredictability of the actual system. Stochastic differential equations can form the basis of time series analysis, but technical complications arise when dynamics are nonlinear and the noise intensity is state-dependent. Here, we discuss the use of the Laplace approximation for estimating both system state trajectories and system parameters, focusing on the case where transition densities are not available in closed form. We demonstrate that consistency is obtained when the problem is cast as estimating the driving noise, and we point out the connection between this problem and that of minimum-effort control. We illustrate the theory with numerical simulation-reestimation examples, involving nonlinear dynamics, state-dependent noise, and non-Gaussian measurement errors. These examples include a predator-prey system with a limit cycle and Poisson-distributed count observations.

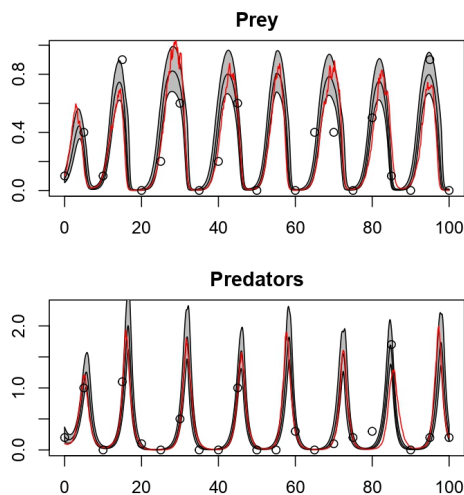


Figure 1: A simulation-reestimation experiment involving a predator-prey system.

# DYNAMIC SIR MODELS WITH EXACT SOLUTION

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We investigate an epidemic model based on Bailey's continuous differential system. In the continuous time domain, we extend the classical model to time-dependent coefficients and present an alternative solution method to Gleissner's approach. If the coefficients are constant, both solution methods yield the same result. In the discrete case, this provides the solution to a new discrete epidemic system [1]. However, the biological significance is not maintained. To address the problem, we derive a nonstandard finite difference scheme for Bailey's Susceptible-Infected-Removed continuous model. We prove that our discretized system is dynamically consistent with its continuous counterpart and we derive its exact solution. We end with the analysis of the long-term behavior of susceptible, infected and removed individuals, illustrating our results with simulations.

*The last part of our talk is joint work with Márcia Lemos-Silva (CIDMA) and Sandra Vaz (CMA-UBI).*

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# MODELING THE IMPACT OF MOBILITY SUPPRESSION AND VACCINATIONS IN CONTAINING EPIDEMICS IN CITIES NETWORK

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In this talk, we consider an agent-based model for the spread of an infection in a network of cities. We investigate the impact of mobility levels in containing the spread of infection with various vaccination coverage and age distributions. The results indicate that mobility reduction is sufficient to control the disease under all circumstances, and full lockdowns are unnecessary. It has to be reduced to different ratios depending on the vaccination level and age distribution. A key finding is that increasing vaccination coverage above a certain level does not affect the mobility suppression level required to control the infection anymore for the cases of young population and heterogeneous age distributions. By investigating several migration and commuting patterns, it is found that shutting mobility in a few local places is favored against reducing mobility over the entire country network. In addition, commuting -and not migration- influences the spread level of the infection.

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# THE ROLE OF BACTERIA IN AN ANAEROBIC DIGESTER

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The process of a real waste treatment plant is modeled, taking into account that in the anaerobic digestion in addition to chemical kinetics and stoichiometry of chemical reactions, bacteria are also involved. This implies the introduction of a biological feature in the model. As the whole process is very complex and essentially little is known about its several phases, we propose four different models to take into account the possible contributions of families of microorganisms operating in the absence of oxygen [1].

The digester substrate is composed by the chemical reagents. The output is given by biogases, of which methane and carbon dioxide represent the main portion, and of digestate compounds, namely water and organic substances, from which with additional processing, fertilizer in the form of compost is finally obtained.

Simulations of the various models are carried out in both non-operational and operational conditions. In static conditions, neither organic waste inputs nor product outputs are modeled, but the steady state is investigated. In particular special attention is paid to its stability sensitivity in terms of the model parameters. The simulated plant daily input are used in operational conditions and the biodigester outputs are compared against real data of the plant.

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# MITIGATING THE NEGATIVE EFFECTS OF EASTERN COTTONTAIL INVASION IN ITALY USING Z-TYPE CONTROL TECHNIQUES

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When alien species spread into new environments they cause ecological disruptions, alteration of native population dynamics and ecosystem dysfunctions. The negative effects can be exerted demographically, by competition, predation and hybridization, or epidemiologically, via new disease transmission.

We consider the specific invasion situation concerning the Eastern cottontail (*Sylvilagus floridanus*) into the northern and central regions of Italy. Affecting the local predator-prey dynamics, this invasion has shifted the natural equilibrium between the indigenous European hares (*Lepus europaeus*) and red foxes (*Vulpes vulpes*), since apparent competition mechanisms exist between the two lagomorphs.

In this framework, we investigate the situation intending to mitigate the negative effects of the invasion. For this task, we apply the Z-type control considering three possible alternatives to act on the ecosystem, in order to possibly give indications to ecosystem managers. At first, we consider predator removal to curb the invasive cottontails causing the hyperpredation effect on hares. We apply an indirect control on the cottontails, acting on foxes to reduce the pressure on hares. Then, we consider the possibility of importing new individuals of the indigenous prey population from outside, employing direct control on this class. This choice sustains the hare population, although it also provides more resources for foxes and it may entail other problems due to the emergence of hybrid species. Finally, we combine the two strategies initially proposed: indirect control on the cottontails, acting on foxes, and direct control on hares [1–3].

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# MATHEMATICAL MODELING OF OPTIMAL ANTI-HORMONAL TREATMENT FOR BREAST CANCER BASED ON MOUSE EXPERIMENTS WITH DIFFERENT DIETS

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Approximately 75% of all breast tumors express estrogen receptor (ER) and anti-hormonal treatment with aromatase inhibitors (AI) is usually preferred to treat ER positive breast cancer patients [2]. ER in breast cancer cells is activated by estrogen and it promotes cell proliferation and tumor growth [5]. Anti-hormonal treatment with AI decreases estrogen levels while anti-estrogen's block directly the action of steroids at the estrogen receptor [7]. High body mass index and high fat mass are known to have an impact on estrogenic activity in patients receiving AI, suggesting a reduced treatment efficacy in obese women [3, 4]. On the other hand, ER positive breast cancer cells can adapt to AI therapy and become resistant to anti-hormonal treatments [6]. Even though higher AI doses for obese patients have been recommended in the clinic, no therapeutic recommendations to eliminate the risk of drug resistance for obese patients with breast cancer exist.

In this study, we propose a mathematical model based on a system of ordinary differential equations [1]. We consider the interaction of tumor cells, estrogen level and adipocytes. We inform the model with data from mouse experiments fed with control and high-fat diet. The model allows to simulate treatment on lean and fat mice, so we investigate optimal hormonal treatment scheduling with drug resistance in each case. Our results suggest that AI treatment for breast cancer should consider adiposity and diet differences into account.

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# INSIGHTS INTO NEURAL OSCILLATOR NETWORK DYNAMICS USING A PHASE-ISOSTABLE FRAMEWORK

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Networks of coupled nonlinear oscillators can display a wide range of emergent behaviours under variation of the strength of the coupling. Of particular interest in this talk are neuronal networks where nodes are single neuron or neural population models. In these cases, interactions may be significant in magnitude compared to the rate of decay to the underlying stable limit cycle. Since the standard technique of first-order phase reduction breaks down beyond the weak coupling regime it therefore fails to capture many important features of the dynamics of these neural networks. Recent work has shown isostable coordinates to be a useful concept to characterise the transient behaviour of oscillators in directions where decay to the limit cycle is slow [3]. An alternative framework using isostable coordinates to obtain higher-order phase reductions has also demonstrated a similar descriptive ability for two oscillators [2].

In this talk we discuss the extension of phase-isostable network equations to an arbitrary but finite number of coupled oscillators, giving conditions required for stability of phase-locked states including synchrony. For examples where the dynamics of the full system are known, we compare the accuracy of the phase-isostable network equations and higher-order phase reductions in capturing bifurcations of phase-locked states. We find the former to be the more accurate and therefore we may employ this framework to investigate the dynamics of a number of globally coupled neuronal networks of varying size for planar node models [1].

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# INTERDEPENDENCE OF TESTS IN STATISTICAL TESTS SUITES: CASE OF STUDY

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There are several areas of knowledge in which it is necessary to work with sequences of random or pseudo-random numbers, for example in simulation studies (which can be applied to biology, physics, statistics, among others) or in security models (as in cryptography). There are different methods that allow such generation either at the bit level or in the interval  $(0,1)$ .

It is essential to verify the goodness of the generated sequences (and therefore, of the generators that produce them) by using sets of hypothesis tests, which are generally grouped in sets called batteries or suites [1]. There is currently a line of research that focuses on the study and design of such suites (see for example [2–4], among others). In this work, we will analyse some techniques used for this purpose and show a case study.

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# WITHIN-HOST MODELS UNRAVELLING THE DYNAMICS OF DENGUE REINFECTIONS

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Caused by four serotypes, dengue fever is a major public health concern worldwide. Current modeling efforts have mostly focused on primary and heterologous secondary infections, assuming that lifelong immunity prevents reinfections by the same serotype. However, recent findings challenge this assumption, prompting a reevaluation of dengue immunity dynamics.

In this study, we develop a within-host modeling framework to explore different scenarios of dengue infections. Unlike previous studies, we go beyond a deterministic framework, considering individual immunological variability. Both deterministic and stochastic models are calibrated using empirical data on viral load and antibodies immunoglobulin M and immunoglobulin G (IgM and IgG) concentrations for all dengue serotypes, incorporating confidence intervals derived from stochastic realizations.

With good agreement between the mean of the stochastic realizations and the mean-field solution for each model, our approach not only successfully captures primary and heterologous secondary infection dynamics facilitated by antibody-dependent enhancement (ADE) but also provides, for the first time, insights into homotypic reinfection dynamics. Our study discusses the relevance of homotypic reinfections in dengue transmission at the population level, highlighting potential implications for disease prevention and control strategies.

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**This work was also presented as a poster.**

# LARVICIDE TREATMENT OPTIMIZATION AT A BOTANICAL GARDEN

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*Aedes albopictus* is a well-known vector of multiple diseases such as dengue, Zika, or chikungunya [3]. This, together with the fact that it is an invasive species in Europe, makes the development and improvement of control techniques of paramount importance [2].

In order to understand the interaction between control interventions and mosquito population dynamics, we develop a metapopulations model of coupled ODEs for *Aedes albopictus* that incorporates Larvae, Adults and the amount of a control agent (such as *Bacillus thuringiensis* [1]) present in the water at each breeding site. In this mathematical framework, control interventions are modeled by Dirac's deltas, since we assume the interventions to be instantaneous compared to the time window studied. The model accounts for the thermal responses of the mosquito biological parameters and rainfall, which are known to shape mosquito population dynamics, as well as the spatial information concerning the distance between the different breeding sites.

The study is based on real data from 35 breeding sites, which are currently undergoing control measures at the Marimurtra botanical garden. We use stochastic optimisation techniques to determine numerically the optimal times for implementing treatments with respect to the seasonal climatic patterns. Additionally, in cases where the treatment of all breeding sites is not feasible due to budgetary or operational constraints, we intend to identify traits in the spatial distribution or in the intrinsic characteristics of breeding sites that make them a priority for treatment.

The goal of our work is to obtain general guidelines aimed at improving the efficacy of mosquito control using *B. thuringiensis* within the Marimurtra botanical garden (Blanes, Girona) during the upcoming 2024 mosquito season. Nonetheless its applicability may be appropriate for other scenarios too.

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# THE MULTILAYER INTERACTION STRUCTURE OF AN ECOLOGICAL NETWORK AND THE LOKA-VOLTERRA MODELS

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The Lotka-Volterra (LV) dynamical models for ecological systems have been considered by various authors [1, 3] to study the relevance of the interaction network and the effects of random fluctuations for the existence and stability of the stationary solutions. In the simplest formulation, one considers  $n$  species interacting in an ecological niche so that the reproduction rate  $r_k$  of the  $k$ -population changes as a function of the possible binary interactions with the other populations

$$\dot{n}_k = r_k(\vec{n})n_k = \left( \gamma_k - \sum_{j=1}^n \Gamma_{kj}n_j \right) \Theta(n_k - n_{min})n_k \quad n_k \geq 0 \quad (1)$$

where one introduces the Heaviside function  $\Theta(\cdot)$  to simulate the extinction dynamics when a population is reduced below the threshold  $n_{min}$ . The interaction matrix  $\Gamma$  can be associated to a weighted graph and it represents different ecological interactions between the species  $k$  and  $j$ , according to the sign of  $\Gamma_{kj}$  and  $\Gamma_{jk}$ . The community equilibrium state  $\vec{n}^*$  follows from the existence of a solution  $\vec{n}^* = \Gamma^{-1}\vec{\gamma}$  in the first quadrant  $n_k^* \geq n_{min}$  and its stability depends on the spectral properties of the interaction matrix  $\Gamma$ . Other equilibrium are possible if some species are extinct. In the seminal work[4], May pointed out as in case of random interactions (i.e.  $\Gamma$  is a random matrix) the limit  $n \rightarrow \infty$  is unstable, suggesting that the complexity of an ecological network has to be associated to specific interaction structures to explain the species abundance distributions [2]. In this contribution we consider the spectral properties of the random matrix  $\Gamma$  when the ecosystem can be divided into two communities (preys and predators) with internal competition:

$$\Gamma = \begin{pmatrix} \Gamma^{(1)} & A \\ -A^T & \Gamma^{(2)} \end{pmatrix}$$

where the matrices  $\Gamma^{(i)}$  define the competition among the predators ( $i = 1$ ) and among the preys ( $i = 2$ ) and the matrix  $A$  represents the predation behavior. The methodology is based on a perturbation approach and the results of Random Matrix Theory [6] together

with numerical simulations. Our aim is to study the stability properties of the community equilibrium of the system (1) and the bifurcation properties when the community interactions change.

We also generalize the model (1) by assuming the existence of a second interaction layer that diffuses a character  $\alpha_{k_2}$  among the preys that modulates the predation behavior.

$$\begin{aligned}\dot{\alpha}_{k_2} &= - \sum_j L_{k_2 j_2} \alpha_{j_2} \\ \dot{n}_{k_1} &= \left( -\gamma_{k_1} - \sum_{j_1} \Gamma_{k_1 j_1}^{(1)} n_{j_1} + A_{k_1 j_2}(\alpha_{j_2}) n_{j_2} \right) n_{k_1} \\ \dot{n}_{k_2} &= \left( \gamma_{k_2} - \sum_{j_2} \Gamma_{k_2 j_2}^{(2)} n_{j_2} + A_{k_2, j_1}^T(\alpha_{k_2}) n_{j_1} \right) n_{k_2}\end{aligned}$$

where  $L_{kj}$  is a Laplacian matrix. In this way we introduce a multiplex structure in the LV dynamics as it has been proposed for ecological systems to model the different nature of the interactions among the species [5]. The diffusion dynamics may simulate the spread of a parasite among the preys or a change in the environment that affects the predation efficiency, and it can change the stability of the community equilibrium.

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# THE EFFECTS OF SPATIAL STRUCTURE ON THE ECOLOGY AND EVOLUTION OF INFECTIOUS DISEASE

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While we now have a wealth of theory on the ecology and evolution of infectious diseases, many mathematical models rely on a mean-field assumption such that there is no accounting for spatial structure within populations. In reality we would expect many processes such as disease transmission and births of offspring to be local processes. There are a variety of ways spatial structure can be built into models. In this talk I will focus on lattice-based methods, where it is assumed host individuals are fixed in space on a grid. Interactions such as disease transmission can then still be ‘global’ across the lattice, or ‘local’ between near-neighbours. Two complementary approaches are taken to analyse these systems: approximate models of differential equations using a pair approximation, and stochastic simulations. I will discuss the impacts of including this spatial structure in a series of models, focussing in turn on the epidemiology, ecology and evolution of infectious disease. These include lowered levels of infection in spatial systems, the potential for disease-driven extinction of host populations, and evolution to more highly-defended hosts. I will finish by highlighting areas of future research with these models.



# SPATIOTEMPORAL DYNAMICS IN TRADE-OFF PREY PREDATOR MODEL WITH DOOMED FUNCTION RESPONSE

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In ecological scenario, predators often risk their lives pursuing dangerous prey, potentially reducing their chances of survival due to injuries [1]. Prey, on the other hand, try to strike a balance between reproduction rates and safety. In our study, we introduce a two-dimensional prey-predator model inspired by Walter Tostowaryk's work [3], specifically focusing on the domed-shaped functional response observed in interactions between pentatomid predators and neo-diprionid sawfly larvae [2]. To account for the varying effectiveness of larval group defense, we incorporate a new component  $cx^2$  into the response equation. Our investigation delves into predator trade-off dynamics by adjusting the predator's mortality rate to reflect losses incurred during encounters with dangerous prey and preys' trade off between safety and reproduction rate [4, 5] incorporating this domed-shaped functional response. Our model demonstrates bistability and undergoes various bifurcations, including transcritical, saddle node, Hopf, Bogdanov-Takens, and Homoclinic bifurcations. Critical parameters impact both predator and prey populations, potentially leading to predator extinction if losses due to dangerous prey encounters become excessive, highlighting the risks predators face for their survival. Furthermore, the efficacy of group defense mechanisms can further endanger predators. Expanding our analysis to a spatially extended model under different perturbations, we explore Turing instability to explain the relationship between diffusion and encounter parameters through both stationary and dynamic pattern formation. Sensitivity to initial conditions uncovers spatiotemporal chaos. These findings provide valuable insights into comprehending the intricate dynamics of prey-predator interactions within ecological systems.

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# A STUDY OF COVID-19 DYNAMICS IN BASQUE COUNTRY AND ITALY

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In this work we wanted to study the effects of COVID-19 pandemic in two different regions using the same frame of work. We focus in Basque Country and Italy because of the quality of the available data and because of their similar demographic characteristics; in particular, they have comparable life expectancy, death rates and age distribution [2, 3]. To replicate the COVID-19 behaviour we established a deterministic SHARD model, which is an extension of a classic SIR adding the number of deaths (D) and where infected are divided into two categories: hospitalized (H) and asymptomatic (A) [1]. We fit the model with the real data from both regions to estimate parameters like the reproduction rate or the mortality ratio that characterises the disease, and compare the values from the countries. We extended the analysis considering the life expectancy of the residents of both countries [4] and the impact of COVID-19 in population groups of comorbidity level. Additionally, we studied the effects of the lockdowns of both regions in the dynamics of the infection and of the mobility restrictions on the disease spread.

As a result, we could conclude how the same pandemic can behave in a distinct way in alike regions; we measured the different impact by country and by population characteristics (age, sex and comorbidity); and we quantified the effects of the contention measures of the countries.

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# MODELING CELL CYCLE DYNAMICS IN CELL CULTURES: IMPLICATIONS FOR CANCER THERAPY IN WELL MIXED AND SPATIAL STRUCTURED MODELS

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The cell cycle is a series of precisely regulated events crucial for cell growth and division. This complexity poses challenges in mathematical modeling and simulation of cell cultures. Particularly, employing an exponentially distributed cell cycle length may lead to erroneous interpretations, as highlighted by Yates et al. [4], “the most probable time for a cell to divide is the current time”. Further, Vittadello et al. [3] have shown that synchronization among individual cells can spontaneously emerge in a cell culture due to the cell cycle, even in the absence of direct intercellular coupling.

In this presentation, we introduce a novel stochastic simulation algorithm designed to model cell populations with realistic cell cycle lengths in well-mixed environments. We particularly explore its applications in cancer therapy scenarios. Based on our lattice based stochastic cell population simulation method [1], we then expand this method to simulate spatially heterogeneous populations. This extension reveals challenges linked to the finite carrying capacity of environments. To address these, we propose four model assumptions that facilitate overcoming these challenges. Finally, we characterize the parameter space, identifying regions where synchronization is evident in spatial models. We conclude by demonstrating the robustness of synchronization effects across different model assumptions. The presentation is partly based on the phd thesis of the author [2].

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# MODELLING OF TUMOR-IMMUNE SYSTEM INTERACTIONS

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The interactions between tumor cells and cells of the immune system can regulate the cancer development, facilitate the tumor progression and influence the tumor response to treatment. According to [1, 2], the tumor-immune system interactions can be summarized in three relevant phases, namely the clearance phase, the equilibrium phase, and the escape phase. The first stage is characterized by the dominance of the immune cells, when they are able to eliminate the new formed cancer cells. In the second stage, the interactions between tumor and immune cells are balanced and the tumor cells are inactive. In the last stage, the tumor cells are equipped with new mechanisms that affect their recognition by immune cells and at the same time they increase their ability to destroy immune cells. However, adoptive cellular therapy is one of the recent effective immunotherapies which can improve the ability of the immune system to destroy tumor cells during the escape phase.

This cellular mechanism is rather complex and mathematical modeling can help to describe and interpret the dynamics. We are interested, in particular, in the escape phase, and we propose a mathematical model that describes the rivalry among tumor and immune cells in the presence of adoptive cells therapy by interleukin. The mathematical model is based on the Kinetic Theory approach that describes the cellular interactions, and then we derive macroscopic equations that describe the global behaviour of the cellular populations. We prove the consistency between the model solution and the biological context, including existence, uniqueness, positivity and boundedness of the solution. We study the stability of the equilibrium states, and investigate the existence of bifurcations in the parameter space. We complement our study with various numerical simulations that show different behaviours of the solution.

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# INFLUENZA MODEL WITH TEMPERATURE-INCIDENCE ASSOCIATION

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Portugal is among the European countries with higher excess of mortality during winter, even though winters are considered to be relatively mild. This excess mortality might be associated with a larger vulnerability of the Portuguese population [4]. Some of this excess mortality can be attributed to Influenza outbreaks [3] during the winter time. Important also to note that influenza activity has also been shown to be negatively associated with temperature [2].

In this work we will present an ODE compartmental influenza model [5] which will include a temperate-incidence association function. The model will then be adjusted to the data available. Data includes weakly incidence of influenza and average temperature for certain regions of Mainland Portugal. Given the relationship between influenza incidence and temperature described in the literature, we aim to find the functional form of the association for linear and non-linear cases that can better characterise this relationship through time and across distinct geographical regions [1].

With the temperate-incidence association function defined we are able to compute  $\mathcal{R}_t$  as a function of temperature covariates. Given temperature forecasts, and defined initial conditions, it is possible to forecast  $\mathcal{R}_t$  for which we test the accuracy of given observed outcomes.

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# SUPERPOSITION OF STATIONARY WAVES IN BRAIN ACTIVITY VARY WITH ANESTHESIA

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Spontaneous fluctuations in signals detected with functional Magnetic Resonance Imaging (fMRI) correlate across spatially distributed brain areas forming functional networks that appear disrupted in numerous psychiatric and neurological disorders, pointing to a key role in brain function [3]. However, the organizing principle driving long-range correlations between brain areas remains unclear. When analyzed across the brain continuum, functional networks exhibit features of stationary wave patterns, pointing to an inherent relationship with resonance phenomena. From a wave perspective, correlated activity is detected among spatially distributed poles (the wave antinodes), with gradually varying phase relationships across space [1]. These wave patterns have been shown to emerge transiently and recurrently during rest, to be selectively recruited during specific tasks, and to replicate across mammals. In this work, we recorded ultra fast ultrahigh field fMRI signals (9.4 Tesla with a temporal resolution of 38 milliseconds) from female rats across three anesthesia conditions. Power at frequencies extending up to 0.3 Hz was consistently detected across rat brains and was found to be modulated by anesthesia level. Principal component analysis revealed a repertoire of modes, in which transient oscillations organize with fixed phase relationships across distinct cortical and subcortical structures, indicative of stationary waves. These oscillatory stationary waves reveal canonical functional networks, whose properties were found to vary between anesthesia conditions, resonating at faster frequencies under medetomidine sedation and reducing both in number, frequency, and duration with the addition of isoflurane. Peaking in power within clear anatomical boundaries, these oscillatory modes point to an emergent systemic property resulting from the superposition of stationary waves. This work provides insight into the origin of oscillations detected in fMRI and the organizing principles underpinning spontaneous long-range functional connectivity in the brain across levels of arousal [2].

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# A MATHEMATICAL MODEL FOR THE FORMATION OF PATTERNS ON TULIP PETALS CAUSED BY THE TULIP-BREAKING VIRUS

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The petals of flowers are full of lively colours and beautiful patterns. It is hard to imagine that viruses can create beauty in plants, but tulips infected with the tulip-breaking virus (TBV) can produce beautiful striped and flamed patterns on their petals. Even though the TBV can make tulips smaller and less likely to reproduce, the beauty of the created patterns enchanted the Dutch in the seventeenth century so much that the price of tulip bulbs experienced an unreasonable and unsustainable growth (a.k.a. Tulipmania). In this work, we will present a mathematical model that provides a dynamical explanation for the formation of pigment patterns on tulip petals due to the TBV. The model comprises a system of partial differential equations that describes the interaction of the tulip-breaking virus, the substrate needed for virus replication, and the tulip pigment, anthocyanin. We will show how the development of spatial patterns in the model results from the complementary effects of a Turing's instability mechanism [2] and a Wolpert's positional information mechanism [1] for pattern formation, and embed this dynamics on a growing domain for the purpose of illustrating the solutions of the model on a growing petal.

