Editorial

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Timeless order

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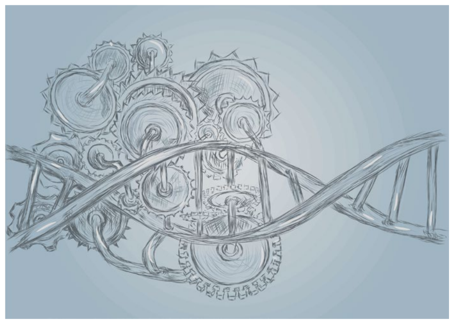
Eighty years on from the publication of Erwin Schrödinger's interdisciplinary analysis on the origin of order in living organisms — *What is Life?* — we look at how physicists and biologists are approaching the topic today.

Based on a series of lectures Erwin Schrödinger delivered at Trinity College Dublin, his book *What is Life? The Physical Aspects of the Living Cell* inspired biologists and challenged the expectations of physicists on the underlying working principles of living systems. It was published in 1944 and explored whether the statistical approach of physics can account for cellular processes in living organisms. On the occasion of its 80th anniversary, we reflect on its efforts to link biology and physics and on how scientists study these phenomena today.

Physical laws rely on order, or "order from disorder", as Schrödinger put it[1]. Although Isaac Newton's description of the planets had become a paradigmatic case of determinism by the time Schrödinger delivered his lectures, advances in statistical physics and quantum mechanics had shown that at the microscopic level lay disorder and indeterminism. Take atoms in a gas, for example. They move randomly, producing varying degrees of thermal disorder; but when averaged over large numbers, their macroscopic properties can be described by exact physical laws. One typical example is diffusion: although it can be modelled as a structured process, it stems from random Brownian trajectories of individual components.

But living and inanimate matter differ in their statistical behaviour. Whereas physicists would expect "a big number of atoms controlling the whole system"[1], an organism's biology is controlled by a relatively small number of atoms making up its genetic material. In this way, genes generate "order from order" by passing hereditary information down a lineage. This concept, together with X-ray crystallography experiments by Rosalind Franklin, inspired James Watson and Francis Crick and led to the discovery of DNA structure and its central role in living cells.



Today, scientists know there is more to order and disorder than meets the eye. For example, cell signalling is coordinated by intrinsically disordered proteins (or regions within proteins). This so-called disorder–function paradigm[2] changed the traditional view on structure–function relationships and proved that proteins can carry out cellular functions without three-dimensionally stable folded structures.

But how is an organism able to maintain any form of collective order given the thermal disorder at its core? In his essays, Schrödinger evoked clockwork as a metaphor. In the same way heat disorder is unable to disturb the solid constituents of clockwork enough to alter its movement, an organism's workings rely on an "aperiodic crystal" (now known as DNA) which is held together by forces that are strong enough to resist thermally driven structural variations. Beyond this illustrative explanation, it all comes down to entropy.

Living systems operate in non-equilibrium conditions to reduce their entropy. This is an organism's secret to avoid the second law of thermodynamics and a relentless descent into a more disordered form. In the pursuit of homeostasis — the dynamic, self-regulating state characteristic of life by which organisms maintain stability against changing conditions — biological systems depart from the physicist's probabilistic framework, which describes inanimate matter, leading to an inherently informational and more deterministic picture.

This mechanism is at play during cellular processes that are paramount to life, such as cell metabolism and the transport of solutes across the cell membrane[3]. Entropy reduction also occurs via the formation of biomolecular condensates and information storage in DNA[3]. Biomolecular condensates are membraneless structures present in eukaryotic cells — cells that contain a nucleus — which perform a range of functions from controlling the rate of chemical reactions to enabling homeostatic cellular responses. Their formation is driven by extracellular stimuli, placing them at the centre of information exchange between a cell and its environment[4].

Today's equivalent of Schrödinger's clockwork-inspired view on biological order may be found in mechanobiology. This field is concerned with the mechanical rather than the thermodynamic aspects of the interaction between living cells and their environment. The processes by which cells sense external mechanical signals and translate them into a response — mechanosensing and mechanotransduction — govern crucial cellular behaviour, such as motility and tissue morphogenesis[5].

From understanding the role of DNA as information carrier and of structure-dependent protein functionalities, to non-equilibrium thermodynamics, biomolecular condensates and mechanobiology, the connection between physics and biology proposed by Schrödinger continues to go from strength to strength. The idea of bringing two seemingly opposite disciplines together was a crucial step to advancing our understanding of life. It has already generated a number of interesting fields that promise to thrive for years to come.

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References

1. Schrödinger, E. *What is Life? The Physical Aspects of the Living Cell* (Cambridge University Press, 1944).
2. Trivedi, R. & Nagarajaram, H. A. *Int. J. Mol. Sci.* **23**, 14050 (2022).
3. Davies, P. C., Rieper, E. & Tuszynski, J. A. *Biosystems* **111**, 1 (2013).
4. Lyon, A. S., Peeples, W. B. & Rosen, M. K. *Nat. Rev. Mol. Cell. Biol.* **22**, 215 (2021).
5. Jansen, K. A. et al. *Biochim. Biophys. Acta* **1853**, 3043 (2015).

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