The physics of morphogenesis

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Biological systems provide a prime example for naturally occurring complex, far from equilibrium, processes that exemplify 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 previous work challenges the ability to reverse engineer biological systems (see [1]). In particular, it demonstrates the difficulty in identifying the relevant degrees of freedom underlying biological phenomena. One of the main reasons for this challenge is the inherent difficulty in separating any given level of organization from the coupled dynamics at all the other levels, including the environment within which the system is embedded. We will discuss these coupled dynamics in the context of morphogenesis—the emergence of form and function in a developing animal, which is one of the most remarkable examples of pattern formation in nature. The current picture of morphogenesis relies on biochemical patterning. However, as we are going to discuss, morphogenesis involves the integrated symbiotic interplay of three type of processes: biochemical, mechanical and electrical, which span all scales from the molecular to the entire organism [2].

In the first part, we will discuss the role of mechanics and the integration of mechanical processes with the biochemical processes, utilizing *Hydra* regeneration as a model. In the second part, we will generalize the discussion, focusing on the ways living systems close the loop to stabilize the emergence of a viable body plan in development. We then utilize *Hydra* again, and study its regeneration under external electric fields. These examples paint morphogenesis as a physical dynamic pattern-forming process and call for a new theoretical framework for this phenomenon.

Specifically, our plan for these two parts is as follows:

Part 1 – Kinneret Keren

Morphogenesis in regenerating *Hydra*: actin dynamics and the influence of mechanical constraints

In this part we focus on the mechanical aspects of morphogenesis using *Hydra*, which provides a flexible platform to explore how mechanical forces and feedback contribute to the formation and stabilization of the body plan during morphogenesis. We will discuss our results showing that structural inheritance of the supra-cellular actin fiber organization directs the alignment of the new body axis in regenerating *Hydra* [3]. We will further describe our efforts to develop a framework relating the dynamics of the nematic organization of these supra-cellular actin fibers to the morphogenesis process [4]. In particular, we show that topological defects in the nematic order act as effective organizing centers in *Hydra* morphogenesis. Finally, we will present our recent studies on the establishment of body axis polarity in regenerating *Hydra,* showing that body axis determination is a dynamic process that involves mechanical feedback together with signaling processes.

Part 2 – Erez Braun
Reversal morphogenesis in Hydra regeneration under external electric fields

The robustness of the morphogenetic process is typically attributed to the presence of a well-defined hierarchy of forward-driven processes, such as threshold-crossing cellular processes and the development of symmetry-breaking fields. Is it possible to modulate the course of morphogenesis in a whole animal on demand and alter its developmental trajectory in a controlled manner? We demonstrate that an external electric field can be tuned to drive morphogenesis in *Hydra* regeneration, backward and forward, around a critical point in a controlled manner [5]. Interestingly, a backward-forward cycle of morphogenesis leads to a newly emerged body plan in the re-developed folded tissue, which is not necessarily similar to the one before the reversal process. Thus, a controlled drive of morphogenesis allows in principle, multiple re-initiation of novel developmental trajectories for the same tissue. We will discuss the main experimental observations and their implications. Controlled reversal trajectories open a new vista on morphogenesis and suggest a novel approach to study the physics of this fascinating process as a dynamic phase transition.

References:

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