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# BEHAVIOR OF A SIR MODEL WITH VACCINATION RULED BY AN IMITATION GAME: FROM EQUILIBRIUM STABILITY TO POSITIVE LYAPUNOV EXPONENTS

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Mathematical modelling of epidemiological behavior has been a major breakthrough in understanding the role of human interaction in the spreading of infectious diseases. The SIR model consists in dividing the population in three major groups: susceptible (S), infected (I) and removed (R), according to how each of these population percentages is affected by an infectious disease at a given time. By deploying a system of ordinary differential equations, one can describe how each of the groups change throughout an epidemic. Additionally, by incorporating a dynamic equation based on game theory, it is possible to model whether vaccinating is the best strategy at a given time, according to how the vaccination risk is perceived relative to the infection risk [2].

This work aims to understand how the system behaves around the endemic equilibrium and how it is destabilized through a Hopf bifurcation, with the only shifting parameters being the social learning rate ( $k$ ) and the relative vaccination risk ( $r$ ). Positive Lyapunov exponents are a good indicator of chaotic behavior in a system [2]. By calculating these exponents for multiple sets of parameters ( $k, r$ ), it is possible to identify chaotic regions and conjecture the social and biological circumstances in which these appear.

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# MODELLING AND OPTIMIZING RESOURCE ALLOCATION TO DEFENCE CHEMICALS AND COUNTER-COUNTER DEFENCE BY ENZYME INHIBITORS IN PARASITIC AND TROPHIC INTERACTIONS

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In numerous interactions between parasites (including pathogens) and their hosts, defence and counter-defence mechanisms in the form of defence chemicals and enzymes degrading those chemicals can be observed [3]. An example is provided by cephalosporins from *Streptomyces clavuligerus*,  $\beta$ -lactamases produced by many bacterial species and an inhibitor of  $\beta$ -lactamases, clavulanic acid, again secreted by *S. clavuligerus* [5]. Related phenomena occur in trophic (e.g. plant-herbivore) interactions. Mathematical modelling is instrumental in understanding such complex interactions [1–4].

Here, we study the question under which conditions it pays, during evolution, to establish a counter- counter defence rather than to intensify or extend the defence. We propose an ODE model describing this phenomenon, based on enzyme kinetics for reversible or irreversible competitive inhibition. We use an objective function based on Haber’s rule, saying that the toxic effect is proportional to the time integral of toxin concentration (Area under the curve, AUC). It is not widely known that the AUC for a Michaelis-Menten type degradation can be calculated analytically, although this had been derived decades ago [7]. Here, we show that, in the case of reversible inhibition, also the optimal allocation to defence and counter-counter defence can be calculated analytically [6]. This yields a threshold value for the inhibition constant. Only if it is below that threshold, that is, in the case of strong binding, it pays to have a counter-counter defence. A bifurcation is also observed for the dependence on the capacity. For the case of irreversible inhibition, an additional ODE has been included and numerical solutions have been derived. Our theoretical predictions should be of interest for computing optimal mixtures of  $\beta$ -lactam antibiotics and  $\beta$ -lactamase inhibitors such as sulbactam in clinical applications, as well as for better understanding plant-herbivore and other molecular-ecological interactions.

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# EXPONENTIAL SYNCHRONIZATION OF KURAMOTO OSCILLATORS WITH TIME-DELAYED INTERACTIONS

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We study the asymptotic synchronization for the Kuramoto oscillators model with time-delayed interactions. The Kuramoto model appears in many biological/physiological applications. Then, often, time delay effects have to be considered. We provide an explicit lower bound on the coupling strength and an upper bound on the time delay in terms of initial configurations ensuring exponential synchronization. Our approach, which relies on continuity arguments and careful estimates of the trajectories, allows us to significantly relax previous thresholds on the time delay size. Moreover, we introduce a graph topology on the structure of the model in order to consider a non-universal interaction among the states.

**This work was also presented as a poster.**

# THE $\beta$ -SEIR APPROACH FOR MODELING INFECTIOUS PANDEMICS, WHEN HUMAN BEHAVIOR IS AN INEVITABLE FACTOR

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In the context of motivation for the COVID-19 pandemic, in [5] to model the observed variability in the transmission rate  $\beta$  an equation of the type

$$\frac{1}{\beta} \frac{d\beta}{dt} = \underbrace{f(\beta, \beta_*)}_{\text{restitution factor}} - \overbrace{g(S, E, I, R)}^{\text{reaction factors}}$$

was introduced and added to the standard SEIR model especially to explain the early main pandemic patterns [4]. That is, without leaving the perspective of a strategic model, it assumes a social reaction as a result of an evaluation of some of the variables that compartmentalize the epidemiological state of the disease (e.g., for the introduction of nonpharmaceutical mitigations). This is in tension with a restitution factor  $f(\beta, \beta_*)$  that depends on the distance between the transmission rate and a theoretical intrinsic one  $\beta_*$ , that is, an expression associated with a loss of compliance [1]. In the present work, we communicate research advances associated with particular cases of the function  $g(\cdot)$  and the justification of the model through its association with psychological theories of human conduct [3], such as the Theory of Planned Behavior [2, 6].

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# BEHAVIOR IN A DYNAMICAL MODEL

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We consider the study of behavior in biology, through a kinematic geometrical method. We use symbolic dynamics techniques to classify and simulate a variety of types of behaviors, generalizing the work developed in [1] and [2], used for the classifications of motion in biology. The classification of behavior in a simple model is obtained considering several coupled discrete dynamical systems, one characterizing the movement and others characterizing distinct aspects of behavior, in particular internal state of the organism, and interaction with the environment.

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## RE-MATING CONSEQUENCES ON THE EFFICIENCY OF THE STERILE INSECT TECHNIQUE

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The Sterile Insect Technique (SIT) is a biological control technique based on mass-rearing, sterilization, and releases of the pest species targeted for population control. Sterile males are released to dilute wild population, so that wild females are more likely to encounter and mate with a sterile male rather than a wild male, thus reducing the number of offspring in the next generation. However, if wild females tend to re-mate, the effectiveness of SIT may be compromised.

The influence of re-mating, i.e. the ability of a female to be inseminated several times, was studied using a model based on differential equations with continuous releases. In the model, the population is structured into larvae, sterile and wild males, and three female stages: unmated, mated with sterile males, and mated with wild males. Sterile matings with sterile males produce no offspring, as opposed to fertile matings with fertile males. We compared a situation in which females mate only once in their lifetime with one in which they can mate and then re-mate after a certain period of time, called the refractory period. Situations in which the refractory periods associated with sterile and fertile matings are not equal have been studied.

The analytical study of the re-mating model revealed a dependency between the existence of infestation equilibria, limiting control capabilities where they exist, and the length of refractory periods. Thus, if the refractory period associated with sterile matings is short, larger releases are needed to control the population. If this refractory period is long, sterile matings will make females unavailable for some time, in addition to the dilution effect of the releases, thus increasing the effectiveness of SIT compared to the previous case. The study highlights the impact of reproduction processes on SIT control effectiveness, and more generally the need for a thorough understanding of the ecology and biology of the target pest.

# ANALYTICAL DETECTION OF STATIONARY AND DYNAMIC PATTERNS IN A PREY-PREDATOR MODEL WITH REPRODUCTIVE ALLEE EFFECT IN PREY GROWTH

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Spatial pattern formation plays a crucial role in understanding the dynamical complexity of biological systems [4]. Turing [5] first explained the formation of spatially heterogeneous stationary pattern in a chemical system involving activator and inhibitor of different diffusion rates. The idea of Turing has been applied using reaction-diffusion theory to a variety of real biological systems that include semi-arid vegetation, plankton patchiness, fish skin, mussel bed, ecological invasion, prey-predator system, etc. A generalized reaction diffusion system for two species  $u(x, t)$  and  $v(x, t)$  can be written as [4].

$$\begin{aligned}\frac{\partial u}{\partial t} &= D_1 \nabla^2 u + F_1(u, v), \\ \frac{\partial v}{\partial t} &= D_2 \nabla^2 v + F_2(u, v), \quad x \in \Omega \subset \mathbb{R}^n,\end{aligned}$$

where  $D_1$  and  $D_2$  are the diffusion coefficient of  $u$  and  $v$ ,  $F_1(u, v)$  and  $F_2(u, v)$  are the reaction kinetics, and  $\nabla^2$  is the Laplacian operator in  $\mathbb{R}^n$ .

Allee effect in population dynamics has a major impact in suppressing the paradox of enrichment through global bifurcation, and it can generate highly complex dynamics [1, 3]. Here, we discuss the influence of the reproductive Allee effect, incorporated in the prey's growth rate of a prey-predator model with Beddington-DeAngelis functional response [2]. Preliminary local and global bifurcations are identified of the temporal model. The spatio-temporal model satisfies Turing instability conditions, but numerical investigation reveals that the heterogeneous patterns corresponding to unstable Turing eigenmodes act as a transitory pattern. Inclusion of the reproductive Allee effect in the prey population has a destabilising effect on the coexistence equilibrium. For a range of parameter values, various branches of stationary solutions including mode-dependent Turing solutions and localized pattern solutions are identified using numerical bifurcation technique. The model is also capable to produce some complex dynamic patterns such as travelling wave, moving pulse solution, and spatio-temporal chaos for certain range of parameters and diffusivity along with appropriate choice of initial conditions.

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# MODELLING BOVINE HORMONE DYNAMICS: A COMPARTMENTAL APPROACH

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Over the years a plethora of different methods have been developed to model bovine hormone dynamics. Previous methods such as by Boer et al. [1] and Stötzel et al. [4] use a set of ODEs and Hill functions to replicate recorded hormone concentration data. Other methods such as by Lacker [2] and Sobleva et al. [3] focus on individual follicular competition within the ovary.

In our proposed model, we adopt a combination of two approaches to effectively capture the dynamics of hormone growth and follicle development. We model each hormone as a system of ordinary differential equations (ODEs), while also modelling the growth of individual follicles and their Estradiol and Progesterone production. To achieve this, we have developed a compartmental model, as depicted in Figure 1.

Here, the cow is divided into distinct compartments, where the growth of each follicle and the production of each hormone are dependent on their previous state and the concentrations of hormones within that specific compartment. Hormones pass between adjacent compartments depending on relative concentration in each. By modelling each follicle separately, we can effectively capture the intricate interactions between hormone dynamics, follicular development, and the occurrence of multiple ovulations, a significant indicator of twinning in cattle. The model was created using MATLAB allowing us to generate an arbitrary number of follicles and implementing the necessary if statements for events and conditional follicular growth within the model. Compartmentalising the model allows us to parameterise more easily, as we can simulate in-vitro experiments by isolating a compartment. We can then compare the behaviour of, for example, our follicle compartment with in-vitro data of follicles administered with varying hormone concentrations.

This model has led to the creation of a “Virtual Ovary” where in-silico experiments can be conducted to determine the impact that varying hormone administrations has on follicular growth and circulating hormone concentrations.

**Acknowledgements** We would like to acknowledge the contributions of the Department of Reproductive Immunology and Pathology, Institute of Animal Reproduction and Food Research, Polish Academy of Sciences for supplying data to calibrate this model.

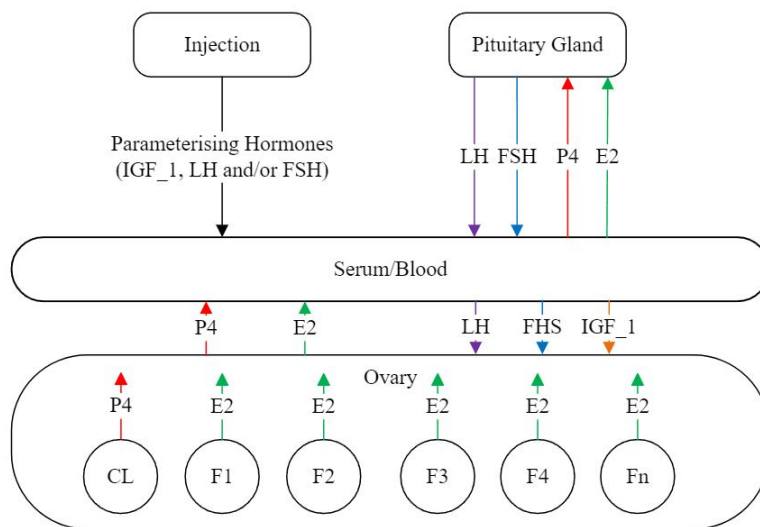


Figure 1: A simplified depiction of the flow of hormones between compartments in our model. Estradiol as E2, Progesterone as P4, Luteinising Hormone as LH, Follicle Stimulating Hormone as FSH and Insulin-like Growth factor 1 as IGF\_1. Follicles are labelled  $F_1$ - $F_n$  and the Corpus luteum as CL.

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# COST-EFFECTIVENESS OF COVID-19 VACCINATION BY MODELING A COUNTERFACTUAL SCENARIO: A CASE STUDY OF THE BASQUE COUNTRY

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Vaccination has played a crucial role in mitigating the effects of the COVID-19 pandemic. In this talk, we will present the results of a retrospective evaluation of the cost-effectiveness of the initial phase of COVID-19 vaccination in the Basque Country, from January to December 2021. We use a deterministic framework to describe different phases of COVID-19 dynamics in the Basque Country, where the changes in biological parameters such as, for example, the transmission and mortality rates are estimated over one year of vaccination rollout. Our model is calibrated with empirical data on hospitalizations, Intensive Care Unit (ICU) admissions and deaths, and the results are compared to the no-vaccine scenario, enabling us to compute the quality-of-life years (QALYs) saved by the vaccination. The costs of infection, vaccination, hospitalization, and ICU admission are then used to evaluate the incremental cost-effectiveness ratio (ICER) from the healthcare system perspective in terms of euros spent per QALY gained, a measure often used as a decision rule in resource allocation.

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**This work was also presented as a poster.**

# A TWO-STAGE SEIRS REINFECTION MODEL WITH MULTIPLE ENDEMIC EQUILIBRIA

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Since the introduction of SIR model by Kermack and McKendrick in 1927, compartmental models have been massively studied and successfully applied to various epidemic processes including characteristics such as quarantine, vaccination, variants, cross-immunity. Recently, a particular attention has been paid to reinfection models in epidemiology. To cite a few, threshold conditions for infection, reinfection and endemicity of various SIRS models are studied in [2], bifurcation analysis for a SIRS model presenting different contact rates for infection and reinfection in [4], and models counting reinfections in [1, 3]. Nevertheless, in most studies on reinfection, the infection and reinfection processes are assumed to behave essentially in the same way, which is quite limitative. With the aim of understanding the effects induced by differences between the stage of primo-infection and further reinfections, we introduce here an 8-dimensional two-stage SEIRS reinfection model in which the parameters characteristic of the disease dynamics are different for the primo-infection and for the following reinfections. The value of the basic reproduction number  $\mathcal{R}_0$  of the model around the (unique) disease-free equilibrium is first derived, and the existence of up to two and three endemic equilibria, respectively in the cases  $\mathcal{R}_0 \leq 1$  and  $\mathcal{R}_0 > 1$ , is theoretically established under appropriate conditions on the system parameters. Finally, numerical testing and simulations are achieved, which in particular exhibit bistability in the cases when multiple endemic equilibria arise.

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# LIMIT CYCLES IN PERIODIC LOTKA-VOLTERRA SYSTEMS MODELING CANCER ADAPTIVE THERAPY

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Treatment resistance is common in almost all cancers and a threat to treatment success. An accepted hypothesis to explain the evolution of resistance is based on the concepts of *resistance cost* and *competitive release*: resistant cells are less competitive due to the cost of resistance and before treatment their growth is suppressed by highly competitive sensitive cancer cells; however, after these are eliminated by therapy, the resistant cells are released to proliferate rapidly. In this context, adaptive therapy is as a promising alternative, aiming to control the evolution of resistance by combining different drugs and/or treatment regimens that allow controlled growth of sensitive cells to suppress resistant cells. Recent works modeled adaptive therapy for prostate cancer [1], but their results are based only on numerical simulations and open some fundamental questions from a mathematical perspective. We approach these questions by modeling adaptive therapy with a three-dimensional Lotka-Volterra system with periodic coefficients,

$$\dot{x}_i = r_i(t)x_i \left( 1 - \frac{\sum_{j=1}^n \alpha_{ij}(t)x_j}{K_i(t)} \right), \quad i = 1, \dots, 3, \quad (1)$$

where  $x_1, x_2, x_3$  represent three different phenotypes of tumor cells,  $r_i$  are reproduction rates,  $K_i$  are carrying capacities, and  $\alpha_{ij}$  are competition coefficients. The functions  $r_i, K_i, \alpha_{ij}$  are periodic with a period  $T = T_1 + T_2$ , where  $T_i$  is the duration of treatment type  $i$ . Each phenotype has different sensitivities to each treatment. We investigate general conditions on the parameters, plausible from a clinical point of view, under which the system (1) has a stable limit cycle, representing the success of adaptive treatment. Such results can provide a better understanding of the mechanisms involved in the occurrence of resistance and how adaptive therapy can be planned to avoid it.

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# DYNAMICS OF A TWO-STRAIN EPIDEMIC MODEL WITH WANING IMMUNITY - A PERTURBATIVE APPROACH

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Many infectious diseases are comprised of multiple strains with examples including Influenza, tuberculosis, and Dengue virus. The time evolution of such systems is linked to a complex landscape shaped by interactions between competing strains. Possible long-term dynamics include the extinction of less competitive strains, convergence to multi-strain steady-states, or self-sustained oscillations.

This work considers a two-strain epidemic model in which the strains can interact indirectly via the immunity response generated following infections, and in which this immune response wanes with time. In particular, we focus on scenarios where the rate of waning immunity is significantly faster than the rate of demographic turnover. The first key result of this study is the explicit computation of the steady states. Such a result is unexpected since the equilibrium point is defined by a nonlinear algebraic system of seven equations, and to the best of our knowledge does not appear elsewhere in the literature considering similar systems. Following this result, we take advantage of the separation of time scales in the problem and use perturbation methods to analyze the stability of the fixed points. In particular, we establish the conditions under which the system gives rise to the coexistence of the two strains and whether coexistence is attained via convergence to an endemic steady-state or via self-sustained oscillations.

Our study exposes the system behavior in a broad parameter regime. In particular, it unveils two parameter regimes of the distinct qualitative behavior of the system and characterizes the separatrix between them. Within the first regime, the system gives rise to oscillatory coexistence for all feasible conditions. In the second regime, the system's behavior is governed by a solution to a quadratic equation, potentially resulting in the convergence to a multi-strain endemic equilibrium or the persistence of oscillatory coexistence.

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# GLOBAL STABILITY OF COEXISTENCE EQUILIBRIA FOR $N$ -SPECIES MODELS OF FACULTATIVE MUTUALISM

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In Georgescu *et al.* [1], a framework for proving boundedness results for  $n$ -species models of facultative mutualism in terms of per-species reproductive numbers that are computed at large population densities, understood as threshold parameters, has been assembled under fairly general assumptions.

We now augment those assumptions with either sublinearity or monotonicity conditions and use a monotone dynamical systems approach to establish stability results for the coexistence equilibria. To this purpose, the boundedness of solutions is of paramount importance, as it drastically limits down a certain trichotomy perspective provided by underlying approach. If the reproductive numbers have a suitable quasi-polynomial form motivated by the specifics of Wolin and Lawlor's model, a single parameter can then be used to formulate a stability condition rather than multiple ones, namely the spectral radius of a certain matrix of coefficients.

Finally, we use these stability results to discuss several  $n$ -species models of facultative mutualism whose 2-dimensional versions are in current use, outlining the details that require the use of a specific additional assumption.

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# THE HISTORICAL ECOLOGICAL BACKGROUND OF WEST NILE VIRUS IN PORTUGAL PROVIDES ONE HEALTH KNOWLEDGE AND OPPORTUNITIES INTO THE FUTURE

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In the context of global anthropogenic trends, such as population growth, socio-economic transformation, and climate change, host-pathogen interactions are undergoing significant shifts, leading to the (re)emergence of infectious diseases. In the context of Portugal, this study focuses on West Nile virus (WNV), a neglected arbovirus and the leading cause of viral encephalitis worldwide. Through ecological modelling based on machine learning algorithms (Random Forest and Boosted Regression Trees), we analyse the association between background variables (N=53) and historical WNV occurrences in Portugal (1969-2023). The comprehensive predictor dataset includes information regarding climate, land types, altitude, mammal, mosquito, avian and human hosts.

Our findings reveal that the south of Portugal is ecologically more suitable for WNV circulation than the north. Warmer temperatures, lower precipitation, high avian diversity, unique land types and prevalence of specific avian species generally define an adequate ecological background. Building on these insights, we propose a novel framework, based on estimated suitability and historical evidence, that identifies spatial opportunities for future optimized surveillance and control for each relevant host group (humans, equines, birds). In a forward-looking approach, we also projected the direct impact of future climate change on ecological suitability up to the year 2050. We uncover a potential increase in suitability across a wide range of the country, pushing the current north-south boundary of ecological suitability northwards. This significant shift underscores the dynamic nature of vector-borne diseases in the face of climate change.

Our study contributes with a novel perspective on the ecology of WNV in Portugal, providing first of a kind valuable insights for decision-making into the future. A shift towards a One Health active surveillance, guided by the proposed suitability and evidence based framework, and inclusion of genomic surveillance is recommended in the near future. Only this way can we close existing gaps in knowledge, enhance our understanding of the evolving emergence of WNV in the country, and prepare for the first human-associated epidemic in Portugal.

**This work was also presented as a poster.**

# CHARACTERIZATION OF THE LONG-DISTANCE DISPERSAL KERNEL OF WHITE-TAILED DEER AND EVALUATING ITS IMPACT ON CHRONIC WASTING DISEASE SPREAD IN WISCONSIN, US

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Chronic Wasting Disease (CWD) is a fatal untreatable neurodegenerative disease that infects cervids. It is highly contagious and caused by abnormal malfunction and assembly of the normal cellular prion proteins (PrPC) into aggregation-prone prions (PrPSc). The center for disease control reports that the prevalence of CWD in free-ranging deer in the US is still relatively low. However, in several states the infection rates exceed 1 deer in 10. Cervids may uptake CWD prions from direct interaction with infected individuals or from the environment. Infected individuals shed prions into the environment through feces, urine, saliva or carcass. Hence, long-distance dispersal of infected deer poses a danger of spreading CWD to new regions. Predictive measures of CWD transmission are required to inform CWD management and surveillance actions. We propose an Integro-Difference Model (IDE) to capture CWD dynamics and the consequences of long-distance dispersal behavior of White-Tailed Deer (WTD). Currently there are no dispersal kernels available to describe the long-distance dispersal behavior of WTD juveniles. Our aim is to characterize long-distance dispersal of WTD juveniles and assess how it may affect CWD spread. We introduce a long-distance dispersal model, based on a diffusion-settling seed transport by vertebrates, accommodating a variety of hypothetical dispersal behaviors of WTD. Four kernels were obtained by solving 2D diffusion-settling PDE models and approximating using Laplace's method. We parameterized the kernels with GPS collar data collected in Wisconsin, US. Using a Maximum Likelihood Estimation approach, we fitted the model parameters, and assessed model fits using the Bayesian Information Criterion. Sensitivity of results was determined using nonparametric bootstrapping and the impact of long-distance dispersal on CWD spread was quantified as indicated by the IDE model. CWD control measures can be developed based on our work quantifying and predicting CWD transmission taking into account long-distance dispersal events.

# DISCRIMINATING TIME SERIES VIA ENTROPY-BASED INDICES, WITH AN APPLICATION TO CARDIOLOGICAL DATA

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We introduce a method for quantifying mutual dependencies in a pair of intertwined data series. We use ordinal patterns that provide a conceptually simple yet very effective method of time series analysis [2]. In addition, since ordinal patterns can be identified with permutations, we take advantage of their algebraic structure through so called transcripts [1].

We develop a method for entropy-based classification of pairs of data series (the ECPS method for short); specifically, we propose a comprehensive collection of indices based on ordinal patterns and entropy that turned out to be very successful in the evaluation of mutual relations between sets of data. In real applications, many of these indices may be correlated with each other and the variability of some others may not be relevant to the actual differences between the data classes upon consideration. Therefore, in our method, we propose to use machine learning in order to select a small number of the most relevant indices and to construct a simple classifier that provides optimal results.

We apply the ECPS method in cardiology. We develop a model that would distinguish patients that suffer from obstructive sleep apnea from healthy subjects based solely on the measurement of their heart rate (HR) and blood pressure (BP) [3]. HR and BP represent two crucial physiological variables that exhibit a close connection. Examining how they influence each other can yield valuable insights into an individual's cardiovascular well-being. In certain instances, changes in the way HR affects BP, or vice versa, can indicate the presence of a serious medical condition. Let us stress that in our research we consider HR and BP taken during an outpatient exam that is conducted during the day, when the patients are awake and the sleep apnea problem does not occur. In particular, as a result of application of the method to the patients' data we obtain a small number of indices that are capable of extracting the differences between the groups considered.

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# ESTIMATING THE RISK OF ARBOVIRUS SPREADING IN NON-ENDEMIC AREAS: BASQUE COUNTRY AS A CASE STUDY

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Human mobility and the global warming contribute not only the invasion and establishment of mosquitoes and other diseases vector species into new geographical regions, but also the emergence and spreading of infectious diseases transmitted by vectors, such as dengue, Zika, chikungunya, and yellow fever. Even in non-endemic areas, disease outbreaks might occur in regions with imported viremic cases and the presence of disease vector. Currently, this threat represents a serious risk to public health in European countries like Spain, France and Italy where local transmission (not travel related) of dengue has been already confirmed [1].

