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Projecting cell polarity into the next decade

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Introduction

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Cell polarity—the intrinsic property of cells to take different shape, migration or growth patterns suited to their function—is one of those things intuitively we are all aware of. It is part of our collective imagination, and indeed if prompted all of us immediately think of cells as anisotropic. It is an absolutely paramount property of life that dictates how all cells divide, grow, populate and form all healthy tissues and organs, and as such it holds the key to understanding how many human diseases develop and can be cured.

To trace the origins of cell polarity, one could probably go back to the birth of the cell theory itself with the first observations of cells under a light microscope. For instance, Robert Hooke's original 1665 microscopy drawings [1] display cork 'cells' that contain global asymmetries, which one could take as a first evidence of polarity (figure 1*a*). That feature is even more obvious from the monumental work that ensued by Antoni van Leeuwenhoek, whose detailed microscopy drawings—collected over five decades from the 1670s to the 1720s in this very journal, *Philosophical Transactions of the Royal Society*—demonstrated that cells come in innumerable morphological varieties that mirror in number their functional diversity [2–5] (figure 1*b–e*).

However, the concept of 'polarity'—which might have originated in simple experiments with inverted plants carried out before Christ by Greek botanists [6]—was only applied as a scientific, biological term for the first time by George J. Allman in 1864, who used it for describing how a segment of the hydroid *Tubularia* regenerates a new anterior end on the side of the segment that lies nearest the old anterior end, and a new posterior end on the side of the segment that lies closest to the old posterior end ([7], cited in [8]). From then, it gradually became widespread and studied across plants and animals, eventually also unicellular developing organisms like eggs and spores [6], and championed by physiology heavyweights such as Jacques Loeb and Thomas H. Morgan, who helped cement it as a fundamental and universal biological phenomenon [9].

The earliest recorded PubMed entry of 'Cell Polarity' in the title of a publication is in 1926, describing work on the polarity of cell division in rabbit fibroblasts [10], followed by another in 1939, on polarity and differentiation [11]. Since then the field of cell polarity has been a growing area of research with over 12 000 online listed publications today (figure 2). Looking at the most common new keywords in the publication titles—using for example the free online tool AntConc (http://www.antlab.sci.waseda.ac.jp/)—one can retrace the most prominent trends of progress in the field per decade: 1920s, cell division; 1930s, differentiation; 1970s, development, mouse, chick, embryo; 1980s, gene, membranes, transport mechanisms, microtubule cytoskeleton, epithelia, rat, humans; 1990s, protein, secretion, receptors, factor localization, actin, sorting, kinase, yeast, neurons, *Drosophila*, MDCK, growth; 2000s to present, signalling, asymmetric, migration, PAR, cdc, Wnt, planar, cancer, *C. elegans*.

These testify how this growing field has gone from descriptive to molecular and mechanistic, from anecdotal and divergent to universal, and from biological to biomedical and therapeutically relevant.

