

# Order from disorder in biological systems at different levels of organization

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**Lecture Description:** Biological systems provide a prime example for naturally occurring complex, far from equilibrium, processes showing the emergence of order from the underlying microscopic disorder. The approach to this complexity reflects the tension between a reductionist, reverse engineering stance and the more abstract, systemic one attempting to uncover the organization principles underlying living matter. Our work challenges the ability to reverse engineer biological systems. In particular, it demonstrates the difficulty in identifying the relevant degrees of freedom underlying biological phenomena. We will explain the challenge, mainly concentrating on the microscopic-macroscopic degeneracy and the inherent difficulty in separating the dynamics at any given level of organization from the coupled dynamics of the other levels, including the environment within which the system is embedded. By discussing two examples from our recent experimental research, we will briefly sketch an alternative methodology to the programmatic, reverse engineering approach, based on exploratory self-organization dynamics.

First, we will discuss the organization of cells leading to their well-defined morphology, metabolism and function. Cell-state organization is a dynamical process in which the genome does not determine the ordered cell state; rather, it participates in this process by providing a set of constraints on the spectrum of regulatory modes, analogous to boundary conditions in physical dynamical systems. We will demonstrate that the underlying physics of cell-state organization, in the context of a cell population, is based on exploratory dynamics allowing adaptation and convergence on physiological time scales in the high-dimensional variable space.

Second, we will discuss morphogenesis—the emergence of form and function in a developing organism, which is one of the most remarkable examples of pattern formation in nature. We will focus on the dynamic interplay of three type of processes underlying morphogenesis: Biochemical, mechanical and electrical which span all scales from the molecular to the entire organism. We utilize Hydra, a small multicellular fresh-water animal exhibiting remarkable regeneration capabilities, as a model system to show that: **1.** Mechanical forces and feedback shape the body plan during morphogenesis. **2.** An external electric field above a critical value can lead to reversal of morphogenesis: a fully developed animal flows back into its incipient state, which nevertheless can regenerate again when the amplitude of the external electric field is reduced below criticality. Reversal of morphogenesis is demonstrated to result from enhanced electrical excitations of the Hydra tissue. Controlled reversal trajectories open a new vista on morphogenesis and suggest a novel approach to study the physical basis of regeneration.

For each of these examples, we will first discuss the necessary background and then sketch the main experimental findings, followed by their implications and generalized conclusions.