Here, we present a model-data-driven methodology to assess the risk of outbreaks of arboviruses diseases in non-endemic areas. Our model consists of a refined version of the SIRUV model adapted to the typical epidemiological constraints of non-endemic areas. As a case study, we have used the latest entomological and epidemiological available data for the Basque Country, and have estimated the risk of local outbreaks at both provincial and municipal levels. Our risk estimator will be discussed and compared with different estimators used in Public Health. Finally, the interactive GIS dashboard produced to guide the public health authorities to monitor arboviruses in the Basque Country is shown.

**Acknowledgements** This work is supported by the Basque Government through the *Mathematical Modeling Applied to Health* and *ARBOSKADI* projects; BERC 2022-2025 program, and by the Spanish Ministry of Sciences, Innovation and Universities (MICINN): BCAM Severo Ochoa accreditation CEX2021-001142-S/MICIN/AEI/10.13039/501100011033. Maíra Aguiar acknowledges the financial support by MICINN through the Ramón y Cajal grant RYC2021-031380-I.

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# CHAOS IN A SEASONAL FOOD-CHAIN MODEL WITH MIGRATION AND VARIABLE CARRYING CAPACITY

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The carrying capacity's functional dependence illustrates the reality that any species' activities can enhance or diminish its carrying capacity. Migration is the need of many species to achieve better opportunities for survival. In a tri-trophic system, the middle predator often immigrates to consume its prey and often emigrates to secure themselves from predators. This work deals with formulating and investigating a mathematical model reflecting the aforementioned ecological aspects. We perform a detailed analysis to prove the boundedness of the solutions. Further, we examine the existence and stability of equilibrium points, followed by the bifurcation analysis. We explore various global and local bifurcations like Hopf, saddle-node, transcritical, and homoclinic for the critical parameters  $\beta$  (measuring the impact of prey activities on the carrying capacity) and  $k_1$  (measuring the migration rate of a predator). Higher values of  $\beta$  generate unpredictability, which helps explain the enrichment paradox. The presence of a chaotic attractor and bi-stability of node-node type is demonstrated via numerical simulation. The migratory behavior of middle predators can control chaos in the system. Furthermore, we study the proposed model in the presence of seasonal fluctuations. Persistence of the non-autonomous system, existence, and global stability of periodic solutions are proved. The seasonality in  $\beta$  brings the bi-stability of a chaotic and periodic attractor. Moreover, the bi-stability in the autonomous system shifts to the global stability of an equilibrium in the seasonal model. When birth and death rates are seasonal along with  $\beta$ , the extinction of one or more populations is possible. Our findings reveal that the population's intense constructive and destructive actions can allow the basal prey to thrive while eradicating both predators.

# AN EXTENSIVE NUMERICAL APPROACH TO MODEL THE DYNAMICS OF THE ACUTE INFLAMMATORY RESPONSE

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In this study, an algorithm based on a collocation approach is proposed for studying the dynamic model of the acute inflammatory response. The analytical results for the linear stability of the system around the equilibria are presented [2, 4]. The authors Kumar [7], Reynolds [8], and Day [1] introduced a model which aims to explain the dynamics of the body's acute inflammatory response under infection conditions. We examine the problem, deriving the model and numerical solutions from given initial conditions through a numerical method. The method transforms the problem into matrix equations, and point-by-point solutions are obtained in the given interval using collocation points [5]. Additionally, we describe the stability analysis of the dynamic system around the positive equilibrium. Furthermore, an analysis of errors, numerical solution simulations, and bifurcation analysis results are presented to demonstrate the effectiveness and practicality of the method and the behaviour of the model [3, 6].

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# PARASITE INFECTION AND THE EVOLUTION OF HOST SENESCENCE

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Senescence (an increasing mortality rate with age) is found in many species. Why senescence evolves remains a fundamental question in biology, but its evolution in the context of parasite infection is not fully understood. Energy use within a host results in oxidative stress, which contributes to senescence by damaging macromolecules. We expect that the energy dynamics and levels of oxidative stress within an infected host will differ to those within an uninfected one. When infected, a host must increase its use of energy for immune cell proliferation, whilst the parasite will steal energy to replicate. By explicitly considering these processes, we can allow senescence to emerge from within-host dynamics, rather than imposing an additional mortality rate in an infected host. Additionally, we can allow these processes to feedback into the epidemiological dynamics, which depend on the survival and parasite density of infected hosts.

To better understand these interactions, we developed a multiscale model which accounts for within-host and epidemiological dynamics. We found that the amount of energy available to the host determined the relationship between the parasite's growth rate and the lifespan of the host (the virulence-transmission trade-off). Furthermore, the equilibrium infection prevalence in the host population changed non-monotonically as a function of energy availability. Finally, we found that the evolutionary equilibrium for the parasite's growth rate (and therefore senescence) was determined by the host's energy availability and the parasite dose at the beginning of an infection. By considering the within-host dynamics of energy use and oxidative damage, this work reveals how parasites drive the evolution of senescence in their hosts.

## THE RISE OF THE MINI-MODELS

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Zygotic genome activation (ZGA) in the development of flies, fish, frogs and mammals depends on pioneer-like transcription factors (TFs). These TFs create open chromatin regions, promote histone acetylation on enhancers, and activate transcription. Here, we use mathematical modeling in the form of mechanistic ordinary differential equation (ODE) models to investigate the combinatorial mechanisms of ZGA, which were calibrated by fitting the panel of single, double and triple mutants for zebrafish genome activators Pou5f3, Sox19b and Nanog, multi-omics data. We first derived a transcriptional core model which can accurately describe the dynamics of the pioneer-like TF data measured in the different mutants. In a next step, the predictions obtained by the core model for the protein expression of the different TF's were used to analyze how they regulated the gene expression of 1800 genes in early zygotic development. To achieve this, 19 small ODE models, so-called mini-models, were built representing all possible combinations of TF performing every regulatory role and selected the mini-model which best fitted the available data for each gene. The result of that analysis was then cross-validated with an independent data-set, where open chromatin regions were measured. We found that Pou5f3 and Nanog display both synergistic and antagonistic behavior depending on the targeted gene in contrast to their previously assumed purely synergistic action [1].

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# IMMUNE INTERACTIONS AND HETEROGENEITY IN TRANSMISSION DRIVES THE PATHOGEN-MEDIATED INVASION OF GREY SQUIRRELS IN THE UK

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Over the last 20 years mathematical models have played a key role in highlighting the importance of pathogen-mediated invasion, with the replacement of red squirrels by squirrelpox virus (SQPV) carrying grey squirrels in the UK a well known example. The modelling study of Tompkins et al. (2003) [1] was influential in explaining the rapid replacement of red squirrels in the UK. Based on limited data, the Tompkins et al. (2003) [1] study assumed SQPV led to life-long immunity in grey squirrels (SIR dynamics). New field and experimental data now allow the model framework and parameters used by Tompkins et al. (2003) [1] to be refined and updated, in particular to reflect observed reinfection of grey squirrels. We use mathematical models, combined with the new empirical data, to gain a better understanding of the epidemiological dynamics of SQPV in red and grey squirrels. Our key finding is that a model with either partial or waning immunity and reinfection, where individuals become seropositive on the second exposure to infection, that up to now has been shown in experimental data only, can capture the key aspects of the field study observations. Furthermore by fitting to SQPV epidemic observations in isolated red squirrel populations we can infer that infectivity of red squirrels is significantly (4x) higher than the infectivity of grey squirrels and as a result our model shows that disease-mediated replacement of red squirrels by greys is considerable more rapid than replacement in the absence of SQPV. Our findings recover the key results of the previous model studies, which highlights the value of simple strategic models that are appropriate when there is limited data, but also emphasise the likely complexity of immune interactions in wildlife disease and how models can help infer disease processes from field data.

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# DYNAMICS OF CHRONIC MYELOGENOUS LEUKEMIA WITH LOGISTIC GROWTH AND CELL DIVISION DELAY

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We present a nonlinear delay differential equation model that delves into the dynamics of chronic myelogenous leukemia (CML) cell concentration during the resting phase. In our model, we assume that cells leave the resting phase and enter a proliferation phase of duration  $\tau$  at a rate that is smoothly dependent on the present concentration and is modeled by a logistic function. Our results show that delay  $\tau$  can cause stability changes, and the model undergoes a Hopf bifurcation at certain threshold values of  $\tau$  and exhibits symmetric patterns as the time delay increases. The model is shown to be permanent when a certain condition is met, and numerical simulations are presented to illustrate the rich dynamics of the model. The findings conclude that when the delay exceeds a certain threshold value, the positive equilibrium vanishes, resulting in the decay of cancer cells. We support and validate our numerical results with a graphical representation of the model's dynamics, which facilitates the understanding and interpretation of the findings. Overall, the model proposed in this article provides insight into the dynamics of CML cancer cell concentration in the resting phase and sheds light on the role of time delay in cancer growth or decay.

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# OPTIMAL SCHEDULING FOR RELAY INTERCROPPING

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Intercropping is the simultaneous cultivation of two or more arable crop species in the same field. Compared to the standard practice of monocropping, intercropping can produce more yield with less inputs, benefits that are attributed to reduced competition and facilitation. Indirect effects of competition, such as weed suppression, can also result in net facilitation [4, 8, 9]. In particular, relay-intercropping involves asynchronous sowing and harvesting of companion crops, resulting in temporal separation of development, and tends to outperform both monocropping and synchronous intercropping in terms of yield [8]. The effectiveness of crop rotations and relay-intercropping depends on the timing, and as such linear programs constrained by design rules have been formulated to optimize (inter)crop schedules [3, 6]. We present an alternative approach, based on optimal control and explicit growth dynamics: plant biomasses are the state variables, sowing and harvesting choices are decision variables. Competitive Lotka-Volterra (CLV) equations model interactive growth of crops and weeds [5, 7]; we add size-asymmetric competition for sunlight to the CLV model through exponential functions of the size differences between pairs of plant species. Across the planning horizon, which may represent a single season or multiple years, decisions of sowing or harvesting are made for all crops at equally spaced intervals. Sowing and harvesting are treated as instantaneous events, given their fast timescale relative to crop growth dynamics. We discretize the dynamics with a Runge-Kutta fourth-order (RK4) method, and enforce sowing and harvesting as binary tasks, resulting in a mixed-integer nonlinear program, formulated in CasADi [1] and solved with Bonmin [2]. We plan to estimate model parameters and evaluate solutions with functional-structural plant model (FSPM) simulations [10]. The current framework can be extended with a more elaborate model incorporating e.g. soil nutrient dynamics, and additional decision variables such as planting densities, weed control and fertilizer inputs.

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## BIOLOGICAL CONTROL OF DIAMONDBACK MOTH: A MATHEMATICAL APPROACH

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Cabbage is one of the most important vegetables grown in the world. Pest activities result in the loss of a significant amount of its production. The most important of these is the diamondback moth. Several techniques have been developed to limit the damage caused by this pest, such as parasitoid-based biological control. In this work, we build a nonlinear model using ordinary differential equations by considering the biomass of cabbage in the field, the diamondback moth larvae population, and the larval parasitoid population. The growth of parasitoids on larvae is modeled using the Beddington-DeAngelis type functional response characterized by mutual interference of parasitoid  $\beta$  and pest resistance to predation  $\alpha$ . In the first study, we assume that a quantity of parasitoids is introduced into the farm. We show that the best strategy to achieve permanent establishment and sustainable control is to use parasitoids with a long life cycle. In the second study, we assume that the parasitoids are released continuously in the plantation. We show that solitary parasitoids have a better control effect than gregarious parasitoids because of their  $\beta$  low values. Thus, with parasitoids with low mutual interference, we compute a critical release value which represents the minimum rate of parasitoids to be introduced to obtain and maintain a healthy plantation. In addition, the system presents either a transcritical bifurcation or a backward bifurcation depending on the values of parameter  $\alpha$ . Hence, this study provides both qualitative and quantitative foundations for the implementation of parasitoid-based biological control techniques.

# OPTIMAL CONTROL PROBLEM OF EPIDEMIC MODELS BASED ON DEEP REINFORCEMENT LEARNING

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We investigate an optimal control problem of various epidemic models with uncertainty using stochastic differential equations, random differential equations, and agent-based models. We discuss deep reinforcement learning (RL), which combines RL with deep neural networks, as one method to solve the optimal control problem. The deep Q-network algorithm is introduced to approximate an action-value function and consequently obtain the optimal policy. Numerical simulations show that in order to effectively prevent the spread of infectious diseases, it is essential to vaccinate at the highest rate for the first few days and then gradually reduce the rate.



# ON THE STOCHASTIC ENGINE OF CONTAGIOUS DISEASES IN EXPONENTIALLY GROWING POPULATIONS

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The purpose of this paper is to analyze the mechanism for the interplay of deterministic and stochastic models for contagious diseases. Deterministic models for contagious diseases are prone to predict global stability. Small natural birth and death rates in comparison to disease parameters like the contact rate and the removal rate ensures that the globally stable endemic equilibrium corresponds to a tiny average proportion of infected individuals. Asymptotic equilibrium levels corresponding to low numbers of individuals invalidate the deterministic results.

Diffusion effects force probability mass functions of the stochastic model to possess similar stability properties as the deterministic model. Particular simulations of the stochastic model predict, however, oscillatory patterns. Small and isolated populations show longer periods, more violent oscillations, and larger probabilities of extinction.

We prove that evolution maximizes the infectiousness of the disease as measured by the ability to increase the proportion of infected individuals. This holds provided the stochastic oscillations are moderate enough to keep the proportion of susceptible individuals near a deterministic equilibrium.

We close our paper with a discussion of the herd-immunity concept and stress its close relation to vaccination-programs. Further information of the contents of this talk can be found in Lindström [1, 2].

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# FROM A CO-INFECTION SIS MODEL TO THE REPLICATOR EQUATION

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Understanding the interplay of different traits in a co-infection system with multiple strains has many applications in ecology and epidemiology. Because of high dimensionality and complex feedback between traits manifested in infection and co-infection, the study of such systems remains a challenge. In the case where strains are similar (quasi-neutrality assumption), we can model trait variation as perturbations in parameters, which simplifies analysis.

Here, we consider and study such a quasi-neutral model of susceptible – infected – susceptible (SIS) dynamics among  $N$  strains with two levels of infection. For  $N$  strains, the resulting systems consists of a system of  $N^2 + N + 1$  non linear EDO.

Using the theory of singular perturbations [1, 3], we will show how the hypothesis of quasi-neutrality allows to describe the dynamics through the replicator equation, a system of only  $N - 1$  EDO.

Next, we apply this methodology to a SIS model incorporating spatial diffusion [2] and we show how the reduced systems we obtain depends on the speed of the diffusion.

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# MODELLING OPTIMAL THERAPY SWITCHING STRATEGIES TO MITIGATE DRUG RESISTANCE DEVELOPMENT

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Drug resistance is the capacity of a pathogen to become less susceptible to a drug over time due to mutations. A common intervention that physicians use to mitigate resistance is to switch the drug being used. Understanding the time scales of drug resistance development is important to determine how often the therapy has to be changed. We present a model for the efficacy of two simultaneous therapies as a bounded Markov process, in which we incorporate stochastic resetting to represent therapy switching. This process fluctuates until it reaches an absorbing boundary, which indicates the failure of the therapy. The distribution of times for the Markov process to reach the absorbing state is obtained using analytical expressions and Gillespie simulations. We study how varying the rate of therapy switching impacts the mean time to absorption in different parameter regions. Finally, we study the case where the number of therapies is limited. We find a finite reset rate that maximizes the mean absorption time. Our results suggest the existence of optimal therapy switching strategies.

# PEST DETECTION FROM A BIOLOGY-INFORMED INVERSE PROBLEM AND PHEROMONE SENSORS

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One third of the annual world's crop production is directly or indirectly damaged by insects. Early detection of invasive insect pests is key for optimal treatment before infestation. Existing detection devices are based on pheromone traps: attracting pheromones are released to lure insects into the traps, with the number of captures indicating the population levels. Promising new sensors are on development to directly detect pheromones produced by the pests themselves and dispersed in the environment. Inferring the pheromone emission would allow locating the pest's habitat, before infestation. This early detection enables to perform pesticide-free elimination treatments, in a precision agriculture framework. In order to identify the sources of pheromone emission from signals produced by sensors spatially positioned in the landscape, the inference of the pheromone emission (inverse problem) is performed. Classical inference is conducted by combining the data and the so-called direct model [1]. In the present case, this entails combining the data from the pheromone sensors and the pheromone concentration dispersion that is a 2D reaction-diffusion-convection model [2]. In the proposed method, the inference involves not only the coupling of the pheromone dispersion model with the pheromone sensors data but also incorporates *a priori* biological knowledge on pest behaviour (favourite habitat, insect clustering for reproduction, population dynamic behaviour...). This information is introduced to constrain the inverse problem towards biologically relevant solutions. Different biology-informed constraints are tested, and the accuracy of the solutions of the inverse problems is assessed on simulated noisy data.

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# A MATHEMATICAL FRAMEWORK FOR MEASURING AND TUNING TEMPO IN DEVELOPMENTAL GENE REGULATORY NETWORKS

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Development is dynamic, with the timings and sequences of gene expression vital for proper growth. Many of the genetic programs that have evolved to coordinate these sequences are common amongst species; however the timescale of these programs varies greatly between species [1]. Differences in developmental tempo has been observed in both somitogenesis [2] and motor neuron differentiation [3]. In particular, these two studies showed that differences in regulatory sequences do not explain tempo differences between species.

How do different species harness the same genetic programs but execute them at different speeds? Or in other words, what kinds of genetic programs are able to maintain their biological function while keeping the flexibility to change tempo? And ultimately, what mechanisms exist which can tune tempo during development? Since developmental programs are so dynamic and complex, my approach to these fundamental questions is through using the framework of dynamical systems. By recognising these developmental processes as dynamical systems, we are able to investigate the cause and effects of tempo holistically. However, to be able to use this powerful field in mathematics, we need to translate the idea of 'biological function' into mathematical language. In my work, I develop a mathematical framework based on dynamical system theory which can: (a) be used to quantitatively measure the similarity in function between systems (both model systems and through experimental data), and (b) can predict mechanisms which can be used to tune tempo in a case study oscillating system.

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# POPULATION-DYNAMICAL MODEL TO OPTIMISE AGRICULTURAL LANDSCAPE MANAGEMENT FOR NATURAL PEST CONTROL

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Pest-regulating insects often require habitats other than crop fields to persist and be effective. These habitats can e.g. provide hibernation sites, alternative prey, or floral resources. Landscape based population-dynamical modelling can give more insight in the relative importance of these different habitats for the performance of pest-regulating insects.

In this study, we modelled the dynamics of predatory hoverflies (Diptera: Syrphidae) and their aphid prey in a collection of habitats. These hoverflies are dependent on different habitats for different reasons. Whilst their larvae feed on aphids, adult hoverflies require floral resources. Both types of resources are often spatially segregated in agricultural landscapes. In addition, these resources are often only temporarily available in one habitat, so that multiple habitats are required to cover the annual cycle of a hoverfly population. In our model, hoverflies can move between different habitats and select where to feed and where to produce off-spring based on optimal foraging considerations. The model represents habitats common in arable landscapes and is parameterised based on field observations of temporal and habitat-related availability of resources. This model is unique as it combines predator-prey interactions, developmental delays, detailed seasonal forcing and habitat structure.

Our model indicated that optimal hoverfly performance and aphid suppression require a minimum of three different habitats offering resources at different times of the year. A woody habitat with shrubs and trees provides aphids very early in the season, whereas an early crop and a late crop cover the period in between. Model analyses show that different arable crops enhance each others pest control when their aphid populations peak at different times of the year. In addition, these habitats need to provide floral resources simultaneously with the aphids, e.g. in a flowering sub-habitat such as (wild) flower margins.

Visual abstract is shown in [Figure 1](#).



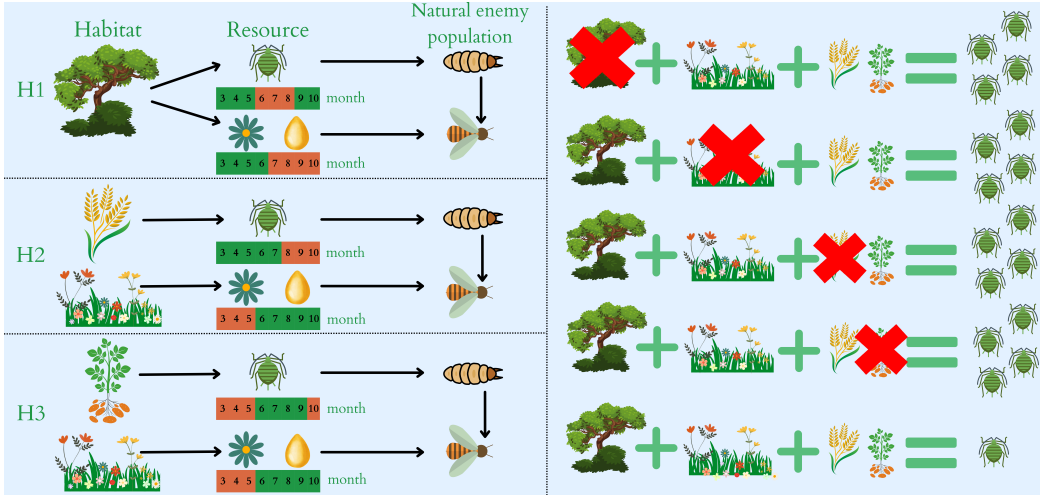


Figure 1: Visual abstract.

# UNREVEALING SPATIAL PATTERNS: PHYSICS INFORMED NEURAL NETWORKS FOR SOLVING THE INVERSE PROBLEM IN TURING SYSTEMS

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The diffusion-driven Turing instability caused by interacting activator and inhibitor morphogens is a potential mechanism for spatial pattern formation in numerous biological systems. However, engineering these patterns experimentally and demonstrating that they are produced by this mechanism is challenging. To address this, we aim to solve the inverse problem in artificial and experimental Turing patterns by recovering the model parameters from the pattern. This task is challenging since high levels of noise corrupt the patterns and slight changes in initial conditions can lead to different versions of the same underlying pattern [2]. Using both least squares and physics-informed neural networks, we demonstrate that the inverse problem can be solved to varying degrees. The least squares method, although simple, is extremely fast and requires only minimal data, which allowed us to explore different aspects of this problem in detail. Nevertheless, as expected, it is highly sensitive to noise. In order to achieve high-noise tolerance, we develop a neural network based on Physics-Informed Neural Networks [3] and using Radial Basis Function kernels as function approximators. We refer to this network as RBF-PINNs. In contrast to Least Squares, RBF-PINNs offer a much greater robustness to noise, reaching biological levels, but at a much higher computational cost. After showing this incremented robustness to noise and a fairer comparison with other traditional PINNs, we demonstrate the applicability of this latter method to several pattern formation models and most crucially to experimental data from chemical patterns [1]. This latter application presents further difficulties, such as missing information regarding the scale and shift of the true pattern, and also more biologically relevant bacterial models. Our results demonstrate the potential of machine learning to guide the design of synthetic biological patterns and other experimental patterns, and deepen our understanding of morphological patterns in biological systems.

**Acknowledgements** We thank Roozbeh H. Pazuki for invaluable support and technical comments, Martina Oliver Huidobro for stimulating discussions and Milos Dolnik for explanations of his experiments.

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# TIME-SCALE SEPARATION AND CENTER MANIFOLD ANALYSIS IN A VECTOR-HOST MODEL

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In vector-borne diseases, due to the considerably different life spans of host and vector, the dynamics of the human host often evolve on a much slower time-scale than the dynamics of the vector transmitting the disease. When this occurs, a time-scale separation argument can be used to reduce the dimension of the system. In this talk, we will use a time-scale separation argument to reduce the dimension of an SISUV model, where an SIS model for the human hosts is coupled with a UV model for the uninfected and infected vectors. This simple model has the advantage of being analytically treatable. Results can be tested numerically and a comparison with the stochastic version given. Using central manifold analysis, we will also show another method for reducing the dimension of the system, which can be generalized to more complicated models where time-scales are more entangled, like the SIRUV or more realistic multi-strain vector-host models [1–3].

**This work was also presented as a poster.**

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# STABILITY FOR A DISCRETE-TIME NONLINEAR DISPERSAL MODEL

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We consider a nonlinear coupled discrete-time model of population dynamics, generalising the model of [1]. This model describes the movement of populations between  $n \in \mathbb{Z}_+$  regions, where each sub-population is modelled by a bounded Kolmogorov map and coupling terms are defined by nonlinear functions taking values in  $(0, 1)$ . These dispersal terms describe the proportion of individuals moving from one patch to another. We will state sufficient conditions for the stability/instability of the extinction equilibrium, for the existence of a positive fixed point, and for ensuring uniform persistence. We also give a sufficient condition for the existence and uniqueness of a locally stable positive fixed point when  $n = 2$ .

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# DYNAMICAL ANALYSIS AND OPTIMAL CONTROL OF HIV MODEL WITH IMMUNE IMPAIRMENT

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Understanding the immunological response with treatment for the Human immunodeficiency syndrome (HIV) is still a desire. The objective of this study is to propose a mathematical model that captures the dynamics of the disease progression by considering the major factors that include functional response, antiretroviral therapy (ART), and immune response delay. Compare to the existing literature [1–4], the HIV model (see Figure 1) includes the immune impairment where, the immune system fails against infection, which eventually leads to extinction of T-cells cause susceptible to various infection. The basic reproduction  $\mathcal{R}_0$  is estimated to govern the disease progression. Further, stability analysis for different situations such as disease-free, immune-free and infection equilibria by Routh-Hurwitz criterion considering with and without delay are performed. The model parameters that play significant role in disease dynamics is identified through bifurcation analysis approach. In addition, this study considers therapy as a control and the corresponding optimal control strategy is proposed through employing Hamilton-Lagrange approach [5, 6]. Furthermore, we perform numerical simulations to validate the theoretical results [7].

