Manifesto for a Cytoplasmic Revolution

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The goals of this extremely readable and cleverly illustrated book are not modest. Gerald Pollack, professor of bioengineering at the University of Washington, begins by demeaning textbook renditions of cell biology as analogous to Ptolemaic epicycles. These renditions, he claims, are pedantic minutiae to be over-thrown by a Copernican revolution that will leave us with a "new, unifying approach to cell function," one unencumbered by the mass of molecular details usually trolled by biologists in search of mechanisms.

Cells, Gels and the Engines of Life is an eloquent and accessible statement of a heresy that has smoldered at the fringe of orthodox biology for about 30 years. Having often watched eyes glaze over as I try to preach that cytoskeletal polymer phase transitions are important for cell motility, I was ready to embrace a work that unabashedly and eloquently celebrates cells as polymer gels, without resorting to a single mathematical equation. Too little imagination, I have thought, has been applied to thinking through possible ways that biological gels (such as fibrin, collagen. elastin, and actin) influence human physiology and disease.

After challenging the notion that pumps and channels manage solute gradients across a continuous membrane envelope at the cell surface, Pollack reviews the physical chemistry of water and solutes and the effects of immobile polymers on this chemistry. He claims that these interactions are sufficient to explain solute partitioning between cells and the outside world. The principles of structured water and the power of cytoskeletal liquid-gel phase transitions then provide specific explanations for a wide range of cellular phenomena: the neural and muscular action potential, the exportation of packaged secretions, cell locomotion, movements produced by molecular motors, mitosis, and muscle contraction. Energy in the form of complex phosphates, rather than running scores of little machines on a highly individualized basis, works primarily to order of layered water.

Though Pollack's interpretations challenge conventional wisdom, such challenges should always be welcome. Sometimes a re-formation must await the right instigator at the right time. Has the time come? Will cell physiologists now throw away their patch clamps and impale themselves on their micropipettes? Probably not. Most cell biologists hardly think of cells as bags of diffusing solutes. Others, studying signal transduction reactions or mining genetic databases for new drug targets, wouldn't necessarily be less productive in their pursuits if they did. Pollack believes that the elegant and powerful equilibrium phase transitions discovered by the late Toyoichi Tanaka, which can do amazing work in applications ranging from disposable diapers to artificial muscles, have similar effects in living cells. A tiny variation in pH, for example, can generate huge changes in volume of a charged polymer gel. The application of these reactions to biology, however, steps into the pitfall of reasoning by analogy. Although physics reigns over biology, biological processes operate far from physical and chemical equilibria. Temperature shifts can expand or contract metal springs, and liquid running down a hill can look like a migrating ameboid cell, but muscle contraction and cell locomotion simply don't work the same way as these similar-looking phenomena.

Biologists' imposition of molecular rigor of chemistry on the underlying polymer physics of cells has predictably multiplied the ingredients in the system. But I believe that these details, rather than being annoying distractions, are the essence of biological meaning. Whereas molecular interactions and molecular machines clearly operate within a context of bulk polymers that strongly influence the aqueous and ionic environment, the subtle differences in molecular interactions and molecular machines are what make yeasts different from humans and humans different from one another. Perhaps someday we may define these interactions in terms of water and ions, but at the moment the fun and profit are in the molecular specifics.

Defenders of pumps, channels, and molecular details will notice that most of the references Pollack cites to support his claims are elderly. I suspect that many of the specific arguments are susceptible to the accusation that the author cherry-picks evidence (a technique not restricted to the heterodox). Mainstream biologists can cite findings from modern molecular genetics that illustrate how genetic point mutations that subtly affect macromolecular functions powerfully influence a cell's behavior without grossly disrupting the structure of its polymers. One example among many is the wobbly weaver mouse, which lacks cerebellar neurons because of a mutation in the pore region of a potassium channel. Another is the ability of the blood's complement system to poke holes in and destroy red blood cells: a tribute to the existence of coherent cell membranes and the basis of an entire industry devoted to assuring that blood transfusions are immunologically compatible.

Although I enjoyed reading Cells, Gels and the Engines of Life, and I believe that it is valuable for directing one's thinking toward cellular machinery in a broad and interesting way, it didn't deliver what I was seeking. I hope that having gotten this book out of his system, Pollack will now write an equally readable but more balanced fundamental cell biology (or physical chemistry) text for students of the health professions. A well-illustrated, lively description of cell biology (without equations) that conveys the big picture about the contributions of physical principles to cellular function might help practitioners better appreciate the beauty and practical relevance of biological science and feel less intimidated by its complexity. These practitioners might then be willing to use their credibility as healers with the public to promote the value of research to our political leaders.