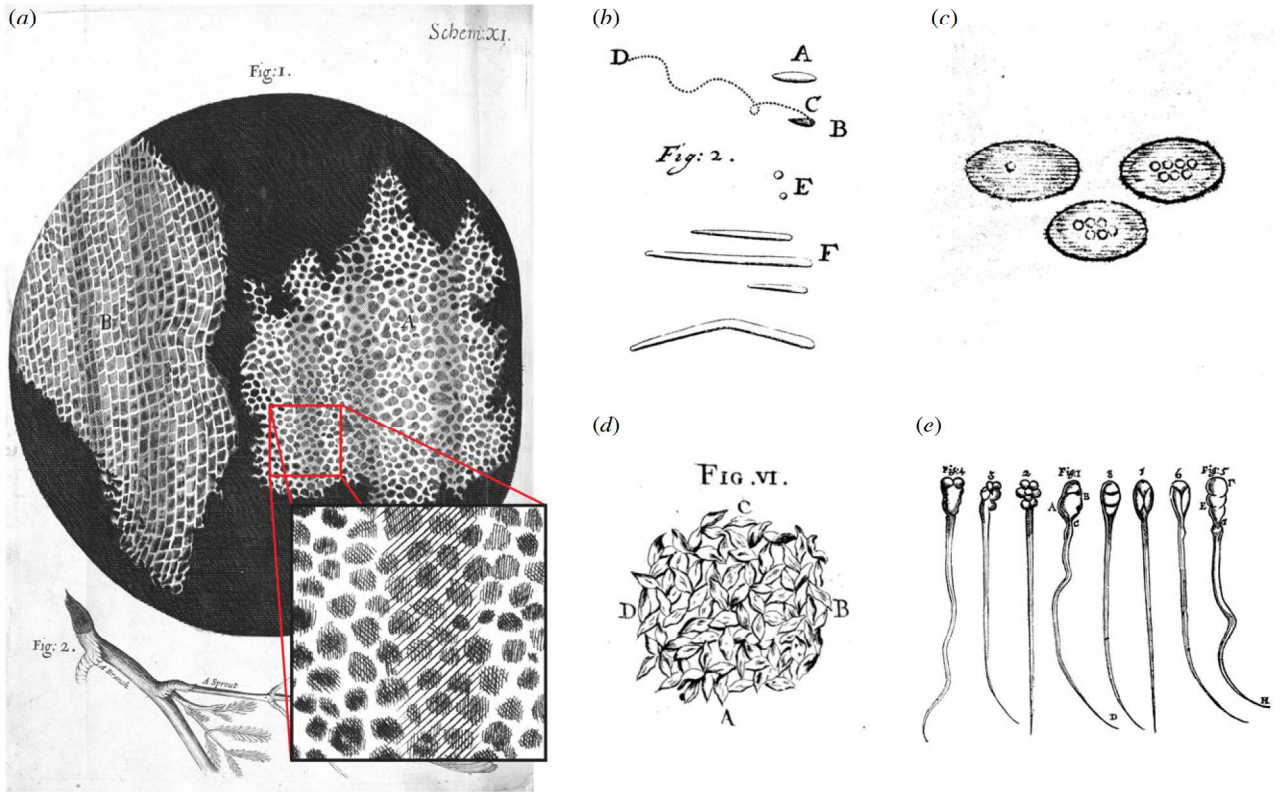

Figure 1. The intrinsic global polarity of cells is already implicit in the earliest microscopic drawings. (*a*) Robert Hooke's original drawing of cork cells from 1665 (bottom right: inset magnification shows varying cell geometries). (*b–e*) Various microscopy cell drawings from Antoni van Leeuwenhoek: (*b*) 'animalcula'—possibly bacteria—from van Leeuwenhoek's teeth, 1693; (*c*) red blood cells from fish with labelled nuclei, 1682; (*d*) dry epithelial cells from van Leeuwenhoek's foot callus, 1722–1723; (*e*) dog (four rightmost) and rabbit (four leftmost) spermatozoa, 1677–1678. Adapted from [1–5]. All images © the Royal Society. High resolution scans of (*a*) and (*c*) courtesy of Joanna Hopkins, Picture Curator, the Royal Society. (Online version in colour.)