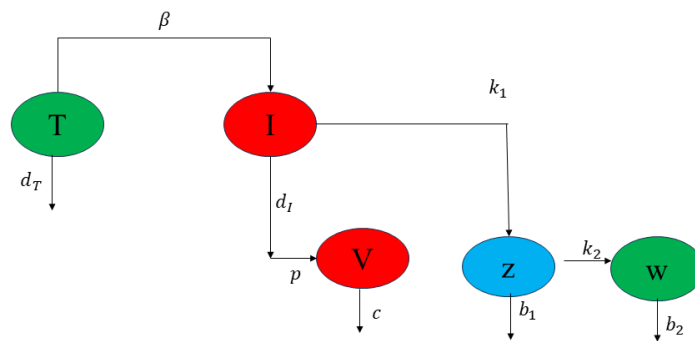


Figure 1: The schematic diagram on HIV immune impairment model

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# THE DYNAMIC OF THE COVID-19 IN THE BASQUE COUNTRY: A MATHEMATICAL MODEL CONSIDERING LOSING AND BOOSTING IMMUNITY, VACCINATION AND CONTROL MEASURES

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Covid-19 is an infectious disease and has spread over more than 200 countries since its outbreak in December 2019 and it has posed the greatest threat to global public health. With different efficacies, COVID-19 vaccines are highly effective in preventing severe forms of the disease after full immunization, and have significantly contributed to reducing hospitalizations and deaths worldwide [1]. Nevertheless, findings of natural waning immunity occurring after vaccination [2] and the emergence of new variants that may escape the existing vaccine immunity, leading to reinfection, require a continuous vaccination rollout with booster doses, to maintain high immunity in the population. Our Goal is to study the dynamic of the covid-19 disease over the first two years taking into account the Public Health and Social Measures (PHSM), as well as the virus-specific immunity acquired after infection, its spontaneous decline over time, and their impact on the severity and the emergence of new waves. To do so, we propose a structured mathematical model called SIR/DS, Susceptible-Infected-Recovered-Death. The recovery class in the model is structured based on specific immunity levels taking into account the opposing effects of immunity decline near the site of infection, as well as immunity boosting after reinfection or vaccination. We validate the model with real data of the Basque Country from March 2020 to March 2022. The analysis of the model uses the generation matrix method to obtain the basic reproduction numbers and the global stability of the COVID-19 distribution model. A detailed sensitivity analysis to identify the key parameters influencing the transmission dynamics of COVID-19 pandemic.

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# UMAP DIMENSIONALITY REDUCTION TO ANALYSE B ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS DATA

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The study we present on Acute Lymphoblastic Leukemia (ALL) is motivated by the fact that this disease accounts for 30% of cancers in pediatric patients. In these patients, around 15–20% of treatments are unsuccessful. Consequently, studies related to relapses are interesting to analyze [3]. Currently, the diagnosis and follow-up of these patients are carried out through data obtained by flow cytometry [1, 5], manually analyzing over twenty cellular biomarkers in samples containing a million cells.

Mathematical tools allow us to analyze and study large datasets using machine learning techniques [4], which applied to flow cytometry can offer a more precise and efficient approach to the diagnosis, follow-up and treatment of the disease [2]. In order to illustrate this, we have collected flow cytometry data from several time points of more than fifty patients and developed a pipeline with UMAP dimensionality reduction technique to enable a simplified representation of the bone marrow samples. In this way, monitoring of these patients is facilitated, allowing us to distinguish between groups of patients with different clinical outcomes.

**Acknowledgements** This work has been partially supported by the Fundación Española para la Ciencia y la Tecnología (FECYT project PR214), the Asociación Pablo Ugarte (APU, Spain), Junta de Andalucía (Spain) group FQM-201, Ministry of Science and Technology, Spain (grant number PID2019-110895RB-I00, funded by MCIN/AEI/ 10.13039/501100011033).

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# HOST MANIPULATION BY PARASITES TO FACILITATE TRANSMISSION

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It may be a surprise to learn that a parasite can evolve to possess some control over a host. However, examples in nature show that to increase their chance of successful transmission, parasites can manipulate their host into changing their behaviour or appearance. These manipulation strategies tend to evolve in parasites that are trophically transmitted. An infected intermediate prey host will have increased vulnerability to predation, allowing the parasite to infect its definitive target host - the predator - more easily.

Mathematical models are used in many disciplines as an essential tool to study disease spread. Here we develop a compartment model based on the framework by Fenton and Rands [1] to investigate when a parasite will most likely evolve these strategies. Manipulation is beneficial for the parasite since it facilitates movement through a stage of the life cycle to the final host. However, increasing the likelihood of predation by manipulation is a costly approach for the parasite which we incorporate in a trade-off with spore production. These spores are vital for transmission since they are released into the environment to be consumed by susceptible prey causing infection or they may be left to decay.

Our results show that fluctuating dynamics are an outcome of this system and that the evolution of manipulation strategies is simultaneously governed by both the size of the susceptible prey population and the perceived threat of predation determined by the size of the entire predator population.

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# MODELLING AN INFECTIOUS DISEASE TRANSMITTED VIA CANNIBALISM - WHITE SPOT SYNDROME VIRUS OUTBREAK IN KURUMA SHRIMP

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White spot syndrome virus (WSSV) triggers white spot disease which causes quite high mortality in farmed shrimp. To control WSSV, understanding WSSV epidemic character is required. To this end, the epidemiological data of WSSV in the setting of aquaculture is required especially for measuring transmissibility including basic reproduction number ( $\mathcal{R}_0$ ). However, the detailed epidemiological data is difficult to obtain due to the rapid and high mortality. In this study we proposed a framework for estimation of transmissibility of WSSV from the combination of i) the epidemiological data in the early phase of outbreak, ii) the infection experiment of WSSV and iii) the feeding experiment of dead shrimp eaten by healthy shrimp using a mathematical model describing WSSV transmission by cannibalism of dead and infected shrimp. We measured the transmissibility of WSSV by  $\mathcal{R}_0$  using the epidemiological data of WSSV outbreak in aquaculture ponds observed in the island in Japan. Our model with the estimate of  $\mathcal{R}_0$  suggests the transmissibility of WSSV in the setting of aquaculture is quite high and the urgent intervention is required when a WSSV infection is confirmed in an aquaculture pond. Also, all shrimps will get infection regardless of the value of  $\mathcal{R}_0$  if the infected and dead shrimps are not removed and  $\mathcal{R}_0$  is larger than one. Thorough cleaning of aquaculture pond is required to control WSSV.

# IMPACT OF FEAR AND GROUP DEFENSE ON THE DYNAMICS OF A PREDATOR-PREY SYSTEM

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To reduce the chance of predation, many species adopt group defense mechanisms. While it is commonly believed that such defense mechanisms lead to positive feedback on prey density, a closer observation reveals that they can indeed influence the growth rates of species. This is because individuals invest more time and effort in defense rather than reproductive activities. In this study, we delve into a predator-prey system where predator-induced fear influences the birth rate of prey, and the prey species exhibit a group defense mechanism. We adopt a non-monotonic functional response to govern the predator-prey interaction, which effectively captures the group defense mechanism. We present a detailed mathematical analysis, encompassing the determination of feasible equilibria and their stability conditions. Through the analytical approach, we demonstrate the occurrence of Hopf and Bogdanov-Takens (BT) bifurcations. We observe two distinct types of bistabilities in the system: one between interior and predator-free equilibrium points, and another between limit cycle and predator-free equilibrium point. Our findings reveal that the parameters associated with group defense and predator-induced fear play significant roles in the survival and extinction of populations.

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# COLONIZATION DYNAMICS OF THE INVASIVE VECTOR AEDES ALBOPICTUS IN SPAIN: THERMAL BIOLOGY AND HUMAN MOBILITY

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Tiger mosquito, *Aedes albopictus*, is an invasive vector of diseases such as Dengue and Chikungunya. The first records in Spain date back to 2004 in Sant Cugat del Vallés [1]. Since then it has invaded the Spanish Mediterranean coast and is moving inland. Studies have shown that these mosquitoes can travel in vehicles [2], allowing them to cover long distances. In this work, we explore the colonization process of *Aedes albopictus* in the last decade with data from the citizen science observatory, Mosquito Alert [3].

We focused on two factors: human movement and habitat suitability. To assess habitat suitability, we computed the Basic reproduction number [4],  $\mathcal{R}_M$ , from a mosquito mechanistic model with three compartments: egg,  $E$ , larva,  $L$  and adult,  $A$ . The mosquito basic reproduction number is given by

$$R_M = \sqrt[3]{f(T) \frac{a(T)}{\delta_A(T)} p_{EL}(T, R, H) p_{LA}(T)}, \quad (1)$$

where  $f$  is the fecundity rate,  $a$  the biting rate,  $\delta_A$  the adult mortality rate and  $p_{XY}$  is the probability from stage  $X$  to stage  $Y$ . Each parameter related to the mosquito life cycle is given as a function of temperature ( $T$ ), rainfall ( $R$ ) and human density ( $H$ ). Therefore, Eq. (1) provides the thermal limit for *Ae. albopictus*, Fig. 1. We combine the mosquito basic reproduction number with human mobility and distance to the invaded regions in a metapopulation model [5] to understand the effect of different dispersal modes in the colonization process. Our findings shed light on the colonization dynamics of *Aedes albopictus* and provide insights into the interplay between human movement, habitat suitability, and distance to the invaded regions. This research has practical implications for the management and control of invasive species, providing valuable information that can inform strategies aimed at mitigating the impact of these disease vectors on human health and the environment.

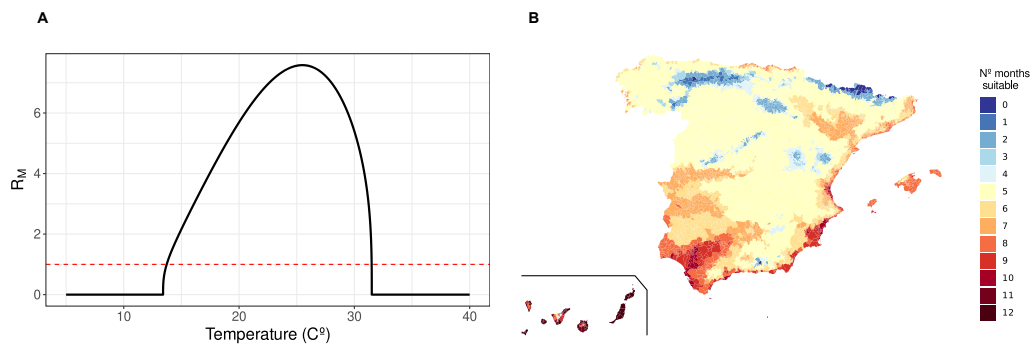


Figure 1: A the mosquito basic reproduction number as a function of temperature. B number of months that  $R_M > 0$  for 2020 in Spain.

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# IDENTIFICATION OF THE PARAMETERS IN A MODIFIED SIRD EPIDEMIC MODEL USING ENSEMBLE NEURAL NETWORKS

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In this talk, we present a parameter identification methodology of the SIRD model, an extension of the classical SIR model, which considers the deceased as a separate category. In addition, our model includes one parameter which is the ratio between the real total number of infected and the number of infected that were documented in the official statistics.

Due to many factors, like governmental decisions, several variants circulating, opening and closing of schools, the typical assumption that the parameters of the model stay constant for long periods of time is not realistic. Thus, our objective is to create a method which works for short periods of time. In this scope, we approach the estimation relying on the previous 7 days of data and then use the identified parameters to make predictions.

To perform the estimation of the parameters, we propose the average of an ensemble of neural networks. Each neural network is constructed based on a database built by solving the SIRD for 7 days, with random parameters. In this way, the networks learn the parameters from the solution of the SIRD model.

Lastly, we validate our approach of parameter identification using real data of Covid19, from March 2020 until December 2021, for Romania, Hungary, The Czech Republic and Poland. Therefore, we manage to obtain estimates of the parameters from real data, for the above period and then we endorse our results by making short-term predictions for different periods of time, from 10 up to 45 days, for the number of deaths. The main goal was to apply this approach on the analysis of COVID-19 evolution in Romania, but this was also exemplified in other countries with similar results. The results are backed by a theorem which guarantees that we can recover the parameters of the model from the reported data. We believe this methodology can be used as a general tool for dealing with short term predictions of infectious diseases or in other compartmental models. The above ideas and the complete methodology are detailed in an exhaustive manner in [1, 2].

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# PANDEMIC PREPAREDNESS, SUPPRESSION AND MITIGATION: HOW DOES INDIVIDUAL BEHAVIOUR PERTURB OPTIMAL SOCIAL DISTANCING?

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After the failures in the COVID-19 response, future pandemic preparedness will require to identify general control principles relying on the two main pillars emerged during the pandemic: the tension between suppression and mitigation and the centrality of social distancing as the critical control measure.

We aim at comparing “abstract” optimal interventions where planners rely on steady population’s adherence to the proposed measures (“behaviour-free” case) with the alternative case where adherence is also affected by individuals’ behaviour (“behavioural” case).

We use open-loop optimal control of a worst-case transmission model for COVID-19 [2] to identify best social distancing policies balancing the direct epidemiological costs of the epidemic with its societal costs, depending on the three key policy factors, namely the (i) prioritization of direct costs (PDC), (ii) adherence to interventions, (iii) timeliness of interventions. In the behaviour-free case we assume a steadily constant adherence, while in the behavioural case adherence is fully endogenous depending on individuals’ risk perceptions of both direct and indirect costs [1, 3, 4].

In the behaviour free case, combinations of decreasing values of PDC, adherence and timeliness force the optimal policy to switch from suppression to “effective” mitigation and eventually to palliative mitigation. Inadequate adherence and timeliness inevitably leave mitigation as the only accessible option even when PDC is high. The behavioural case yields a wealth of results, ranging from the case where policy-resistant behaviour worsens both adherence and timeliness thereby forcing palliative mitigation to be the only policy option even when planners’ PDC is high, up to the case where behaviour can enhance mitigation in the presence of a planner’s low prioritization to direct costs.

Although the complexity of pandemic events is hardly captured by simple models, optimal control analyses with behavioral dimensions offer important insight for future preparedness.

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# INTEGRO-DIFFERENTIAL SIR MODEL WITH LAGRANGIAN APPROACH

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Classical epidemic models are generally described by compartmental models that do not include spatial heterogeneity. Based on the literature review on spatial heterogeneous models, there are mainly two ways to include spatial dependence designated by Eulerian and Lagrangian approaches, or as Distributed-Infectives (DI) and Distributed-Contacts (DC), respectively. In the Eulerian approach, we follow the movement of individuals, assuming that the contacts are local whereas, in the Lagrangian approach, we follow the individuals' contacts and not their movement, maintaining the population constant throughout space.

We will focus on the Lagrangian approach. We consider an integro-differential SIR model with vital dynamics. We determine the basic reproduction number,  $R_0$  based on Diekmann's next-generation operator [1], and we study the stability of the disease-free equilibrium depending on  $R_0$  [1, 2]. Finally, we will show numerical results for the endemic equilibrium.

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# ORDINARY DIFFERENTIAL EQUATION MODELING FOR CONTACT INHIBITION AND THE PROLIFERATION OF MELANOMA *IN SITU*

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This work introduces an ordinary differential equation parameter estimation modeling for contact inhibition and the proliferation of melanoma *in situ*. This phenomenon was previously reported by Morais *et al.* (2017) in the context of *in vitro* experiments where a coculture of cells was designed to mimic the development of melanoma with metastatic potential (human melanoma cell line SK-MEL-147) surrounded by cells from the basal layer of human skin (spontaneously immortalized human cell line HaCaT) [3].

The modeling approach proposed by Morais *et al.* (2017) to study melanoma contact inhibition and the proliferation is based on a spatial discrete stochastic model inspired by statistical physics and molecular chemistry. The study also reported growth curve fits for the cell line populations, but without considering the influence of the cell line populations on each other. Therefore, here we propose to fill this gap by applying the model from mathematical oncology presented by Gatenby & Vincent (2003) [1]. In a more convenient way for our parameter estimation study for contact inhibition, his model reads:

$$\begin{cases} \frac{dN_1}{dt} = r_1 N_1 - b_1 N_1^2 - a_{12} N_1 N_2, \\ \frac{dN_2}{dt} = r_2 N_2 - b_2 N_2^2 - a_{21} N_2 N_1, \end{cases}$$

being  $b_1 \doteq r_1/k_1$ ,  $b_2 \doteq r_2/k_2$ , and  $a_{12} \doteq \alpha_{12}r_1/k_1$ ,  $a_{21} \doteq \alpha_{21}r_2/k_2$ , where  $r_1$  and  $r_2$  are the growth rates of normal (HaCaT) and cancer (SK-MEL-147) cells,  $k_1$  and  $k_2$  are the carrying capacities for each of these cell line populations, and  $\alpha_{12}$  and  $\alpha_{21}$  are the respective competition coefficients affecting normal ( $N_1$ ) and cancer ( $N_2$ ) cells. These competition coefficients also include the effects of mutual contact inhibition between the cells of the lineages. Accordingly, the novelty here is to consider these competition interactions in the data fitting of the growth curves for SK-MEL-147 and HaCaT. For this, we consider the same experimental data reported by Morais *et al.* (2017) [3], and we perform a parameter estimation of the ordinary differential equation model presented above (Gatenby & Vincent, 2003 [1]).

The experimental data include measurements of cell density of each lineage at exact 24-hour intervals, on days 0, 1, 2, 3, 4, 5, 6, 7, and in triplicates in wells (I, II, III). For each well, on each day, ten images were taken at randomly selected positions in the field of

view. The number of cells of each line was registered for each image of the coculture. In order to properly deal with variations, the mean of the ten values found in each image was considered as one point of the time series data used in the fitting.

For parameter estimation we use the nonlinear mixed effects (NLME) framework [2], which allows to model fixed and random effects on parameters. The error matrix  $\Sigma$  was chosen as a diagonal matrix with diagonal entries  $[s_1 N_1(t)]^2$  and  $[s_2 N_2(t)]^2$ . The covariance matrix for the parameters  $\Omega$  was also chosen to be diagonal. Its entries are also estimated, as well as  $s_1$  and  $s_2$ . Since we are interested in estimating  $a_{12}$  and  $a_{21}$ , we set  $r_1 = 6.680 \cdot 10^{-1}/\text{day}$ ,  $r_2 = 8.568 \cdot 10^{-1}/\text{day}$ ,  $b_1 = 3.268 \cdot 10^{-4}/\text{cells/day}$  and  $b_2 = 5.558 \cdot 10^{-3}/\text{cells/day}$ . Fittings and numerical and biological parameter values with respective errors are shown in Figure 1. Even considering the standard errors, we found  $a_{21} < a_{12}$ , which agrees with previous results of a lesser inhibition contact effect on cancer cells (SK-MEL-147) over the growth dynamics [3]. Moreover, we also found that the values of both  $r_1$  and  $r_2$  are greater than those found by us in (omitted) fittings for single cultures of HaCaT and SK-MEL-147. More details on that will be given at the conference.

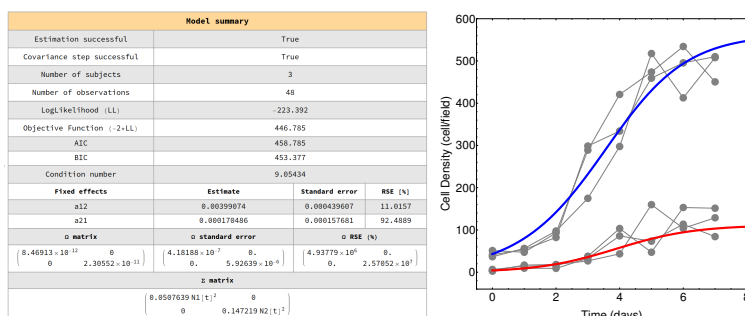


Figure 1: (a) Numerical and biological parameter values and standard errors estimated by NLME [2] and (b) Curve fitting for coculture of normal (blue) and cancer (red) cells considering all three time series data.

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# LOCAL AND GLOBAL DYNAMICS OF A PREDATOR-PREY MODEL WITH MATURATION DELAY IN GENERALIST PREDATOR

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The primary goal of this study is to explore how delayed maturity in generalist predators qualitatively affects the dynamics of a predator-prey system. To illustrate, we consider a predator-prey model with generalist predators and Holling type II functional response to characterize the generalist predator's grazing behavior to their primary prey. The basic model is

$$\frac{dx}{dt} = x(1-x) - \frac{\beta xy}{1+\alpha x}, \quad (1a)$$

$$\frac{dy}{dt} = y\rho(1-y) + \frac{\gamma e^{-\delta j\tau} x(t-\tau)y(t-\tau)}{1+\alpha x(t-\tau)}. \quad (1b)$$

We find various parameter regimes for the non-delayed system where we find either no coexistence, single coexistence, or multiple coexistence of prey and their generalist predators. Rich dynamics, induced by various local and global bifurcations, are displayed for the non-delayed system. The inclusion of a maturation delay in the model system causes the system's qualitative properties to alter, such as shifting bifurcation thresholds and a reduction in the region of multi-coexistence in a parametric domain. Our analysis demonstrates that the delayed maturation of generalist predators does not act as a destabilizing factor; instead, it promotes stable coexistence. Inclusion of maturation delay results in shift of various bifurcation thresholds and there is a reduction in the region where the system has multiple positive equilibrium points. The delayed system has potential of exhibiting both absolute stability and conditional stability of positive equilibrium points.

Proof of global stability for unique locally stable coexistence equilibrium points with the help of a suitable Lyapunov function is an interesting research problem for predator-prey type models. The proof of global stability becomes challenging for the models which admit more than one coexistence equilibrium point. We prove the global stability of the coexistence equilibrium point for system (1). With the help of the Lyapunov function and Bendixson-Dulac criteria under two different parametric restrictions  $\alpha \leq 1$  and  $\alpha > 1$  respectively, we establish global stability of unique coexistence equilibrium point of the non-delayed version of the model. Further, we use a Lyapunov functional and apply LaSalle's invariance principle to prove the global stability of the coexistence equilibrium point of the delayed model, with maturation delay.



# ON THE ROLE OF THE OBJECTIVE FUNCTIONAL ON OPTIMAL CONTROL OUTCOMES FOR A SIR-TYPE MODEL WITH VACCINATION

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The choice of the objective functional in optimization problems coming from biomedical and epidemiological applications plays a key role in optimal control outcomes. In this study, we investigate the role of the objective functional on the structure of the optimal control solution for an epidemic model for sexually transmitted infections that includes a core group with higher sexual activity levels than the rest of the population. An optimal control problem is formulated to find a targeted vaccination program able to control the spread of the infection with minimum vaccine deployment. Both  $L_1$ – and  $L_2$ –objectives are considered as an attempt to explore the trade-offs between control dynamics and the functional form characterizing optimality. The results show that the optimal vaccination policies for both the  $L_1$ – and the  $L_2$ –formulation share one important qualitative property, that is, immunization of the core group should be prioritized by policymakers to achieve a fast reduction of the epidemic. However, quantitative aspects of this result can be significantly affected depending on the choice of the control weights between formulations. Overall, the results suggest that with appropriate weight constants, the optimal control outcomes are reasonably robust with respect to the  $L_1$ – or  $L_2$ –formulation. This is particularly true when the monetary cost of the control policy is substantially lower than the cost associated with the disease burden. Under these conditions, even if the  $L_1$ –formulation is more realistic from a modeling perspective, the  $L_2$ –formulation can be used as an approximation and yield qualitatively comparable outcomes [1].

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# IMPROVING MATHEMATICAL MODELS OF CANCER THROUGH GAME-THEORETIC MODELLING: A STUDY IN NON-SMALL CELL LUNG CANCER

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We examined a data set of 590 Non-Small Cell Lung Cancer patients treated with either chemotherapy or immunotherapy using a game-theoretic model that includes both the evolution of therapy resistance and a cost of resistance. We tested whether the game-theoretic model provides a better fit than classical mathematical models of population growth (exponential, logistic, classic Bertalanffy, general Bertalanffy, Gompertz, general Gompertz). To our knowledge, this is the first time a large clinical patient cohort (as opposed to only in-vitro data) has been used to apply a game-theoretic cancer model. The game-theoretic model provided a better fit to the tumor dynamics of the 590 Non-Small Cell Lung Cancer patients than any of the non-evolutionary population growth models. This was not simply due to having more parameters in the game-theoretic model. The game-theoretic model was seemingly able to fit more accurately patients whose tumor burden exhibit a U-shaped trajectory over time. We explained how this game-theoretic model provides predictions of future tumor growth based on just a few initial measurements. Using the estimates for treatment-specific parameters, we then explored alternative treatment protocols and their expected impact on tumor growth and patient outcome. As such, the model could possibly be used to suggest patient-specific optimal treatment regimens with the goal of minimizing final tumor burden. Therapeutic protocols based on game-theoretic modeling could potentially improve patient outcome in the future. In particular, our model invites evolutionary therapies that anticipate and steer the evolution of therapy resistance.

# SEIR MODEL IN CONTACT NETWORK OF URBAN POPULATION

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The aim of our work is to study the dynamics of a new virus in a population of a big city where virus transmission is modeled in a complex network. Basing on the data concerning population composition [2, 3], numbers of educational and working places [6], and on the studies on the contact patterns [1, 5] we constructed complex network for Moscow population. The vertices of the network can be attributed to one of the  $m$  classes depending on their degree. Following the approach suggested by Moreno et al. in [4], we developed SEIR model in the constructed network. Thus, each of the traditional compartments such as susceptible  $S$ , exposed  $E$ , infected  $I$ , and recovered  $R$ , can be subdivided into  $m$  compartments according to the individuals' degrees as follows

$$\begin{aligned}\frac{dS_k}{dt} &= -\beta k S_k \Theta, \\ \frac{dE_k}{dt} &= \beta k S_k \Theta - \sigma E_k, \\ \frac{dI_{uk}}{dt} &= \sigma E_k - (\delta + \gamma_u + \mu_u) I_{uk}, \\ \frac{dI_{dk}}{dt} &= \delta I_{uk} - (\gamma_d + \mu_d) I_{dk}, \\ \frac{dR_k}{dt} &= \gamma_u I_{uk} + \gamma_d I_{dk}\end{aligned}$$

Here, the compartment of infected individuals is slitted into  $I_{uk}$  and  $I_{dk}$ , infected undetected and infected detected, respectively. This subdivision is crucial because for any infection there are undetected cases which can include both sub-clinical and asymptomatic forms of disease. In contrast, the incidence rate is generally available and the dynamics of infectious detected individuals,  $I_d = N \sum_k I_{dk}$ , can be fitted. The probability of link with an infected individual given by  $\Theta = \frac{\sum_k k p_k I_{uk}}{\sum_k k p_k}$  allows to consider network heterogeneity. As a rule, the data on mortality caused by the infection are available that makes it possible to estimate the rate of disease-caused mortality,  $\mu_d$  unlike the rate of death in undetected group,  $\mu_u$ , which can be estimated using additional data on excess mortality.

The parameters of the model were identified to fit the dynamics of COVID-19 in Moscow for the period from March 15 to April 30, 2020. On April, 30 the strict epidemiological measures were imposed. So, the network was transformed in such a way as to delete 75% of links corresponding to professional and educational social contacts. It was shown that the solution strongly depends on the degree distribution.

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# MODELLING THE FEAR FACTOR AS DELAY SPATIOTEMPORAL EPIDEMIC MODEL

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This paper examines a Susceptible-Protected-Infected-Recovered (SPIR) epidemic model. This model incorporates a composite diffusion framework which encompasses both local and nonlocal diffusions focusing on the analysis of the influence of fear of infectious transmissions within the population. Our main goal in this investigation is to establish a mathematical model which is sound i.e. entails the validation of the existence, positivity, and uniqueness of its solution. A pivotal aspect of our analysis revolves around deriving a variational expression for the basic reproduction number ( $\mathfrak{R}_0$ ). This parameter takes on the fundamental role of a threshold quantity for the dynamics of the epidemic. Specifically, when  $\mathfrak{R}_0$  falls below 1, we substantiate that the epidemic will eventually diminish which indicates the global asymptotic stability of the disease-free equilibrium state. Conversely, when  $\mathfrak{R}_0$  exceeds 1, we explain that the solution will persist uniformly, and endemic equilibrium state will exist. The global stability of this endemic equilibrium is demonstrated by employing Lyapunov function techniques. We consider two distinct cases: in the first case we consider that the diffusion coefficient for susceptible population is null i.e. zero, and second one corresponds to the case when the diffusion coefficient for infected population is null. In addition, we made a comparative analysis with the classical SIR epidemic model to elucidate the required protective measures necessary for disease control. And this is attempted through the reduction of  $\mathfrak{R}_0$  below unity. The success of our goal depends on the implementation of suitable protective measures.

# ASSESSING THE TRANSMISSION POTENTIAL OF MPOX IN EAST ASIA DURING 2022-2023: A FOCUS ON TAIWAN, CHINA, JAPAN, AND SOUTH KOREA

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This study aims to estimate the transmission potential of mpox in East Asia, focusing on the hardest-hit nations: Taiwan, China, Japan, and South Korea [2]. We utilized six phenomenological dynamic growth models to fit the case incidence during the initial 30 epidemic days. The best-suited model for each country was identified through performance comparison. Parameters and the reproduction number ( $\mathfrak{R}_t$ ) were then estimated by calibrating the top-performing model to the outbreak's early growth phase using the mean serial interval from a previous study on mpox transmission. Additionally, we used the latest case data and a Bayesian framework to compute the instantaneous effective reproduction number by applying the Cori et al. method [1]. During the early phase, China demonstrated the highest estimated  $\mathfrak{R}_t$  of 2.89 (95% confidence interval (CI): 1.44–3.33); followed by South Korea, 2.18 (95% CI: 0.96–3.57); Japan, 1.73 (95% CI: 0.66–3.94); and Taiwan, 1.36 (95% CI: 0.71–3.30). However, by June 30, 2023, estimated  $\mathfrak{R}_t$  dropped below 1 in all countries: China at 0.05 (95% credible interval (CrI): 0.02–0.10), Japan at 0.32 (95% CrI: 0.15–0.59), South Korea at 0.23 (95% CrI: 0.11–0.42), and Taiwan at 0.41 (95% CrI: 0.31–0.53), indicating the potential decline of the outbreak. Thus, our analysis shows effective containment by each country. Furthermore, it is crucial to sustain the effective management to ensure the ultimate eradication of the outbreak.

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# HYBRID SYSTEMS MODELING OF ECOLOGICAL POPULATION DYNAMICS

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Discrete-time models are traditional for capturing the population dynamics of antagonistic interactions between two insect species - a host and its parasitoid. These models are characterized by an update function that connects the population densities from one year to the next. While previously these update functions were chosen phenomenologically, here we introduce a hybrid approach for obtaining the update functions by solving ordinary differential equations that mechanistically capture the ecological interactions between the host and the parasitoid. This hybrid approach is used to study the suppression of host density by a parasitoid. Our analysis shows that when the parasitoid attacks the host at a constant rate, then the host density cannot be suppressed beyond a certain point without making the population dynamics unstable. In contrast, when the parasitoids attack rate increases with increasing host density, then the host population density can be suppressed to arbitrarily low levels. These results have important implications for biological control where a natural enemy, such as a parasitoid wasp, is introduced to eliminate a pest that is the host species for the parasitoid. Finally, we further generalize these hybrid models to consider multi-species interactions, where multiple parasitoids attack a common host, or a single parasitoid attacks multiple host species.



# THE EFFECT OF AUTO-TOXICITY IN PLANT-GROWTH DYNAMICS: A CROSS-DIFFUSION MODEL

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In population dynamics, cross-diffusion describes the influence of one species on the diffusion of another and, surprisingly, even though the reaction part does not present the activator–inhibitor structure, cross-diffusion terms are often the key ingredient for the appearance of spatial patterns [1]. Furthermore, from the modelling perspective, cross-diffusion terms naturally appear in the fast-reaction limit of a “microscopic” model (in terms of time scales) presenting only standard diffusion and fast-reaction terms, thus incorporating processes occurring on different time scales [4].

We exploit this technique to model the auto-toxicity effect in plant growth dynamics [2], i.e. negative plant–soil feedback due to the decomposed biomass of the plant on its own growth. The “macroscopic” model presents a cross-diffusion term that allows the formation of spatial patterns without introducing water as a variable [3]. A deeper understanding of the conditions required for non-homogeneous steady states to exist is provided by combining a detailed linear analysis with advanced numerical bifurcation methods via the continuation software `pde2path` and numerical simulations.

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# BIFURCATION AND CHAOS IN BIOLOGICAL PHENOMENA WITH SECONDARY HOMOLOGOUS AND HETEROLOGOUS INFECTION FOR TWO STRAIN DENGUE MODEL

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The spread of dengue fever (DF) has caused significant economic and social costs in many countries around the world, making it a major public health concern. Mathematical models that aim to explain the irregular behavior of dengue epidemics have primarily focused on the antibody-dependent enhancement (ADE) effect and temporary cross-immunity. These models analyze available data from Chiang Mai, Thailand, with the goal of describing and understanding the transmission of dengue viruses. Our study focuses on a non seasonal (autonomous) and seasonally forced (non-autonomous) model with temporary cross-immunity and possible secondary infection, motivated by dengue fever epidemiology. We extend two strain model by adding secondary homologous and heterologous infection [1–3]. A comparative study between three different scenarios (non-seasonal, low seasonal and high seasonal with a low import of infected individuals) is performed. The extended models show complex dynamics and qualitatively a good agreement between empirical DHF monitoring data and the obtained model simulation. We discuss the role of seasonal forcing and the import of infected individuals in such systems, the biological relevance and its implications for the analysis of the available dengue data. With minimum number of parameters, it is giving a promising perspective on parameter values inference from the DHF case notifications. Also we provide some mathematical results such as equilibrium and stability analysis for non seasonal (autonomous) model. The model shows Hopf bifurcations, symmetry breaking bifurcations of limit cycles, coexisting isolas, and two different possible routes to chaos, via torus bifurcations.

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# INDIVIDUAL-BASED MODELING OF DAY CARE CENTERS PREDICTS OPTIMAL SURVEILLANCE STRATEGIES AGAINST SARS-COV-2

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During the recent SARS-CoV-2 pandemic, governments worldwide have implemented several interventions to prevent the viral spread, such as the closure of day care centers for children. This resulted in negative effects on children's health and well-being [6]. Therefore, we aim to identify optimal surveillance strategies that prevent the closure of day care centers while minimizing the viral spread.

In previous studies, we developed a stochastic individual-based SIR-type model that simulates the infection spread in a day care center [1, 2]. We could show that the infection spread is governed by various testing regimes and infection surveillance policies such as test frequency, quarantine policy, and specific test days.

In the current study, we extend our model for other variants, test types and consider vaccination of individuals. Infection spread is modelled by a susceptible individual becoming infected with a specific infection rate based on the current viral load of already infected individuals [5]. Thus, for each individual, the corresponding temporal viral load kinetic needs to be simulated, which is done using a piecewise linear model [4]. Herefore, the underlying parameters are sampled from distributions established by using a linear mixed effect model that was fitted to experimental data [3].

With this model we are able to predict optimal surveillance strategies that are required to allow child care centers to remain open during pandemic situations. It also allows the identification of common viral characteristics and how they affect the spread of infection, making it a valuable tool for other infectious diseases.

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# EXTREME VALUES AND RELATED HITTING PROBABILITIES IN EPIDEMIC MODELS ANALYZED VIA LEVEL-DEPENDENT QUASI-BIRTH-DEATH PROCESSES

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In this communication, we present the study of extreme values in epidemic models represented as a level-dependent quasi-birth-death process  $\mathcal{X} = \{(I(t), J(t)) : t \geq 0\}$  on a countable state space  $\mathcal{S}$ . The aim is to characterize the joint probability law of the random vector  $(\tau_{\max}, I_{\max}, J(\tau_{\max}))$  by assuming that the first passage from any initial state  $(i_0, j_0) \in \mathcal{S} \setminus l(0)$  to level  $l(0)$  occurs in a finite time almost surely, where  $I_{\max}$  is the maximum level visited by the process  $\mathcal{X}$  before the first visit to  $l(0)$ ,  $\tau_{\max}$  is the first time to reach this maximum number  $I_{\max}$ , and  $J(\tau_{\max})$  is the phase at time  $\tau_{\max}$ . Our algorithmic solution is based on the block-Gaussian elimination technique, and we offer efficient algorithms for computing the marginal distribution of  $I_{\max}$  and restricted Laplace-Stieltjes transforms of  $\tau_{\max}$  on the sample paths process  $\mathcal{X}$  satisfying  $\{I_{\max} = i, J(\tau_{\max}) = j\}$ . Analytical and algorithmic results are applied to the SIS model with vertical and horizontal disease transmission and the SIR model with constant population size. In this context, we illustrate numerical scenarios related to the duration of a life cycle in a population and of an epidemic outbreak, respectively.

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# CAUSAL DISCOVER FOR STOCHASTIC DYNAMIC SYSTEMS, A NEW MARKOV CHAIN APPROACH

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Our proposed method for causal discovery for stochastic dynamic systems is designed to overcome the limitations of existing methods in detecting hidden and common drivers. The method is based on a simple principle and is presented in a non-parametric structural vector auto-regressive modeling framework. The method is applied to synthetic and real life data.

# IMPACT OF TARGETED TESTING IN EARLY HIV INFECTION ON REDUCING TRANSMISSION AMONG MEN WHO HAVE SEX WITH MEN IN THE NETHERLANDS

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To further curb HIV transmission in near-elimination settings, such as among men who have sex with men (MSM) in the Netherlands, refining screening and testing strategies is crucial. Early HIV diagnosis and immediate antiretroviral treatment (ART) initiation prevent the decline of immune functions and may reduce onward HIV transmission. We



aim to provide guidance on the potential impact of the national implementation of an intervention that combines targeted testing and ART initiated within 24 hours for MSM with early HIV infection (EHI). We developed an agent-based model of HIV transmission among MSM in the Netherlands. The model integrates demographic processes, sexual network dynamics, HIV infection progression and transmission, and current practices of HIV care and prevention. We calibrated the model to the sexual partner rate data (EMIS–2017) and to the yearly incidence of HIV infections (Stichting HIV monitoring reports, 2016–2022). From 2022 onward, we simulated the different levels of uptake of targeted testing where MSM with EHI get diagnosed faster than at the baseline scenario and start ART immediately. Our model predicts that the expected maximum impact is a decrease of cumulative HIV incidence by a median of 138 (Interquartile range (IQR): 72–194) and 240 (IQR: 165–280) new infections after four and eight years, respectively (Figure 1a and 1c). The decrease in the incidence will also be reflected in the reduction of new diagnoses three years following the start of the intervention (Figure 1b). To maximize the impact of the intervention, the testing rate of individuals with EHI must increase 30-fold (Figure 1c).

Targeted testing of MSM with EHI, complemented with immediate ART initiation, potentially could reduce HIV transmission among MSM. Our results suggest that a 30-fold increase in testing by individuals with EHI is required for this intervention to reach its maximum effectiveness.

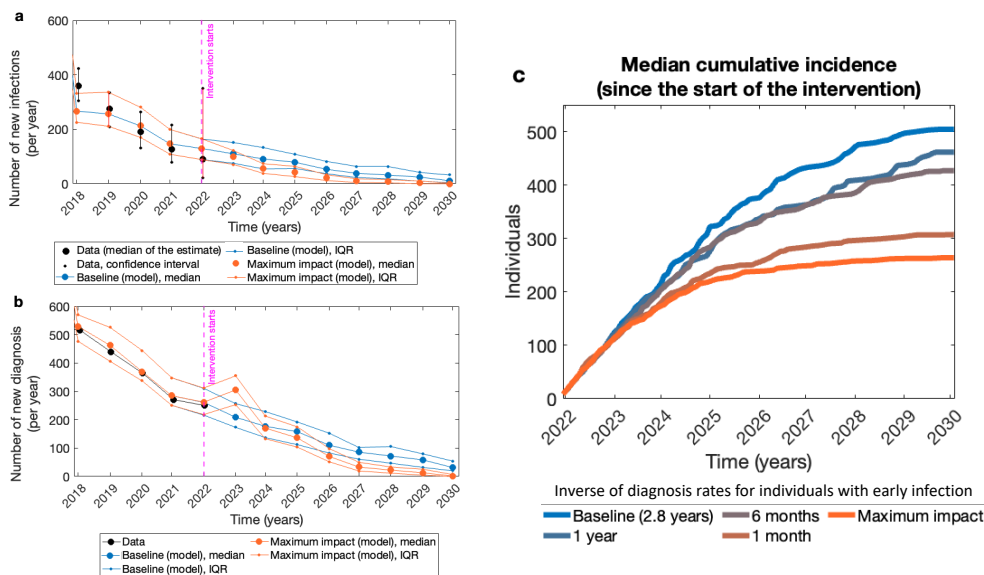


Figure 1: Maximum expected impact of the targeted testing of recently infected individuals on the dynamics of HIV. Intervention starts in 2022.

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# MODELING POPULATION DYNAMICS AND CONTROL STRATEGIES FOR A UNIQUE SPECIES EVOLVING IN HETEROGENOUS LANDSCAPE

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We study a single-species metapopulation model with patches connected by linear diffusion. Inspired by the framework inaugurated by Takeuchi in [7] and Takeuchi and Lu in [4], and using tools of cooperative system theory [6], we show that under appropriate conditions, the sign of the stability modulus of the Jacobian of the system at the origin determines the asymptotic behaviour of the solutions. If it is non-positive, then the population becomes extinct in every patch. Conversely, if it is positive, then there exists a unique nonnegative equilibrium, which is positive and globally asymptotically stable.

In the latter case, given a subset of ‘controlled’ patches where human intervention is allowed, we study whether introducing additional mortality terms in these patches can result in population elimination in every patch. We characterize this possibility by an algebraic property on the graph of the residual, uncontrolled, system. When the population persists whatever the control, we assess the minimal attainable positive equilibrium value. When extinction is possible, we study the optimization problem consisting in achieving this task while minimizing a certain cost function, chosen as a nondecreasing and convex function of the mortalities added in the controlled patches. Using the (strict) convexity properties of the spectral radius of a non-negative matrix with respect to its diagonal elements [1, 3, 5], we show that such minimization problem admits a global minimizer, which is unique when not every patch is controlled.

This presentation stands within the framework of an ongoing project, AttracTIS, in Réunion island, which aims at studying a combination of vector control tools against *Bactrocera dorsalis*, including the Sterile Insect Technique [2]. This pest, also called oriental fruit fly [8], invaded Réunion island in 2017 and since then has been impacting significantly the production of fruits, in particular mangos.

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# A TEMPORAL REFUGE FROM PREDATION CAN CHANGE THE OUTCOME OF PREY SPECIES COMPETITION

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Generalist predators whose primary prey undergoes cyclic fluctuations, will predate on alternative food sources when the abundance of their primary prey is low. This can have implications for the interactions and dynamics of alternative prey species. To examine this we present a general model of a predator that switches predation between its primary prey and two alternative, competing, prey species [1]. When the primary prey is at high abundance, predation of the alternate prey species is low, which provides a temporal refuge for the alternate prey from predation. When the inter-specific interactions between the alternative prey species lead to different dynamical outcomes in the presence and absence of predation, increasing the duration of the temporal refuge promotes dominance of a competitively superior species that is vulnerable to predation.

The general theoretical framework was extended to consider a key case study system of pine marten predation on red and grey squirrels. In the absence of predation, grey squirrels out-compete red squirrels. However, preferential predation by pine marten on grey squirrels can suppress grey squirrel density and allow red squirrel recovery. A temporal refuge for both squirrel species can arise due to prey switching by pine marten in years when field voles, their primary prey in the UK, are abundant. The duration of the temporal refuge, quantified as the relative length of the multi-annual vole population cycle where vole density is above a population threshold, is a critical factor determining the persistence of red and grey squirrels. Our findings therefore provide insights for the conservation of the endangered red squirrel in the UK and the Republic of Ireland and more generally on the influence of the population dynamics of primary prey species in determining community composition.

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# DSABNS 2023

14th INTERNATIONAL CONFERENCE  
DYNAMICAL SYSTEMS APPLIED TO BIOLOGY  
AND NATURAL SCIENCES (DSABNS)

## **Minisymposia**

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**Minisymposium Title:**  
RECENT ADVANCES IN MATHEMATICAL MODELING OF  
INFECTIONS DISEASES AT THE INDIVIDUAL AND  
POPULATION LEVELS

**Organizers:**  
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Mathematical modeling of disease is a useful tool for studying emergence, propagation, and control of diseases at various scales. Among many other utilities, models can help us understand how individual immune systems affect individual disease, how environmental drivers contribute to disease emergence and transmission, and how treatments and vaccine allocations impact dynamics of infectious and non-infectious diseases. In this minisymposium, we bring together researchers developing new tools in disease modeling as well as those applying their work to questions of transmission and control.

## WAITING FOR THE PERFECT VACCINE

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Vaccination has proven to be the most effective public health measure in the fight against various infectious diseases. For emerging or re-emerging diseases, a highly efficacious vaccine may not be available at the start of an outbreak. Timelines for availability of a safe and effective vaccine may significantly affect disease dynamics, its burden, and the healthcare resource utilization. Mitigating this impact may then rely on low-efficacy vaccines that may be rapidly produced and distributed to at-risk populations at the early stages of an outbreak. With the expectation for arrival of a more effective vaccine at a later stage of the outbreak, the optimal vaccination coverage with the existing, low-efficacy vaccines is elusive. While flattening the outbreak if a significant proportion of the susceptible population is vaccinated with a low-efficacy vaccine, the overall infections may not be minimized if a small proportion of the population left unvaccinated when a highly efficacious vaccine becomes available. The optimal coverage for early vaccination could thus depend on several parameters including the efficacy of the currently available vaccines, arrival timing of a more effective vaccine and its efficacy, and the transmissibility of the disease. Here, we develop a deterministic system of differential equations to investigate the optimal vaccination coverage with a low-efficacy vaccine within the aforementioned parameter space. Despite simplifying assumptions, we illustrate that minimizing the overall infections does not necessarily correspond to the highest coverage of early vaccination. However, a high vaccination coverage, even with a low-efficacy vaccine, may still contribute to alleviating severe disease outcomes and reducing healthcare resource utilization.



# UNDERSTANDING SHORT AND LONG-TERM DYNAMICS OF HEPATITIS B VIRAL KINETICS FOLLOWING THERAPY

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Hepatitis B virus is a major medical problem worldwide, with at least 257 million people persistently infected. Current treatment options focus on removing circulating HBV DNA but are suboptimal in removing hepatitis B s- and e-antigens. ARC-520, an RNA interference drug, has induced substantial hepatitis B s- and e- antigen reductions in animals and patients receiving therapy. We study the effect of ARC-520 on hepatitis B s- and e-antigen decline by developing mathematical models for the dynamics of intracellular and serum viral replication, and compare it to patient data from a clinical trial with one or multiple ARC-520 injections. We examine biological parameters describing the different phases of viral marker decline and rebound after treatment initiation, and estimate ARC-520 efficacy. Most importantly, we propose mechanisms of action explaining post-treatment control in a small number of treated patients. The results can help identify treatment markers of cure.

# REPELLENT-BASED MITIGATION MEASURES FOR VECTOR-BORNE DISEASES: A CONTROL THEORY APPROACH

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One strategy for reducing the burden of vector-borne diseases (malaria, dengue, zika, yellow fever, etc.) in an environmentally-friendly way is the use of personal protection based on mosquito repellents in textiles or household items. The repellent action reduces the mosquito biting rate and the transmission probability of the pathogen. The efficacy of such mitigation strategies in simple compartmental models for vector-borne diseases is studied from the point of view of control theory. The two types of controlled non-autonomous system under consideration have the structure of a) Susceptible-Infected; b) Susceptible-Infected-Recovered for the human host, and Susceptible-Infected-type for the vector. The first type corresponds to the classical Ross-Macdonald model for malaria. Transient dynamic behaviour of the model solutions is studied under the following constraints: an upper bound on the control given by the maximum proportion of the host population employing the repellents, and an upper bound on the phase variable (size of the infected host compartment). The first task is to determine those initial states of the dynamical system such that the solutions of the controlled system meet these constraints for all future times. The set of such initial states is the viability kernel associated to the constraints. Theoretical analysis based on comparison theorems for quasi-monotone dynamical systems allows us to distinguish the cases when the viability kernel has positive or zero Lebesgue measure in the phase space. Viability kernels with positive Lebesgue measure are approximated numerically via the solution of associated Hamilton-Jacobi-Bellman equations. The second task is to perform reachability analysis. This helps find the optimal controls that can reduce the number of infected hosts below a certain cap in the shortest time possible if the initial state of the system lies outside the viability kernel. This analysis allows an evaluation of the chosen mitigation strategy that is constrained in time by the duration of repellent action on textile or household items.

# A MATHEMATICAL MODEL OF CHRONIC INFECTION AND IMMUNE EXHAUSTION

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The mathematical modeling of chronic infections across their entire time course is made challenging by the need to incorporate three distinct dynamic behaviors on different time scales. Rapid acute infection dynamics are followed by a long period of pseudo-steady state behavior, eventually leading to loss of immune control and late-stage symptoms. While many models are able to capture portions of these dynamics, simple models that incorporate all three phases are less common. In this work, we present a novel mathematical model based on an analogy to chemical buffer to simulate the slow deterioration of immune control over time, followed approach catastrophic loss of control and viral expansion. We also discuss possible immunological mechanisms for the observed dynamics.



## Minisymposium Title:

# THEORETICAL MODELS IN SUSTAINABLE AGRICULTURE: INTEGRATING ECOLOGY, EVOLUTION AND ECONOMICS

## Organizers:

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Weeds, animal pests, and pathogens have challenged crop production since agriculture's origins. These pests reduce crop productivity, leading to economic losses for the farmers and threatening global food security [5]. First, farmers relied solely on manual and mechanical measures for controlling weed populations and animal pests [5]. Diseases caused by pathogens were imperceptible, with no effective treatments available [5]. Chemical measures, specifically herbicides, insecticides and fungicides, have improved pest control and enabled intense farming [7]. However, the overreliance of modern agriculture on pesticides has caused the evolution of resistance in various species globally [3]. The potential loss of pesticide efficacy imposes a significant challenge to agriculture and threatens food security [3]. Moreover, chemical measures adversely affect the environment, off-target species and human health [7]. Sustainable agriculture necessitates economically producing enough good-quality crops while minimising environmental impacts and delaying resistance evolution [5]. Mathematical modelling is crucial in predicting long-term economic, ecological and evolutionary outcomes under various management regimes and environmental conditions [1, 2, 4, 6]. To better understand and influence this complex dynamical system of sustainable agriculture, we bring together the expertise from theoretical models in economics, ecology, and evolution.