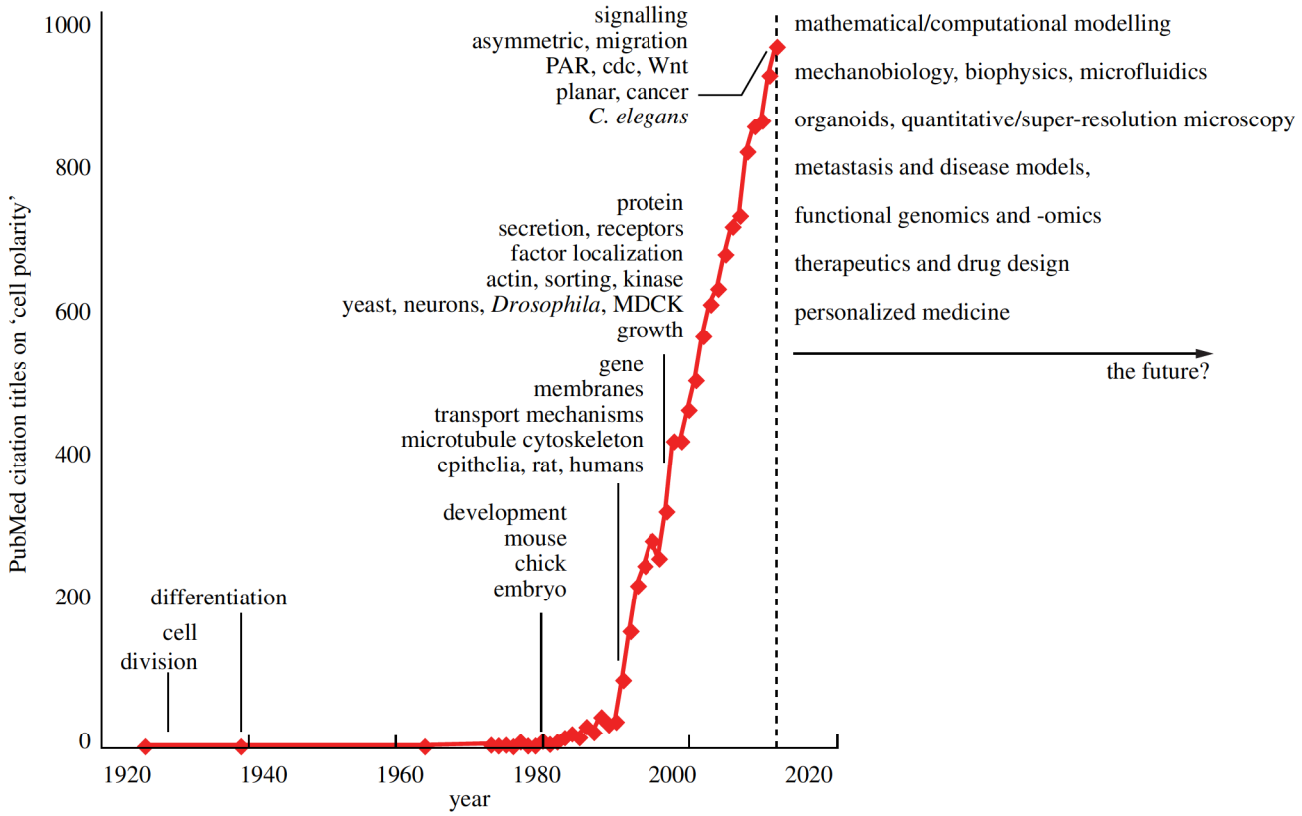

Figure 2. Whence and whither? The graph represents the number of PubMed publication titles with the words 'cell polarity' per year, from 1926 to present. Prominent keywords for each decade are shown above the graph. Future trends are indicated, based on the current research in the field showcased at two recent Royal Society Scientific Discussion Meetings on the topic, as well as on the articles found in this issue. Statistics were extracted freely from the US National Library of Medicine database PubMed (http://www.ncbi.nlm.nih.gov/pubmed/). (Online version in colour.)

So where is the field going?

We recently organized two Royal Society Scientific Discussion Meetings on cell polarity, to get a notion of the Zeitgeist of the research community and seek an answer to that question by canvassing the views of leaders in the field. This Theme Issue of *Philosophical Transactions of the Royal Society B*, which contains contributions from some of those researchers, embodies partly that answer and reflects the diversity and exciting progress of this timeless and timely field of endeavour.

It starts with a preface from Lewis Wolpert, who asks the provocative question of polarity versus asymmetry, then follows a collection of manuscripts exemplifying trends likely to shape the field in the decade to come. First is a review on the evolution of mathematical models of cell polarity regulation, from minimal mechanistic ones to complex molecular four-dimensional models [12]. This is followed by two research articles [13,14] and five reviews [15–19] on the mechanisms of symmetry breaking and polarity establishment, touching upon the point raised by Wolpert on the connections between these events. Next, a research article and a review deal with the adaptive signalling networks regulating cell migration [20,21]. Finally, four reviews and a research article focus on the role of cell polarity in cancer formation and especially on metastasis [22–26]. An emerging picture is that cell polarity establishment as well as loss or re-establishment of polarity all have roles in cancer development. As metastasis is the major cause of cancer-related death and metastasis needs migration, which requires polarity establishment, many see that polarity establishment could be an important drug target for cancer treatment.

New and forthcoming concepts and approaches in cell polarity research are discussed, and the importance of cell polarity establishment and re-establishment during cancer is a major highlight. Asymmetry establishment, the role of feedback loops and mechanosensing are also discussed and tools spreading in the field, such as functional genomics approaches, biophysical methods, mathematical modelling, computer simulations, organoids and disease models, quantitative and super-resolution microscopy and microfluidics, are introduced.

Finally, the scope of the issue is also highlighted in its cover. It encapsulates our firm belief that increased interdisciplinary cross-breeding among researchers in cell polarity working with diverse models and organisms is key to developing future therapies and drugs against cell polarity-related diseases.

We hope you enjoy this issue.

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