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# MATHEMATICAL MODELLING FOR SUSTAINABLE CROP PROTECTION

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Crop pests, pathogens and weeds have a major economic impact and threaten food security. Their control still heavily relies on chemical pesticides, which are harmful to both the environment and public health, and induce pest resistance, hence the need for eco-friendly sustainable alternatives. The aim of this talk is to present modelling studies which implement alternative control methods, in particular resistant crops and biocontrol agents. These studies focus on how “best” to deploy such control methods to limit damages cost-efficiently or in seeking some sort of bioeconomic optimum by means of a yield proxy. The models are dynamical systems derived from classical epidemiological models adapted to the pathosystem considered. Optimisation or optimal control methods are used to determine appropriate deployment strategies. To efficiently control the disease and avoid resistance breakdown, susceptible and resistant crops can be alternated in space or time, depending on the pathosystem under study. An example of optimal resistance deployment in time will be given to control root-knot nematodes in horticultural crops [3]. Optimising cropping practices, as in the case of banana burrowing nematode management [4], is another example of alternatives to chemical pesticides. Several biocontrol methods can be implemented, which will be illustrated for coffee crop pests: fungus-based biopesticides to control coffee berry borers [2], or predators to control coffee leaf rust [1]. Finally, several general issues, such as “small data”, and perspectives will be discussed.

**Acknowledgements** Results detailed in this presentation were obtained as part of the PhD theses of Samuel Nilusmas, Israël Tankam Chedjou, Yves Fotso Fotso and Clotilde Djuikem, as well as co-authors cited in the associated references. EPITAG, and Inria associate team with universities in Cameroon, supported part of their research (<https://team.inria.fr/epitag/>).

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# MODELING *XYLELLA FASTIDIOSA* DISEASES: TRANSMISSION DYNAMICS, GLOBAL SPATIOTEMPORAL RISK PREDICTIONS AND DESIGN OF CONTROL STRATEGIES

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*Xylella fastidiosa* (Xf) diseases pose a significant threat to agricultural ecosystems, causing widespread damage to crops and subsequent economic losses [6]. Understanding the transmission dynamics of Xf diseases, predicting its spatiotemporal distribution and designing control strategies are crucial for effective disease management. This work delves into an interdisciplinary approach to model Xf diseases (see Figure 1), integrating ecological and epidemiological principles with advanced computational methods and climatic data to provide useful insights into different aspects of Xf epidemiology. We present the most advanced epidemiological model for Xf diseases [3], encompassing the population dynamics of its main European vector, *Philaenus spumarius*. We will show the importance of introducing this dynamic feature into the model [1], its ability to characterize different Xf diseases, such as ALSD and OQDS, and the strategic insights it provides for disease control. Furthermore, the model can be adapted to perform global spatiotemporal risk predictions based on transmission dynamics coupled to climatic variables [2], such as temperature, in both current and future climate scenarios [2, 4]. Finally, we introduce a recently developed tool for forecasting the hatching of *Philaenus spumarius* eggs, employing similar mathematical and computational techniques [5]. Our research provides a means to advance the management of Xf diseases by offering a cutting-edge epidemiological model, a global risk assessment framework, and a predictive tool for key vector control, which are essential components in safeguarding agricultural ecosystems against this formidable threat.

**Acknowledgements** A.G.R and M.A.M. acknowledge the grant PID2021 - 123723OB-C22 (CYCLE) funded by MCIN/AEI/10.13039/501100011033 and by “ERDF A way of making Europe”.

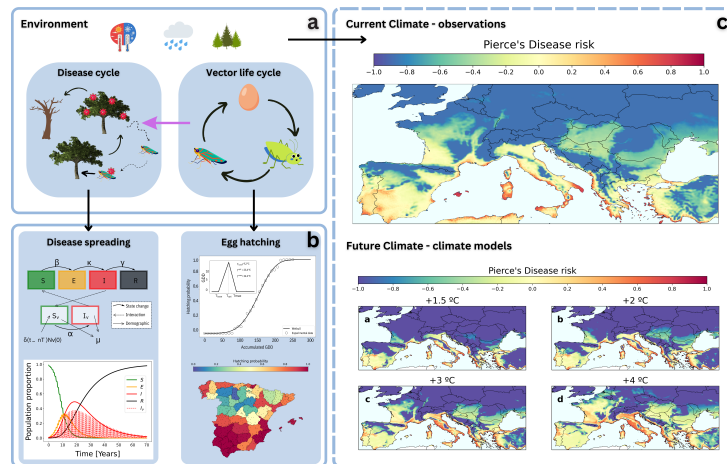


Figure 1: Summary of the modelling framework for *Xylella fastidiosa* diseases.

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# TUNING SPATIAL DISTRIBUTION OF PESTICIDE TO MINIMISE THE RATE OF RESISTANCE EMERGENCE

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Combatting pests with pesticides prompts an evolutionary response: the emergence of resistance to the pesticide. What measures can be taken to suppress the emergence of resistance while not foregoing the benefits of population control? We here ask whether the spatial distribution of pesticide can be tuned to minimise the rise of an existing resistant subpopulation. Existing models of pesticide application typically employ assumptions which reduce the impact of spatial heterogeneity in the model. Incorporating explicit spatial considerations gives rise to novel dynamics which are otherwise not present. Here, we employ a one-dimensional model with pests undergoing diffusive migration, with pesticide applied temporarily on a sub-region only. We find that an optimal size of this sub-region exists, which minimises resistance emergence per area protected over a single generation. We supplement numerical solutions with analytical bounds for the location of the optimum, providing insight into the emergence of this optimum. Moving beyond an isolated area protected by pesticides, we investigate environments consisting of equally spaced sub-regions where pesticide is applied temporarily. In this case, we demonstrate that for a given area of pesticide application, there exists an optimum spatial distribution which minimises the initial rate of resistance emergence. This allows us to answer how a large agricultural region can be subdivided to optimally suppress resistance emergence. These findings are a step towards optimised protocols for pesticide application that protect the crop and suppress the emergence of resistance at the same time.

**Acknowledgements** Thomas Tunstall was supported by an EPSRC DTP PhD studentship and Syngenta.

# MULTITYPE GALTON-WATSON PROCESSES FOR HERBICIDE RESISTANCE EVOLUTION

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Weeds are a major threat to crop production, causing the highest potential yield losses among pests. Since the late 1960s, conventional agriculture has primarily relied on herbicides for weed management. This overreliance on herbicides has led to the widespread evolution of herbicide resistance in various weed species. The evolution of herbicide resistance is an example of rapid adaptation under strong selection, where the source of variation within a population influences the rate and probability of adaptation. When developing strategies to manage herbicide resistance, we thus first need to identify the source of adaptive variation - standing genetic variation vs *de novo* mutations. Perennial weed species are challenging to manage due to their two pathways of reproduction: sexually via seeds and asexually through rhizomes. The seeds of various species are dormant and can stay viable in the ground for several years, forming a seed bank which acts as a buffer, altering eco-evolutionary dynamics. Using a multitype Galton-Watson branching process, we model the lifecycle of perennial weeds to study the eco-evolutionary dynamics of herbicide resistance evolution and the probability of herbicide failure. We analyse the role of standing genetic variants and *de novo* mutations. Further, we show how including the explicit details of weedy traits, such as seed bank dynamics, self-pollination and asexual propagation, alters the relevance of the different sources of adaptive variation.

**Minisymposium Title:**  
**SLOW-FAST SYSTEMS IN BIOLOGY: GEOMETRIC  
SINGULAR PERTURBATION THEORY APPLICATIONS  
AND NEW PERSPECTIVES**

**Organizers:**

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In real world scenarios, the natural phenomena usually evolve on time scales differing by various orders of magnitude. Such separation in time-scales can be found, for example, in the field of chemical oscillations [7], neuroscience [3], ecology [9], epidemiology [6] or opinion/information spreading [2]. In this context, Geometric Singular Perturbation Theory (GSPT) is a powerful approach a powerful analytical technique which fully exploits the underlying time-scale separation. In the following we briefly recap the main results of the theory.

Consider a system of ODEs of the form

$$\begin{aligned}x' &= \varepsilon f(x, y, \varepsilon), \\y' &= g(x, y, \varepsilon),\end{aligned}\tag{1}$$

where  $' = \frac{d}{dt}$ ,  $x \in \mathbb{R}^l$ ,  $y \in \mathbb{R}^k$  and  $f$  and  $g$  are sufficiently regular functions. The small parameter  $0 < \varepsilon \ll 1$  gives the separation of the time-scales. Rescaling the system from the time-scale  $t = \tau/\varepsilon$  to  $\tau$ , we obtain

$$\begin{aligned}\dot{x} &= f(x, y, \varepsilon), \\ \varepsilon \dot{y} &= g(x, y, \varepsilon),\end{aligned}\tag{2}$$

where  $\dot{\phantom{x}} = \frac{d}{d\tau}$ . The time-scale given by  $t$  is said to be fast and (1) is called the *fast system*, whereas  $\tau$  is the slow time-scale and (2) is called the *slow system*. These systems are equivalent until  $\varepsilon \neq 0$  and for  $\varepsilon \rightarrow 0$  systems correspond to distinct limits

$$\begin{aligned}x' &= 0, & \text{and} & & \dot{x} &= f(x, y, 0), \\y' &= g(x, y, 0), & & & 0 &= g(x, y, 0),\end{aligned}\tag{3}$$

called the *layer equations* (fast) and the *reduced system* (slow), respectively. The equation  $g(x, y, 0) = 0$  defines the so-called *critical manifold*.

The main goal is analysing the dynamics of system (1) with  $0 < \varepsilon \ll 1$  by combining the dynamics of the two limit systems (3). To this aim, Fenichel [4] proved that if  $\mathcal{M}_0$  is a manifold contained in the critical manifold and it is uniform hyperbolic, then this manifold persists for  $0 < \varepsilon \ll 1$  as locally invariant slow manifold  $\mathcal{M}_\varepsilon$  of the full problem (1) that is  $O(\varepsilon)$  close to  $\mathcal{M}_0$ , and the restriction of the flow (1) to  $\mathcal{M}_\varepsilon$  is a small perturbation of (3). For more complicated techniques when uniform hyperbolic is lost, more complex dynamics

may appear or there are more than two time-scale, we refer to [8] and in particular to [5] and [1] for applications in mathematical models of natural phenomena.

The aim of this minisymposium is to showcase recent applications of models in biology using GSPT techniques. Each of the speakers has made substantial contributions to the analysis and practical application of GSPT in various biological contexts, and they will highlight their most recent advancements in these fields.

*In this MS, we invited researchers from different countries, ensuring gender balance.*

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# FRONT PROPAGATION IN TWO-COMPONENT REACTION-DIFFUSION SYSTEMS WITH A CUT-OFF

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The Fisher-Kolmogorov-Petrovskii-Piscounov (FKPP) equation with a cut-off was popularised by Brunet and Derrida in the 1990s as a model for many-particle systems in which concentrations below a given threshold are not attainable. While travelling wave solutions in cut-off scalar reaction-diffusion equations have since been studied extensively, the impacts of a cut-off on systems of such equations are less well understood. As a first step towards a broader understanding, we consider various coupled two-component reaction-diffusion equations with a cut-off in the reaction kinetics, such as an FKPP-type population model of invasion with dispersive variability due to Cook, a FitzHugh-Nagumo-style model with piecewise linear Tonnelier-Gerstner kinetics and, finally, a more general predator-prey model with a cut-off in both components that is motivated by standard Lotka-Volterra-type dynamics. Throughout, our focus is on the existence, structure, and stability of travelling fronts, as well as on their dependence on model parameters; in particular, we determine the correction to the front propagation speed that is due to the cut-off. Our analysis is for the most part based on a combination of geometric singular perturbation theory and the desingularisation technique known as “blow-up”.

# MODELING FAST INFORMATION AND SLOW(ER) DISEASE SPREADING: A GEOMETRIC ANALYSIS

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In the era of social networks, when information travels fast between continents, it is of paramount importance to understand how the evolution of a disease can be affected by human behavioral dynamics influenced by information diffusion. For decades, from the early 20th century, the evolution of epidemics are modelled and studied via ordinary differential equations (ODEs) systems. The compartmental models are important tools for a better understanding of infectious diseases and they have been introduced in 1927 by Kermack and McKendrick [2], in fact they can be used to predict how the disease spread, or obtain information on the duration of an epidemic, the number of infected individuals, etc., but also to identify optimal strategies for control the disease.

In this work, we focus on the interplay between fast information spreading and slow(er) disease spreading using techniques from Geometric Singular Perturbation Theory (GSPT). Since the pioneering papers written by N. Fenichel [1], GSPT has proven extremely suitable to describe systems evolving on multiple time scales, and analyse their transient and asymptotic behaviours. Here, we introduce an SIRS compartmental model with demography and fast information and misinformation spreading in the population. Considering the speed at which information spreads in the age of social media, we let our system evolve on two time scales, a fast one, corresponding to the information “layer” and a slow one, corresponding to the epidemic “layer”. We completely characterize the possible asymptotic behaviours of the system we propose with techniques of GSPT. In particular, we emphasise how the inclusion of (mis)information spreading can radically alter the asymptotic behaviour of the epidemic, depending on whether a non-negligible part of the population is misinformed or skeptical of misinformation.

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# MULTIPLE-TIMESCALE DYNAMICS IN SLEEP-WAKE REGULATION AND REM-NREM ALTERNATIONS

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Sufficient and good-quality sleep is an integral component of a healthy lifestyle. Chronically implementing “bad” sleep habits can lead to a number of problems, such as cardio-vascular diseases, increased fatigue-levels, cognitive decline, and others.

Sleep-wake regulation, i.e. roughly when we go to sleep and when we wake up, has been described as the result of the interaction between circadian and homeostatic processes. These latter processes also affect the alternation between rapid-eye-movement (REM) episodes and non-REM (nREM) episodes during sleep.

In this talk, we will discuss some models of circadian rhythms and REM-nREM alternations, with a focus on the multiple-timescale structure of these phenomena.

# FAR-FROM-THRESHOLD DYNAMICS IN SLOPED SEMI-ARID ENVIRONMENTS DRIVEN BY AUTOTOXICITY EFFECTS

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In this talk, we focus on the investigation of far-from-threshold vegetated dynamics in sloped semi- arid environments in the presence of autotoxicity. To this aim, an extension of the 1D Klausmeier model that accounts for the toxicity compounds is considered and the occurrence of travelling stripes is analysed. Numerical simulations are first carried out to capture the qualitative behaviour of the pulse-type solutions and, then, geometric singular perturbation theory is used to prove the existence of such travelling pulses by constructing the corresponding homoclinic orbits in the associated 4- dimensional system. A scaling analysis on the investigated model is performed to identify the asymptotic scaling regime in which travelling pulses can be constructed. Some biological observations are extracted from the analytical results, in particular enlightening the role played by autotoxicity in the structure of the travelling patterns. Finally, the analytically constructed solutions are compared with the numerical ones, leading to a good agreement that confirms the validity of the conducted analysis. Numerical continuation with respect to the main system parameters linked to autotoxicity are also performed using the software AUTO in order to gain additional information on the emerging vegetation dynamics.

**Minisymposium Title:**  
STATISTICAL PHYSICS TOOLS APPLIED TO STOCHASTIC  
MODELS IN POPULATION DYNAMICS AND EPIDEMIC  
SPREADING

**Organizers:**  
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Many dynamical systems in (bio-)chemistry, nuclear, and particle physics incorporate interactions that cause an identity change of their constituents. Reactive processes also capture the kinetics of condensed matter quasi-particles or of agents in ecology and epidemiology. The dynamics of reacting particles is often described through deterministic nonlinear rate equations. These result from the fundamental stochastic master equations via a factorization of space-time correlators. Since this mean-field approximation neglects spatial correlations and temporal fluctuations, its validity must be assessed. The versatile tools of nonequilibrium statistical physics have been applied to characterize the effect of intrinsic noise on reaction kinetics [4, 8] and population dynamics [2]. Naturally, fluctuations become important near population extinction and epidemic thresholds, not just because the number of individuals becomes small, but also owing to their discrete nature and critical correlations [8]. Away from continuous phase transitions, reactive processes may generate strong spatio-temporal (anti-) correlations and induce pattern formation [2, 4] that is not apparent in reaction-diffusion partial differential equations. This minisymposium will begin with an overview of analytical and numerical studies of fluctuation effects in population dynamics and epidemic spreading. Four detailed talks will then discuss recent advances: M. Swailem describes how coarse-graining stochastic reactive processes inevitably introduces renormalized parameters, and how effective macroscopic rates can be extracted from lattice Monte Carlo simulations [7]. The subsequent two presentations will address critical behavior near the epidemic threshold of the paradigmatic susceptible-infectious-recovered model for disease spreading: R. Mukhamadiarov demonstrates that lattice dilution, modelling immunization, does not alter the critical properties governed by the dynamic isotropic percolation universality class [5], whereas G. Ódor identifies nonuniversal power-law scaling on hierarchical modular networks [6] and considers the effects of super-spreader hot-spots and mobility of individuals [1]. Finally, Ll. Hernández-Navarro explores how combined environmental noise and demographic fluctuations alter fixation regimes in an eco-evolutionary dynamical model for cooperative antimicrobial resistance [3].

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# FLUCTUATIONS AND SPATIAL CORRELATIONS IN CHEMICAL REACTION KINETICS, POPULATION DYNAMICS, AND EPIDEMIC SPREADING

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The kinetics of chemical reactions, competing populations, and infectious diseases are mathematically captured by the unified framework of stochastic interacting particle systems, governed by (linear) master equations for the configurational probabilities. Applying a ‘mass action’ factorization of moments and correlations leads to the ubiquitous description in terms of coupled nonlinear differential rate equations, or partial differential reaction-diffusion equations in spatially extended settings. While such mean-field approximations provide valuable insight into the dynamics of complex stochastic reacting particle systems, they may turn out quantitatively insufficient or even fail qualitatively when the reaction kinetics generates strong temporal and/or spatial correlations that invalidate the well-mixed assumption [5, 8]. Prominent examples include the drastically decelerated density decay in diffusion-limited pair coagulation in low dimensions  $d \leq 2$  [3]; segregation and the emergence of sharp reaction zones in two-species annihilation for  $d \leq 4$  [4]; and the related spontaneous formation of noise-induced activity fronts in Lotka–Volterra predator-prey coexistence [6] and spiral structures in the May–Leonard model for cyclic three-species competition [1]. Near continuous phase transitions from active to absorbing states, exemplified by population extinction or fixation, long-range critical correlations induce large fluctuations described by universal power laws distinct from mean-field predictions, but closely related to critical percolation theories [8]. Correspondingly, demographic fluctuations are crucial near epidemic thresholds, and the susceptible-infectious-recovered model rate equations also turn out inadequate in the late stages of disease spreading on spatial networks [7]. Fluctuation-driven phenomena and correlation effects in complex interacting / reacting particle systems are efficiently studied via agent-based Monte Carlo simulations [2], and can be treated analytically by means of path integral representations of the underlying stochastic processes and systematic field-theoretic tools [8].

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# COMPUTING MACROSCOPIC REACTION RATES IN REACTION-DIFFUSION SYSTEMS USING MONTE CARLO SIMULATIONS

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Stochastic reaction-diffusion systems serve as versatile models for many complex physical, societal, and ecological systems [3]. The effective coarse-grained reaction rates in continuum descriptions for such systems represent macroscopic parameters that need to be either measured experimentally or determined numerically. In an agent-based Monte Carlo simulation of stochastic reaction-diffusion systems, the control parameters are the prescribed microscopic probabilities for certain events to happen. They ultimately define the large-scale behavior and long-time states of the system, as well as relaxation rates and other relevant time scales such as oscillation frequencies. To match the results of numerical simulations to experiments, a mapping is required between the microscopic probabilities that define a Monte Carlo simulation and the macroscopic reaction rates. This constitutes in general a non-trivial problem, and there exists no systematic method to obtain the functional dependence of the macroscopic rates on the microscopic probabilities and interaction rules. Here we introduce an algorithmic approach using Monte Carlo simulations to evaluate the macroscopic reaction rates by counting how many events occur per simulation time step [4]. Our technique is first tested on known simple examples such as simple birth reactions, coagulation, and pair annihilation [2, 5]. We then investigate how the microscopic reaction probabilities become coarse-grained into macroscopic rates in more complicated models such as the Lotka–Volterra predator-prey model, the rock-paper-scissors or cyclic Lotka–Volterra model, and the May–Leonard model for cyclic competition of three species [1]. This work aims towards a deeper understanding of coarse-graining in stochastic reaction-diffusion systems with a focus on ecological models, and improved Monte Carlo simulation techniques to fit experimental or observational data.

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# EFFECTS OF LATTICE DILUTION ON THE NONEQUILIBRIUM PHASE TRANSITION IN THE STOCHASTIC SIR MODEL

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We investigate how site dilution, as would be introduced by immunization, affects the properties of the active-to-absorbing nonequilibrium phase transition in the paradigmatic susceptible-infectious-recovered (SIR) model on regular cubic lattices. According to the Harris criterion [3], the critical behavior of the SIR model, which is governed by the universal scaling exponents of the dynamic isotropic percolation universality class [1, 2, 4], should remain unaltered after introducing impurities [6]. However, when the SIR reactions are simulated for immobile agents on two- and three-dimensional lattices subject to quenched disorder, we observe a wide crossover region characterized by varying effective exponents [5]. Only after a sufficient increase of the lattice sizes does it become clear that the SIR system must transition from that crossover regime before the effective critical exponents asymptotically assume the expected dynamic isotropic percolation exponent values. We attribute the appearance of this exceedingly long crossover to a time lag in a complete recovery of small disconnected clusters of susceptible sites, which are apt to be generated when the system is prepared with Poisson-distributed quenched disorder. Finally, we demonstrate that this transient region becomes drastically diminished when we significantly increase the value of the recovery rate or enable diffusive agent mobility through short-range hopping.

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# SUPER-SPREADER HOT-SPOTS, MOBILITY AND LOCK-DOWN EFFECTS ON THE DYNAMICS OF SIR EPIDEMIC MODELS

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Power-law time dependent infection growth has been reported in many COVID-19 statistics. In simple susceptible-infectious-recovered (SIR) models the number of infections grows at the outbreak as  $I(t) \propto t^{d-1}$  on  $d$ -dimensional Euclidean lattices in the endemic phase, or follow a slower universal power law at the critical point, until finite size causes immunity and a crossover to an exponential decay. Heterogeneity may alter the dynamics of spreading models: Spatially inhomogeneous infection rates can involve slower decays, posing a threat of a long recovery from a pandemic. COVID-19 statistics have also provided epidemic size distributions with power law tails in several countries. We have investigated SIR like models on hierarchical modular networks, embedded in two-dimensional lattices with the addition of long-range links [2]. Simulations show that in case of finite graph dimensions, prevalence, at the critical point, grows with degree-dependent power laws. Super-critically, we found the same power law exponents as for regular graphs, but topological disorder alters the critical behavior. This is also true for the epidemic size distributions. The addition of super-spreader hot-spots or other quenched disorder does not change the growth exponent and the exponential decay in the herd immunity regime. Mobility of individuals on the  $d = 2$  lattice changes slightly the critical behavior, as the consequence of breaking the duality symmetry of the SIR epidemic [1].

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# COUPLED ENVIRONMENTAL AND DEMOGRAPHIC FLUCTUATIONS SHAPE THE EVOLUTION OF COOPERATIVE ANTIMICROBIAL RESISTANCE

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The rise of antimicrobial resistance is a global threat responsible for millions of deaths [3]. Therefore we have a pressing need to better understand how microbial populations respond to antimicrobial drugs, and to find mechanisms to possibly eradicate antimicrobial-resistant cells. The inactivation of antimicrobials by resistant microbes can often be viewed as a cooperative behavior leading to the coexistence of resistant and sensitive cells in large populations and static environments. This picture is however greatly altered by the fluctuations arising in volatile environments, in which microbial communities commonly evolve. This talk presents the eco-evolutionary dynamics of a population consisting of an antimicrobial resistant strain and microbes sensitive to antimicrobial drugs in a time-fluctuating environment, modeled by a carrying capacity randomly switching between states of abundance and scarcity [1, 2]. We assume that antimicrobial resistance is a shared public good when the number of resistant cells exceeds a certain threshold; see Figure 1(a). Eco-evolutionary dynamics is thus characterized by demographic noise (birth and death events) coupled to environmental fluctuations which can cause population bottlenecks. By combining analytical and computational means, we determine the environmental conditions for the long-lived coexistence and fixation of both strains, and characterize a *fluctuation-driven* antimicrobial resistance eradication mechanism, where resistant microbes experience bottlenecks leading to extinction; see Figure 1(b-c). Finally, I will discuss the possible applications of our findings to laboratory-controlled experiments and drug treatments.

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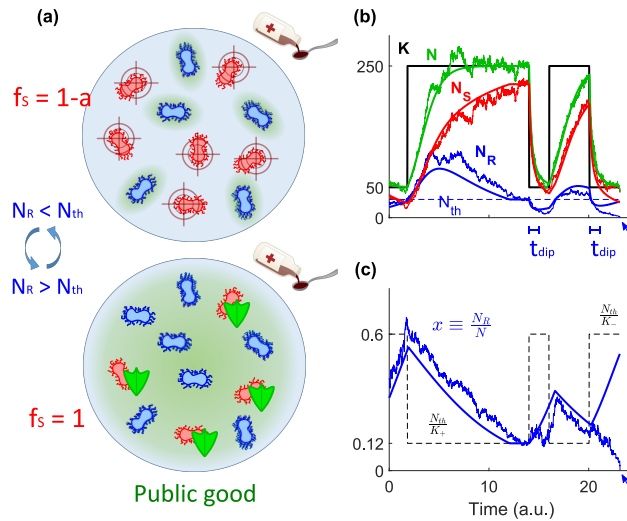


Figure 1: Microbial community model. (a) Top: When the abundance of resistant microbes ( $R$ , blue) is below the cooperation threshold  $N_{th}$ , antimicrobial drug hinders the growth fitness of sensitive microbes ( $S$ , red), as  $f_S = 1 - a > 0$ , and  $R$  cells have then a growth fitness advantage ( $1 > f_R > f_S$ ). Bottom: Antimicrobial resistance becomes cooperative when the number of  $R$  exceeds  $N_{th}$  and these generate enough *resistance enzyme* (public good in green shade) to hydrolyze the antimicrobial drug for the whole medium, so that protection against the drug is shared with  $S$  (with green shields), which have then a growth advantage ( $f_S = 1 > f_R$ ). (b) Example temporal eco-evolution dynamics of the microbial community (number of individuals on the vertical axis); thick black line shows the sample path of the time-switching carrying capacity  $K(t)$ , with a cooperation threshold  $N_{th} = 30$  (dashed blue line); thick solid lines depict the expected behavior when demographic noise is neglected for the total microbial population ( $N$ , green), number of  $R$  ( $N_R$ , blue), and number of  $S$  ( $N_S$ , red); noisy lines show an example stochastic realization of the full model under the joint effect of demographic and environmental fluctuations. In the presence of environmental fluctuations,  $R$  can experience bumps and dips (thick blue line);  $t_{dip}$  indicates the time to reach the bottom of a dip from its inception under no demographic noise. In the presence of demographic noise, fluctuations about the dip can lead to the extinction of  $R$  (blue arrow). (c)  $R$  fraction  $x = N_R/N$  for the same sample path of varying environment as in (b); line styles as in panel (b); the dashed black line shows the stable  $R$  fraction in each environment as  $K(t)$  switches in time.



# DSABNS 2023

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# MODELLING THE EFFECT OF VACCINATION STRATEGIES AGAINST BOVINE BRUCELLOSIS

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Female bovines, due to their important role in the transmission and maintenance of brucellosis, were the target of the serological surveys of the Brazilian Program to Control and Eradicate Bovine Brucellosis and Tuberculosis.

Based on information obtained in Brazilian states where the serological surveys were carried out and prevalences higher than 2% were observed (e.g. [2]), we have developed a compartmental model [1] to simulate the dynamics of brucellosis in herds of female bovines, to analyse the effects of vaccination strategies.

The model assumptions were: routine vaccination scheme; no vaccinated animals at time  $t = 0$ ; homogeneous mixing for the transmission of brucellosis; and vaccination of newborn calves.

The following results were observed: a) for low vaccination coverage (around 30%), the time to reduce the prevalence to 2%, adopted as a reference, may be long, approximately twice as long as the time observed for a higher coverage (90%); b) the time to reduce the prevalence to levels of 1% or 2%, adequate to start the eradication phase, may reach a decade; c) a high proportion of vaccinated females in calf-bearing age may be reached after approximately 10 years of vaccination, because only newborns are vaccinated.

Based on the model, we intend to estimate the effective vaccination coverage for vaccination against bovine brucellosis, using prevalence estimates obtained from surveys carried out at two different times.

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# ANALYZING HIGHER-ORDER MOMENTS AND STATISTICAL DISTRIBUTIONS IN MODELING NATURAL PHENOMENA

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The probability generating function tells us everything about the distribution of random variables concentrated on the nonnegative integers and moments, associated with random variables are quite informative about their distributions offering valuable insights into probability distributions [1]. The focus of this presentation will be on central moments, as they provide significant information about the distribution's shape and symmetry. For instance, the first two moments of the distribution tell us about the location of the distribution and the spread, or degree of concentration, of that distribution about the mean [2, 3]. For example, the kurtosis moment indicates the thickness of the distribution's tails and the presence of outliers. We will show how moments of a distribution aid in obtaining a deeper understanding of its overall pattern and shed light on specific features that may not be immediately apparent.

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# OPTIMAL CONTROL MODEL OF IMMUNOTHERAPY FOR RECURRENT AUTOIMMUNE DISEASE

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In this work, we develop a mathematical model describing the impact of drug therapies on recurrent autoimmune disease. We describe the immune system interactions at the macroscopic level of self-antigen presenting cells, self-reactive T cells, immunosuppressive cells, and Interleukin-2 (IL-2) cytokines. The drug therapy consists of an intake of Interleukin-2 cytokines which boosts the effect of immunosuppressive cells on the autoimmune reaction. We formulate an optimal control problem relative to the model so that the quantity of both the self-reactive T cells that are produced in the body and the Interleukin-2 cytokines that are administrated is simultaneously minimized based on [1]. Moreover, we perform some numerical tests in order to investigate optimal treatment strategies and the results reveal that the optimal control approach provides good-quality approximate solutions and shows to be a valuable procedure in identifying optimal treatment strategies.

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# ON THE ROBUSTNESS OF RANDOM FORESTS FOR GENOMIC PREDICTION AND SELECTION IN BREEDING STUDIES

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The analysis of real data is often vulnerable to the violation of underlying model assumptions, which can be especially exacerbated by data misspecifications such as errors or outliers. In the context of linear regression, the presence of even a single outlier can disrupt the normality assumption, leading to compromised parameter estimation and subsequent also compromised hypothesis testing. Machine learning methods, including Random Forests, are not immune to data contamination, and existing literature has recognized the need for robust statistical techniques to address this issue [2], particularly in high-dimensional data analysis, which includes variable selection and prediction.

While data contamination can manifest at both the response (*output*) and covariate (*feature*) levels, this project primarily focuses on the former. In this study, we will assess the performance of the classical Random Forest method via simulation, while plugging in robust techniques to enhance its resilience against data contamination. Specifically, we will employ a synthetic animal dataset from the literature [1], introducing various plausible contamination scenarios. This study aims to shed light on the implications of data contamination in genomic prediction and selection for breeding studies, offering insights into possible robust adaptations of Random Forests that will help mitigate the challenges posed by certain types of contamination.

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# TACKLING MALARIA IN INDIA: AN EPIDEMIC MODEL WITH BEDDINGTON-DEANGELIS INCIDENCE RATE AND SATURATED TREATMENT

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Malaria is a life-threatening disease prevalent in many regions of the world, including India, and is primarily transmitted through the bite of infected Anopheles mosquitoes. Prompt and effective treatment is crucial to prevent fatal outcomes. In this study, a modified SIR model is proposed to investigate the transmission dynamics of malaria, taking into account the Beddington-DeAngelis incidence rate and saturated treatment function. Incorporating the nonlinear incidence rate helps in indulging the inhibition measures for both susceptible and infected population in order to resist the disease transmission. The inclusion of a saturated treatment function reflects the practical challenges in regions with limited resources. In our study, we delve into the existence and stability of different equilibria within this proposed model. These equilibria represent states where the disease may be absent or endemic, and understanding their stability provides valuable insights into the dynamics of disease transmission. The basic reproduction number ( $R_0$ ) plays a pivotal role in determining the potential of the disease to spread within a population, when  $R_0$  falls below unity, a backward bifurcation emerges. This implies that simply reducing  $R_0$  to less than one may not suffice to eradicate the disease entirely from the population, demanding additional measures and strategies. The essential model parameters have been estimated using the least-squares method employing the data of various states in India. Furthermore, we conduct sensitivity analysis, leveraging the Partial Rank Correlation Coefficient (PRCC) method, to pinpoint the parameters that wield the most substantial influence over disease prevalence. Our numerical simulations bring our analytical findings to life, providing a visual representation of how varying scenarios and parameter adjustments impact malaria transmission.

## PROCEDURE FOR ANALYZING NETWORKS OF RANDOMIZED BLOCK DESIGNS

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Comparison trials of cultivars (cultivated varieties) tend to be integrated into networks. Joint Regression Analysis (JRA) is one of the most widely used techniques for interpreting randomized block networks. In this study, we will introduce a variant of this technique that increases its flexibility. We will consider the adjustment and validation of test networks. We will then study the problem of specific interactions. It was thus possible to generalize the fundamental results of the JRA to the case where different weights were given to the various tests that made up the network. This generalization is of great practical interest as it allows agrological situations with very different weights to be considered simultaneously, which makes it possible to include fewer representative cases in the test networks without distortion.

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# MODELING CAR-T CELL IMMUNOTHERAPY: INSIGHTS WITH DIFFERENTIAL EQUATIONS

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CAR-T cell immunotherapy is an anti-tumor treatment consisting on extracting immune system cells from a cancer patient's, modifying them to enhance their ability to find and attack tumor cells, and subsequently injecting them back into the patient. The clinical interest in this therapy made it an excellent subject for mathematical modeling. Indeed, on the one hand, there is the availability of quantitative data, as clinical studies regularly measure patients' responses. On the other hand, there is the need to better understand the interactions between the involved cell types and the mechanisms underlying the clinical observations. In this poster, I will present results obtained by our interdisciplinary research groups with Brazilian researchers from LNCC, Instituto do Câncer de SP, and UNIFEI [1, 2]. Initially, I will present a model that describes and explains the multi-phasic response observed in CAR-T cell therapy by identifying and separating the time-scales in the dynamics of CAR-T cells into four phases with distinct behaviors, namely distribution, expansion, contraction, and persistence. Fitting the model to patient data, we identify the underlying biological mechanisms for each phase. The results contribute to a better understanding of the phenomenon and suggest possible markers that can be observed in the short-term but have predictive value for therapy responses in the long-term. I will also present the results of the nonlinear analysis of such model, which exhibits Hopf and Bogdanov-Takens bifurcations. Finally, I'll present a recent extension of the model that consists of adding two different building blocks describing both the phenomena of cytokine release syndrome and resistance to CAR-T cell therapy. While the former is the main toxicity issue in CAR-T therapy and occurs in almost all patients in the short-term, the latter occurs when there is persistence of tumor cells resistant to the therapy, leading to treatment failure in the long-term. Our results show how the application of dynamical systems may provide important qualitative and quantitative insights in real-world medical problems.

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# FITNESS COST IN CONTEXT: DECOMPOSITION USING THE REPLICATOR EQUATION WITH INVASION FITNESSES FOR MULTISPECIES SYSTEMS

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Measuring fitness differences between competitors growing in the same medium is a key challenge across many biological systems, from microbiology to epidemiology, as well as other population or environmental contexts. The most widely used comparative assay for such fitness differences is based on the exponential model for growth of two competitors starting at a ratio of 50:50. However, the fitness cost, estimated as a selection coefficient from this method can vary if the medium conditions where the growth takes place change. In particular, interpretation of such differences becomes difficult when the medium is a complex biotic system composed of other ecological partners, potentially interfering and acting on the competition between the two newly inoculated members of the community. To measure and interpret fitness cost in such context, we propose the use of a replicator equation with invasion fitnesses [1], able to quantify, parameterize and predict relative growth biases between two competitors. We provide the theoretical foundations for such method, and illustrate an application on real data.

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# MODELLING TWO VACCINATION DOSES IN SEIR MODEL

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In this work, we study a SEIR (Susceptible-Exposed-Infected-Recovered) model [1] using stochastic Cellular Automata (CA) [3]. This work is a revision of Ref. [2] where two vaccination doses were included in the SEIR model. To study the effects of vaccination, we consider three different scenarios: (i) unlimited doses, (ii) limited doses into susceptible individuals, and (iii) limited doses randomly distributed overall individuals. (i) represents a situation in which the vaccination supply is unlimited and is applied continuously in the  $S$  population. (ii) simulates a situation in which an amount of vaccine is applied intermittently in different  $S$  groups. (iii) is similar to (ii), however, the vaccine is applied randomly to the whole population. From (i), the results show that the better way to contain the disease spread is to start the campaign earlier and vaccinate as many individuals as possible. We show that the time to start the vaccine campaign is more relevant than the efficacy, delay between first and second doses, and delay between vaccinations in different groups. Our results from (ii) show that the spread of disease is better controlled if the entire vaccination supply is divided into small application campaigns. For the scenario (iii), if the vaccination supply is divided into many applications, the number of wasted doses increases linearly with the number of applications.

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# DEFORMABLE DYNAMICAL SYSTEM APPLIED TO MEDICAL IMAGE ANALYSIS

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Recent advancements in medical imaging have catalyzed a burgeoning field in image processing, driven by the core objective of enhancing medical diagnosis through the analysis of segmented images [3]. Specialized techniques have been devised to pinpoint and delineate distinct structures within medical images. Among these techniques, deformable dynamical systems [1, 2, 4–8], known for their adaptability to image features, are of particular interest. The deformable dynamical system excels in achieving precise object segmentation in images, regardless of complex backgrounds, diverse shapes, and positions, without the need for model training. This work explores coupled deformable dynamical system and their applications in medical imaging, enhancing diagnostic precision and medical condition understanding. By incorporating fractional derivatives into our proposed system, we devised an effective segmentation model tailored for images with multiplicative noise and intensity inhomogeneity. The proposed dynamical system seamlessly combines image denoising and segmentation, allowing us to address noise and inhomogeneity challenges simultaneously. We validated the effectiveness of the proposed dynamical system through experiments on various ultrasound images. The proposed system effectively highlights abnormal tissues in medical images, demonstrating its robustness. Moreover, the proposed system outperforms other existing dynamical systems, showcasing notable enhancements in measures like the Hausdorff distance and the dice similarity coefficient, both visually and quantitatively.

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# STOCHASTIC DIFFERENTIAL EQUATIONS MIXED MODEL WITH INCLUSION OF GENETIC VALUES

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Stochastic differential equations (SDE) models adequately describe the dynamics of individual growth in a randomly fluctuating environment. We have applied it to model cattle weight evolution using real data from the Mertolengo cattle breed. The model parameters are the average transformed weight at maturity  $\alpha$ , a growth parameter  $\beta$ , and the intensity of the effect of environmental fluctuations  $\sigma$ . To incorporate individual characteristics of the animals, we have considered that the model parameters may vary randomly from animal to animal, resulting in SDE mixed models. We have developed SDE mixed models that can incorporate specific individual characteristics of each animal. Here we consider SDE mixed models, allowing  $\alpha$  to be a function of the genetic values of the animal. The main goal is to develop more realistic models where the individual genetic value becomes an important component in the estimated growth curve. We applied the maximum likelihood estimation theory to estimate the model parameters, and present the estimates and the asymptotic confidence intervals of the parameters. We compare our mixed effects with genetic characteristics model with two other models: the mixed effects model without genetic characteristics and the fixed effects model. We found that, for some genetic characteristics, its incorporation on the model provides a significantly better performance in explaining the animals growth curves [1].

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# CONTROLLING INFECTIOUS DISEASES: THE DECISIVE PHASE EFFECT ON A SEASONAL VACCINATION STRATEGY

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In the context of epidemiology, *chaos* is often regarded as an undesirable phenomenon associated with the unpredictability of infectious diseases. As a consequence, the problem of converting chaotic motions into regular motions becomes particularly relevant. In this article, we consider the so-called *phase control method* applied to the seasonally forced SIR epidemic model to suppress chaos. Interestingly, this method of controlling chaos has a clear meaning as a weak perturbation on a seasonal vaccination strategy. Numerical simulations show that the phase difference between the two periodic forces –contact rate and vaccination– plays a very important role in controlling chaos [1].

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# MODELLING INFECTION DYNAMICS IN THE HOST TO DESIGN OPTIMAL TREATMENT

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Mathematical models have been successfully adopted to describe the in-host evolution of infectious diseases and plan the optimal treatment of both viral [1, 6] and bacterial [2, 11] infections.

First, following [7], we consider mpox virus infection and treatment opportunities using drugs such as *cidofovir* and *tecovirimat*, which target different stages of viral proliferation in the host, respectively production and shedding [3, 10, 12]. We model in-host viral infection dynamics by distinguishing between the two processes, so as to explore the distinct effect of the two drugs. We show that reducing the model order via timescale separation leads to the classical target-cell limited model, with a lumped viral proliferation rate depending on both production and shedding. After analysing the qualitative behaviour of the full model, we explicitly introduce the effect of the two drugs, and we formulate and solve an optimal control problem that leverages the model dynamics in order to schedule optimal combined treatments [7].

Then, we consider in-host bacterial infection dynamics and we focus on the phenomenon of antimicrobial resistance [5], which is a particularly alarming global health problem: resistant bacteria are among the leading causes of death worldwide and are projected to cause 10 million deaths each year by 2050 [9, 13]. We briefly discuss a model that describes the onset and proliferation of antibiotic resistance among bacteria in a host, due to mutation and selection under intense antibiotic exposure, as well as the spread of antibiotic resistance in bacterial populations via horizontal transfer [8], which we model as a contagion phenomenon. We also consider the interplay between infection dynamics and the host immune system response. The insight provided by the model can suggest optimal treatment schedules [4, 6].

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# MATHEMATICAL MODELING AND CONTROL OF NEMATODE IMPACT ON BANANA PRODUCTION

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The production of bananas and plantains is one of the most important agricultural activities in many countries around the world. A major constraint for this production is due to the serious damage caused by a nematode called *Radopholus similis*. This nematode spends most of its life cycle in the roots of the banana plant, which makes it quite difficult to control. Our aim is to tackle this issue by a modeling approach.

In this work, a 4-compartment model describing the banana-nematode interactions is formulated. The originality of this model is that we consider both infected root and infesting nematodes which allows variable nematode densities in the roots. First, considering that root infestation is fast compared to the nematode development, we use Tikhonov's theorem on slow-fast systems theory to reduce the dimension of our system.

Then we analyse the reduced model. More precisely, we derive a threshold  $\mathcal{R}$  which classically determines the stability of the disease-free equilibrium and identify backward or forward bifurcations at its threshold value 1. Hence,  $\mathcal{R} < 1$  may not be sufficient to eradicate the disease, as a stable endemic equilibrium may exist.

In the third part, the reduced model is extended to include a control strategy consisting in reducing the root infestation rate. The goal of our control is to maximize the banana production while minimizing the control costs and the final infected biomass that will impact the infestation during the next growing season. The existence of an optimal control is demonstrated and necessary optimality conditions are carefully established. Finally, numerical simulations are presented, using a forward-backward sweep method to solve the optimal control problem, which show the effectiveness of the control.

# A HYBRID ROBUST-WEIGHTED AMMI MODELING APPROACH WITH GENERALIZED WEIGHTING SCHEMES

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The AMMI model and its variations have proven to be excellent in identifying genotypes with specific adaptability and stability under certain environmental conditions, making it a valuable tool in crop improvement breeding programs. However, the presence of atypical data points in crop data, which can be a result of various sources, such as measurement errors, genotype characteristics, diseases, or climate phenomena, may seriously undermine the performance of the AMMI model, as these data points most times interfere with the underlying assumptions of the model (e.g., the violation of the normality assumption) [1, 2]. It is, therefore, crucial that the AMMI model is equipped with statistical tools that enable it to provide reliable inferential results even when small departures from the model's assumptions occur, so that the AMMI model can maintain its effectiveness in supporting decisions related to crop improvement. This work proposes a hybrid AMMI modeling framework (RW-AMMI) that combines robust and weighted algorithms to model the genotype by environment interaction. Additionally, we introduce a comprehensive set of nine weighting schemes for the weighted (W-AMMI; [1]), robust (R-AMMI; [2]), and robust-weighted AMMI (RW-AMMI) models. To evaluate the performance of our proposed approach, we conduct a Monte Carlo simulation considering both contaminated and uncontaminated data with and without heterogeneous error variance, and compare the proposed method against the AMMI, W-AMMI, and R-AMMI models while using the nine weighting schemes. Furthermore, the effectiveness of our approach is validated via a real crop data application.

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# HOW GENETIC TRADE-OFFS AFFECT THE EVOLUTION OF PESTICIDE RESISTANCE: A MODEL APPROACH

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Agricultural pests pose a serious threat to crop yields and can rapidly develop resistance to applied pesticides [8]. This is due to pesticides exerting strong selection pressures that act as selectors for alleles underlying survival against the pesticide [2, 6], until eventually the pesticide is no longer effective. Long-term sustainable agriculture requires pest management strategies that mitigate the effects of resistance evolution while still protecting crops from pest consumption. Biopesticides (biological agents that can act as insecticides) offer promising alternatives to chemical pesticides in that living organisms exert more complex selection pressures on pests [7]. While most pesticide models assume single-gene resistance [5], biopesticides may require pests to evolve polygenic resistance [3] that trade-off with other life history functions [1]. Using a network of digital genes to represent complex polygenic traits and their associations, I observed resistance evolution in different genetic architectures and with imposed genetic trade-offs. Modeling was performed in reevol [4], an R package that uses individual-based modeling to simulate the pest population on a varied landscape. I explored the extent to which genetic associations could impact evolutionary trajectories in complex landscapes with fluctuating selection. My results suggest that the ability to constrain resistance evolution depends on both the strength of genetic associations and the complexity of the landscape. These results can contribute to the development of sustainable biopesticide use.

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# TOPOLOGICAL ANALYSIS ON LEUKAEMIA DATA: PREDICTIONS FOR ALL RELAPSE

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Detecting early relapses in acute lymphoblastic leukemia (ALL) poses a significant challenge in clinical practice. Despite advances in treatments, approximately 20% of ALL patients experience relapses, underscoring the importance of identifying this phenomenon [1]. In this context, the application of mathematical methods to multidimensional data, such as those generated by flow cytometry, has proven to be a promising tool.

This study is an extension of previous research, focusing on combining topological data analysis (TDA) with machine learning techniques [2]. The goal is to identify predictive biomarkers for relapse and classify high-risk patients at the time of diagnosis. This combination seeks not only to improve the accuracy of early relapse detection but also to provide personalized interventions for patients. This approach represents a significant step toward precise and personalized management of ALL, with the aspiration to transform clinical care and enhance outcomes.

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# ORGANISM MOTION IN THREE DIMENSIONS: SYMBOLIC DYNAMICS APPROACH

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We consider the study of motion in biology, through a kinematic geometrical method. We use symbolic dynamics techniques to describe, classify and simulate a variety of types of movements in three dimension using the methods introduced in [1] and [2]. The classification is based on the symbolic dynamics of bimodal families of iterated maps of the interval, namely the kneading invariants. Several global characteristics of the motions are analyzed and a dictionary of typical motions is produced.

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# PROSPECTS OF HIV ELIMINATION AMONG MEN WHO HAVE SEX WITH MEN: A SYSTEMATIC REVIEW OF MATHEMATICAL MODELS

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**Background:** We assess the current state of mathematical models for HIV dynamics among MSM in diverse geographical, socio-economical and age-specific contexts. We systematically reviewed recent modelling studies that assess the impact of interventions on the prospects of HIV elimination among MSM to provide a comprehensive overview of (i) MSM population subgroups and geographical settings where HIV elimination may or may not be achieved, (ii) interventions required, and (iii) HIV elimination definition/criteria used.

**Methods:** EMBASE and MEDLINE were searched between 01/01/2021 until 07/08/2023 using permutations of: HIV, MSM, transgender, bisexual, gay, model, framework, simulation, treatment, prevention, mathematical, transmission and computational. Studies assessing the population-level impact of HIV interventions among MSM using a dynamic mathematical transmission model were included. Data extraction focused on the demographic characteristics of the MSM population, interventions evaluated, public health guidance, elimination criteria, elimination prospects, model structure.

**Results:** Out of 604 articles screened, 37 were eligible and included in the review (Figure 1). Studies focused on Northern America (28 studies), Western Europe (1), East Asia (2), Africa (4) and Central America (2). 8 studies focused on the general MSM population in the country, 29 considered smaller geographical settings such as cities or regions. 10 studies considered population subgroups such as young MSM, and 18 considered different ethnic groups. The majority of studies evaluated interventions such as ART (18) and/or PrEP (17). We identified 8 definitions of HIV elimination, with 15 studies including some definition of elimination. 9 of which were able to successfully

model elimination.

Conclusions: There is an under representation of modelling studies that address HIV elimination among MSM outside Northern America or in specific population subgroups (e.g, young MSM, ethnic minorities, etc.). A common definition of HIV elimination is needed for transmission models to provide meaningful guidance to policymakers on HIV elimination among MSM.

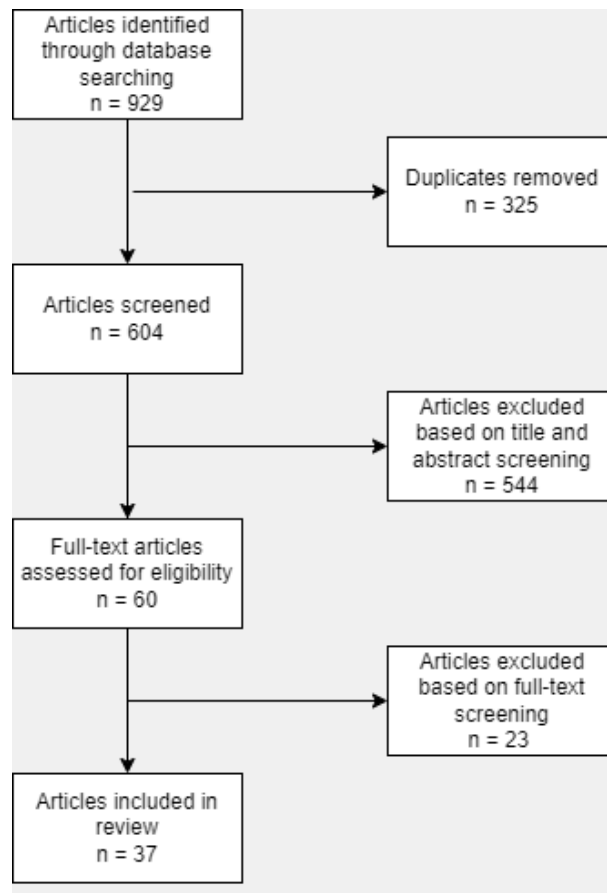


Figure 1: PRISMA flow diagram

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# ANALYSING THE WEIGHT CARRIED BY A SOLDIER, ACCORDING TO HIS FUNCTION, FOR THE DEVELOPMENT OF EXOSKELETONS

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Military personnel are subject to carrying loads that have physiological impacts on their bodies, which may compromise their ability to perform their tasks effectively during operations [1, 3–5, 7]. Challenges in the development of exoskeletons include the specific nature of the equipment carried by soldiers, the variety of associated movements and the physical environment in which these systems must be able to operate. In order to be applied in military operations, an exoskeleton must, among other things, help carry loads to mitigate injuries associated with the weight of the equipment and reduce the level of fatigue [7]. This work is part of the ELITE project, which aims to develop a passive exoskeleton, to reduce the risk of injury to soldiers and increase their readiness level. The following research aims to analyse and characterise the effort of transporting military loads within the infantry section in an operational environment [5, 7, 8]. The sample consisted of 181 soldiers from the Portuguese Army, belonging to the 6th to 12th National Forces mobilised in the Central African Republic from 2020 to 2023. Military personnel were grouped according to their roles within the Infantry section. Considering the weight associated with equipment and weaponry, the aim is to analyse the associated level of overload and compare different functions during military operations. An overall analysis of the force is also considered to understand the proportion of soldiers under stress/ workload during peacekeeping operations in an International environment [5, 6, 8]. Descriptive statistical techniques were used, and resorting to parametric statistical methods for hypothesis testing development, considering the One Way Analysis of Variance (ANOVA) test and Kruskal-Wallis test, both with multiple pairwise comparisons, the study is performed [2]. Therefore, the development of lower limb exoskeletons that can enhance the capabilities of military personnel to meet all operational needs becomes evidente [5, 6]. Future research should analyse other National Contingents detached abroad since the operational environment and mission typologies significantly vary and may impact exoskeleton's performance [1].

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# A GEOMETRIC ANALYSIS OF THE IMPACT OF LARGE BUT FINITE SWITCHING RATES ON VACCINATION EVOLUTIONARY GAMES

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In contemporary society, social networks accelerate decision dynamics causing a rapid switch of opinions in a number of fields, including the prevention of infectious diseases by means of vaccines [3]. This means that opinion dynamics can nowadays be much faster than the spread of epidemics. Hence, we propose a Susceptible-Infectious-Removed epidemic model coupled with an evolutionary vaccination game embedding the National Public Health System effort to increase vaccine uptake. This results in a global system “epidemic model + evolutionary game” [2].

The epidemiological novelty of this work is that we assume that the switching to the strategy “pro vaccine” depends on the incidence of the disease. As a consequence of the above-mentioned accelerated decisions, the dynamics of the system acts on two different scales: a fast scale for the vaccine decisions and a slower scale for the spread of the disease.

Another, and more methodological, element of novelty is that we apply Geometrical Singular Perturbation Theory (GSPT) to such a two-scale model and we then compare the geometric analysis with the Quasi-Steady-State Approximation (QSSA) approach, showing a criticality in the latter. Later, we apply the GSPT approach to the disease prevalence-based model already studied by Della Marca and d’Onofrio in [1] via the QSSA approach by considering medium-large values of the strategy switching parameter.

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# ANALYZING THE INFLUENCE OF EXPLICIT VECTOR DYNAMICS ON DENGUE TRANSMISSION MODELS

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The study of epidemiological scenarios characterized by chaotic dynamics is an important area of research, as it can help us better understand the spread of diseases and make more accurate predictions about disease control measures. The SIRSIR-UV model we propose, which captures differences between primary and secondary infections, is a promising approach to studying these dynamics. The stability analysis of the SIRSIR-UV model using linearization theory and the detailed bifurcation analysis that we have performed are important steps in understanding the qualitative behavior of the system. The formalization of the backward bifurcation using the center manifold theory provides a rigorous mathematical framework for analyzing this behavior. The computation of the Hopf and global homoclinic bifurcation curves, as well as the derivation of analytical expressions for the transcritical and tangent bifurcations, adds to the depth of the qualitative analysis. The observation of chaotic behavior after including seasonal forcing in vector population highlights the importance of considering external factors that can influence disease spread, such as climate and weather patterns. Overall, our study provides valuable insights into the dynamics of infectious diseases by adding vector dynamics. Nevertheless, our findings demonstrate that the bifurcation structures identified in this study align and is comparable with those from the previously analyzed SIRSIR model [1, 2]. Consequently, this research provides valuable insights into the mathematical modeling of dengue fever, highlighting the importance of employing simplifying assumptions, such as only including the implicit vector dynamics, in constructing mathematical models, when no vector control is applied. This assumption allows us to handle complex models more easily, significantly enhancing the manageability of the mathematical analysis and modeling process.

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# SPECIFIC OSCILLATORY ACTIVITY IN THE SIMPLEST NEURON MODEL WITH DISCRETE TIME

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We study complex dynamics of the simplest neuron-like model that is the Chialvo map [1, 4, 5]. We analyze structure of parameter plane, bifurcation lines. Special attention we paid to the Neimark-Sacker bifurcation, torus destruction. We also indicate special regions corresponding to singular discrete chaotic Shilnikov attractors that we consider as a new type of the so-called snap-back repellers (over an unstable focus) [2, 3]. The study of time series was carried out in which there were classified patterns of specific oscillatory activities in the cases when homoclinic orbits to the unstable focus exists and, when such orbits were not yet formed but a strange attractor already exists.

Figure 1a shows example of singular discrete Shilnikov attractor for the Chialvo map. The attractor was developed as a result of torus destruction. The phase portrait allows us to conclude that the phase trajectories come very close to the unstable focus. For a more accurate analysis, enlarged fragments of the attractor were analyzed, which shows that a very small neighborhood of the unstable focus remains unfilled. Corresponding to this attractor time series is depicted in Fig. 1b. Despite of the absence of homoclinic orbit, interval of specific behavior related to the influence of unstable focus can be distinguished in time series (marked with blue color in Fig. 1b).

In the poster we present different types of such attractors, describe scenario of their development, demonstrate attractors appeared on the base of different invariant curves and propose a characteristics which allow to analyse specific oscillatory activity.

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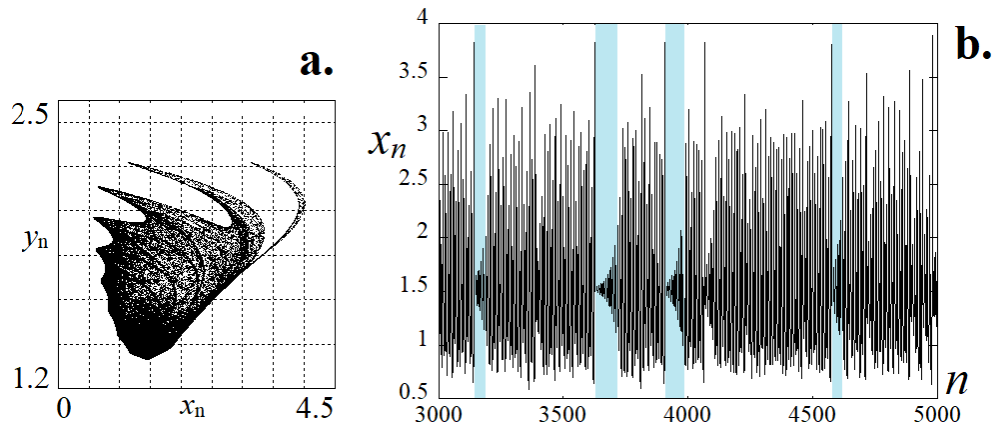


Figure 1: Specific oscillatory activity of Chialvo map. a) Phase portrait of the Chialvo map demonstrating singular discrete Shilnikov attractor; b) corresponding time series with character patterns oscillatory activity

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# CONDENSATION PATTERNS ON SUBSTRATES WITH DIFFERENT DENSITY OF NUCLEATION SITES

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Breath figures (BF) are dropwise patterns that appear on a surface due to the condensation of water vapour [1]. This phenomenon can occur when the surrounding air is supersaturated with humidity at the surface temperature, and will remain as long as the saturation condition is maintained. When condensation takes place on a clean, homogeneous and hydrophobic surface, BF can show up to six stages: 1) Initial nucleation. 2) Isolated droplet growth due to vapour absorption, when the distance between droplets is much larger than their radii. At this stage the droplet radius grows as  $t^{1/2}$ . 3) Vapour absorption with overlapping of concentration profiles around each droplet. In this situation, the interaction between droplets through the atmosphere reduces the absorption of individual droplets and the average population radius increases as  $t^{1/3}$ . 4) Coalescence-dominated growth. When two or more droplets come into contact, they coalesce to form a new, larger droplet and, as these events become more frequent, the average droplet radius will grow as  $t^1$ . 5) New droplet nucleations, in the empty spaces left by previous coalescences. 6) Deformation and/or detachment of large droplets by gravity. Some of these stages may overlap or be absent depending on the particular experimental conditions.

In this work, we report experimental results on the condensation of water vapour on substrates with different density of initial condensation nuclei. The substrates are glasses, clean or coated by immersion in a solution of octadecyltrichlorosilane in hexamethyldisiloxane which leaves the surface with a hydrophobic behaviour accompanied by impurities that promote nucleation [2]. The results of the clean substrate and three cases with coatings with different nucleation densities are analyzed by comparing the surface droplet density and the average radii. We observe that high initial densities produce fast growth dynamics, but with smaller droplets on average.

The dynamics observed in all cases has been rationalised using a growth model that assumes that in the first instants tiny randomly distributed droplets are formed. The validity of this hypothesis has been verified by checking that the positions of the condensation nuclei show complete spatial randomness at different scales, using the Ripley-Besag L-function. For each substrate, an initial density and a characteristic time were calculated and used to adimensionalise the spatial and temporal variables. After rescaling, the curves corresponding to each substrate collapse into one curve (except for very long dimensionless times, where new nucleations occur). In conclusion, the evolution of the condensation pattern is determined by the initial density of nuclei, and the scaling constants (even if calculated for short timescales) describe what happens at longer timescales [3].

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# CONTROLLABILITY OF NEUTRAL HILFER SOBOLEV-TYPE DIFFERENTIAL SYSTEM OF ORDER $\varrho \in (0, 1)$ VIA MEASURE OF NONCOMPACTNESS

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This paper aims to establish a set of sufficient conditions for the existence and exact controllability results for the neutral Sobolev-type differential system using Hilfer fractional derivative [3] with nonlocal initial conditions in a Banach space. We investigate the existence of a mild solution for the proposed control problem and then we derive the exact controllability results. For this purpose, the neutral Hilfer Sobolev-type differential system of order  $\varrho \in (0, 1)$  is transferred into an equivalent fixed point problem via an integral operator and the Sadovskii's fixed point approach is applied. We will establish the theoretical framework necessary for understanding the controllability properties of the differential system under consideration and present key results that cast light on the conditions under which exact controllability can be achieved. The set of sufficient conditions is established by using the concept of fractional calculus [5], the theory of measure of noncompactness [1, 2], propagation family of linear operators [4] and fixed point approach [6]. Finally, the application of the proposed results is presented by giving an example.

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# EXISTENCE OF CYCLIC TREATMENT ROUTINES ON CANCER ADAPTIVE THERAPIES

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Cancer therapy has witnessed a transformative shift in recent years with the advent of adaptive models that enable the tailoring of treatment strategies to the unique characteristics of individual patients [1]. A central concept on adaptive therapies is that instead of trying to eradicate the tumor, one controls its composition by exploiting the competition between different cell types, preventing treatment-resistant cells from emerging [3]. That being said, the success of this sort of treatment relies heavily on the capacity of designing treatment routines that will keep the tumor composition stable and, to that end, extensive mathematical and computational modeling is required.

Due to the key role competition takes in these therapies, competitive models such as Lotka-Volterra [5] and replicator equations [2] have been used to study the dynamics of malignant cells within the tumor under different treatment regimens and determine how they should be scheduled in order to have a cyclic cell composition. Up to this moment we have been working with planar versions of both Lotka-Volterra and replicator equations, i.e. two cell types for Lotka-Volterra and three cell types for replicator, but we intend to increase the number of cell types. In this simplified setting, we derive sufficient conditions for which said cycles can be designed from a given starting point and propose a method to do so. We also present numerical results on the stability of the cycles in each model and discuss how they affect stochastic versions of the models [2, 4] that would better represent a clinical trial.

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## RISK CLASSIFICATIONS FOR SEVERE COVID-19; THE EUROPEAN, DUTCH, AND NORWEGIAN APPROACHES

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Age and pre-existing chronic conditions continue to be the most relevant risk factors for severe COVID-19 outcomes such as hospitalization. These risk factors largely determine which individuals are targeted by post-pandemic SARS-CoV-2 vaccination campaigns. Currently, there is a European guideline for risk classification by the European Centre for Disease Prevention and Control [1], but individual European countries have developed their own guidelines, introducing the potential for discrepancies. Our objective is to compare the European, Dutch [3], and Norwegian [2] risk classifications for severe COVID-19 by risk due to chronic conditions.

Dutch and Norwegian national population registry data from 2020-2021, linked on individual level, were analyzed with regard to the general population and COVID-19 hospitalizations by risk classification. Countries have access to different data sources. Chronic conditions were defined using ICD-10 codes in the European and Dutch classification, and ICD-10 and ICPC-2 in the Norwegian. The populations of both countries, as well as the hospitalized population, were categorized as high, moderate, or low-risk based on their chronic conditions according to the European, Dutch, and Norwegian risk classification.

The European classification covers a broader range of chronic conditions than national classifications from Norway and the Netherlands. Consequently, a larger proportion of both the general and hospitalized populations fall into the high-risk category in the European classifications compared to the national ones (Figure 1). Among Dutch and Norwegian hospitalizations, 44% and 41% were classified as high-risk respectively, and 2% and 3% as moderate-risk according to the European classification. In contrast to the Dutch and Norwegian classification, that classified 16% and 13% as high-risk and 35% and 32% as moderate-risk respectively.

To conclude, there are substantial differences between European, Dutch, and Norwegian risk classifications for severe COVID-19, which have important implications for vaccination strategies. European classification indicates more people are at high-risk and need to be vaccinated.

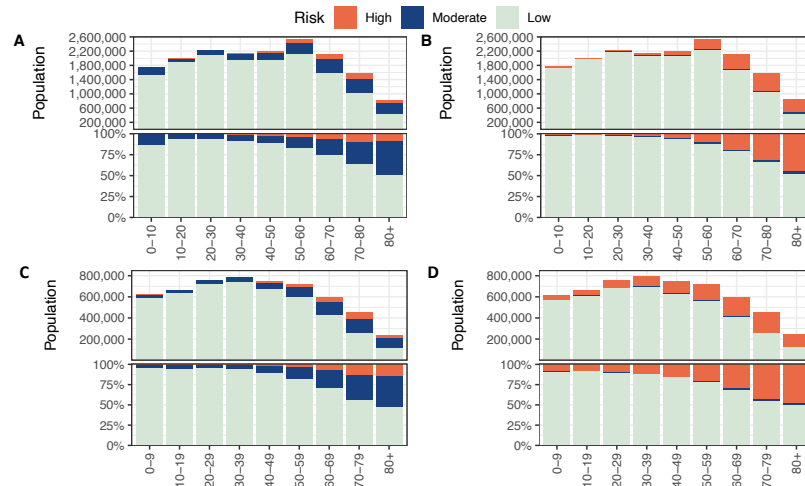


Figure 1: Overview of population in January 2020 for the Netherlands (Panels A-B) and Norway (Panels C and D). Panel A uses the Dutch risk classification, Panel C uses the Norwegian risk classification, and Panels B and D use the European risk classification.

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# A HIGHER ORDER FINITE ELEMENT METHOD FOR COUPLED REACTION DIFFUSION MODELS ARISING IN BIOLOGY

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The coupled reaction-diffusion models arise frequently in various real-life scenarios, particularly in biology. For instance, formation of complex spatial patterns from tissue interactions is modelled through coupled reaction-diffusion equations [1, 2]. Due to nonlinear nature of such models, the analytical solutions are not easily found. Therefore, the advanced methods capable of providing accurate approximations are much sought after. The Galerkin finite element method uses polynomials to approximate solutions, and it is known to yield more accurate results when used with quadratic basis functions instead of linear basis functions [3]. In this article, therefore, we approximate the following coupled reaction-diffusion model using finite element method with quadratic basis functions.

$$u_t - d_1 \Delta u = f(u, v), \quad (1)$$

$$v_t - d_2 \Delta v = g(u, v), \quad (2)$$

where  $u$  and  $v$  are unknowns and  $d_1$  and  $d_2$  are diffusion coefficients. Further, a scheme is proposed by combining the Crank-Nicolson and the predictor-corrector methods for the time discretization. Some numerical examples are considered to illustrate the accuracy and efficiency of the proposed scheme. It is found that the scheme is third-order convergent, whereas the order of convergence with linear basis functions as obtained in the literature is two [4].

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| Cinzia Soresina                | University of Trento                              | Italy    | CT   |
| Cristina Januário              | Instituto Superior de Engenharia de Lisboa        | Portugal | P    |
| Cristina Dias                  | Instituto Politécnico de Portalegre               | Portugal | P    |
| Dana Lauenroth                 | Max Planck Institute for Evolutionary Biology     | Germany  | MS   |
| Diana Paulina Taipe Hidalgo    | Universidad Complutense de Madrid                 | Spain    | CT   |
| Diego Samuel Rodrigues         | University of Campinas                            | Brazil   | CT   |

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|------------------------------|--|----------------------|----|
| Elena Almaraz Luengo         | Universidad Complutense de Madrid                              | Spain                | CT |
| Elizabeth Howell             | Maxwell Institute  | UK                   | CT |
| Enrique Chipicoski Gabrick   | State University of Ponta Grossa                               | Germany              | P  |
| Eunha Shim                   | Soongsil University  | Republic of Korea    | CT |
| Fearghus Downes              | Atlantic Technological University                              | Ireland              | CT |
| Fernando Córdova-Lepe        | Universidad Católica del Maule                                 | Chile                | CT |
| Francesca Acotto             | Università di Torino   | Italy                | CT |
| Gergely Röst                 | University of Szeged   | Hungary              | MS |
| Geza Odor                    | Research Institute for Materials Science and Technical Physics | Hungary              | MS |
| Ghilmana Sarmad              | United Arab Emirates University                                | United Arab Emirates | CT |
| Giulio Pisaneschi            | University of Pisa   | Italy                | CT |
| Grzegorz Graff               | Gdansk University of Technology                                | Poland               | CT |
| Gustavo Carrero              | Athabasca University   | Canada               | CT |
| Hee-Dae Kwon                 | Inha University  | Republic of Korea    | CT |
| HongSung Jin                 | Chonnam National University, Korea                             | Republic of Korea    | A  |
| Hyundae Lee                  | Inha University  | Republic of Korea    | A  |
| Ilse Westerhof               | University Medical Center Utrecht                              | Netherlands          | P  |
| Iulia Martina Bulai          | University of Sassari  | Italy                | MS |
| Jack Woodruff                | University of Sheffield  | UK                   | A  |
| Jacob Aiden Roberts          | University Medical Centre Utrecht                              | Netherlands          | P  |
| Jacques Hermes               | Albert-Ludwigs Universität Freiburg                            | Germany              | CT |
| Jesús Bellver Arnau          | Centre d'Estudis Avançats de Blanes                            | Spain                | CT |
| Joana Ribeiro Barbosa Cabral | University of Minho  | Portugal             | CT |
| Jonathan Forde               | Hobart and William Smith Colleges                              | USA                  | MS |
| Jonathan Hamley              | University of Bern   | Switzerland          | CT |
| Jorge das Neves Duarte       | Instituto Superior de Engenharia de Lisboa                     | Portugal             | A  |
| Juan Antonio Magalang        | University of Bern   | Switzerland          | CT |

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|---|--|-------------------|------|
| JYOTIRMOY ROY                             | Indian Institute of Technology Kanpur  | India             | CT   |
| Kamilia Azib                              | University of Minho  | Portugal          | P    |
| Kaue Rodrigues Alves                      | Basque Center for Applied Mathematics  | Spain             | A    |
| Kemayou Mangwa Frank Bagio                | Université Côte d'Azur   | France            | P    |
| Laid Boudjellal                           | University of Minho  | Portugal          | CT   |
| Laura Mansier                             | University of Amsterdam  | Netherlands       | CT   |
| Lluís Hernández Navarro                   | University of Leeds  | UK                | MS   |
| Maarten Nicolaas de Jong                  | Delft University of Technology   | Netherlands       | CT,P |
| Sten Madec                                | University of Tours  | France            | CT   |
| Magda Stela de Jesus Rebelo               | NOVA School of Science and Technology  | Portugal          | A    |
| Mahmoud A. Ibrahim                        | University of Szeged   | Hungary           | CT   |
| Manon de la Tousche                       | Sorbonne Université  | France            | CT   |
| Marcel FANG                               | National Institute for Research in Digital Science and Technology                    | France            | CT   |
| Marcos Amaku                              | Sao Paulo University   | Brazil            | P    |
| Marian Petrica                            | Institute of Mathematical Statistics and Applied Mathematics of the Romanian Academy | Romania           | CT   |
| Mariana Riera Ramos                       | Instituto Superior Técnico   | Portugal          | P    |
| Marine Courtois                           | National Institute for Research in Digital Science and Technology                    | France            | CT   |
| Marta Pardo Araujo                        | CEAB-CSIC  | Spain             | CT   |
| Martim Geraldes                           | University of Lisbon   | Portugal          | CT   |
| Matheus Hansen Francisco                  | NOVA School of Science and Technology  | Portugal          | A    |
| Megan Oliver                              | University of Sheffield  | UK                | CT   |
| Mennatallah Gouda                         | Utah State University  | USA               | CT   |
| Miguel A. Zavala                          | Universidad de Alcalá  | Spain             | A    |
| Miguel Tomás Beirão Antunes Moreira Braga | NOVA School of Science and Technology  | Portugal          | P    |
| Minhye Kim                                | Kyungpook National University  | Republic of Korea | A    |

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|-----------------------------------|--|--------------------|------|
| Monica Salvioli                   | Maastricht University  | Netherlands        | CT   |
| Nataliya Stankevich               | HSE University   | Russian Federation | A    |
| Nelson Tchingui Jamba             | Universidade de Évora  | Angola             | P    |
| Nikola Popovic                    | University of Edinburgh  | UK                 | MS   |
| Nir Gavish                        | Israel Institute of Technology   | Israel             | CT   |
| Panagiotis Kaktamanos             | University of Edinburgh  | UK                 | MS   |
| Paolo Freguglia                   | University of L'Aquila   | Italy              | A    |
| Patrícia Alexandra Robalo Antunes | University of Beira Interior   | Portugal           | P    |
| Paul Georgescu                    | Technical University of Iasi   | Romania            | A    |
| Paula Cristina Pires Simões       | Academia Militar Portuguesa  | Portugal           | P    |
| Peter Boldog                      | Wigner Research Centre for Physics   | Hungary            | CT   |
| Peter Rashkov                     | Bulgarian Academy of Science   | Bulgaria           | MS   |
| Philipp Städter                   | Leibniz Institute for Natural Product Research and Infection Biology           | Germany            | CT   |
| Pierre-Alexandre Bliman           | National Institute for Research in Digital Science and Technology              | France             | A    |
| Preeti                            | Atal Bihari Vajpayee Indian Institute of Information Technology and Management | India              | P    |
| Ricardo Castelhana                | NOVA School of Science and Technology  | Portugal           | A    |
| Robert Allen                      | University of Nottingham   | UK                 | CT   |
| Roberta Coletti                   | NOVA School of Science and Technology  | Portugal           | A    |
| Rocío Picón González              | Universidad de Cádiz   | Spain              | P    |
| Rubén Blasco-Aguado               | Basque Center for Applied Mathematics  | Spain              | CT   |
| Ruddy Eglee Urbina Sulbarán       | University of Navarra  | Spain              | P    |
| Ruslan Mukhamadiarov              | Ludwig Maximilian University of Munich   | Germany            | MS   |
| Ryosuke Omori                     | Hokkaido University  | Japan              | CT   |
| Sabrina Spigno                    | University of Naples Federico II   | Italy              | A    |
| Sara Sottile                      | University of Trento   | Italy              | MS;P |

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|-----------------------------|---|--------------------|----|
| Soumitra Pal                | Banaras Hindu University, Varanasi                                | India              | CT |
| Stanca Ciupe                | Virginia Tech   | USA                | MS |
| Subit Kumar Jain            | National Institute of Technology Hamirpur                         | India              | P  |
| Subrata Dey                 | Indian Institute of Technology Kanpur                             | India              | CT |
| Suman Chakraborty           | Friedrich Schiller University                                     | Germany            | MS |
| Suzanne Touzeau             | National Institute for Research in Digital Science and Technology | France             | MS |
| Syed Abbas                  | Indian Institute of Technology Mandi                              | India              | A  |
| Tatiana Sannikova           | Marchuk Institute of Numerical Mathematics RAS                    | Russian Federation | CT |
| Thibault Malou              | National Institute for Research in Digital Science and Technology | France             | CT |
| Thomas Tunstall             | University of Exeter  | UK                 | MS |
| Tomás Ferreira Amaro Freire | Instituto Superior Técnico  | Portugal           | P  |
| Torsten Lindström           | Linnaeus University   | Sweden             | CT |
| Uwe C. Tauber               | Virginia Tech   | USA                | MS |
| Vanda M. Lourenco           | NOVA School of Science and Technology                             | Portugal           | P  |
| Vassil M. Vassilev          | Bulgarian Academy of Sciences                                     | Bulgaria           | A  |
| Yongkuk Kim                 | Kyungpook National University                                     | Republic of Korea  | A  |
| Yuri Garcia Vilela          | Federal University of Minas Gerais                                | Brazil             | P  |

