Evidence for Critical Fluctuations in the Establishment of the Body Plan of a Simple Animal

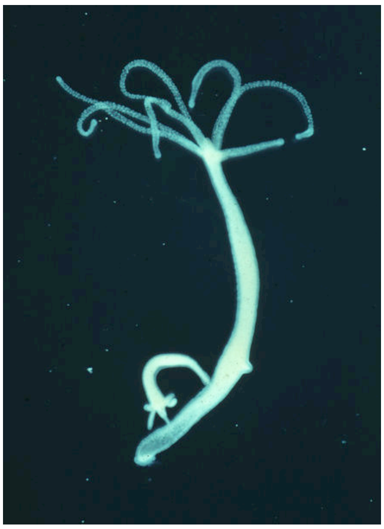
Hydro Molecular Network Reaches Criticality at the Symmetry-Breaking Axis-Defining Moment
Authors: Jordi Soriano, Cyril Colombo, and Albrecht Ott

Physical Review Letters **97**, 258102 (2006)

Recommended with a Commentary by Raymond E. Goldstein, University of Cambridge

One of the most fascinating issues in biology is the generation of broken symmetries in the development of organisms. We are all familiar with the fact that our hearts are typically on the left, but it is worth pausing to reflect on the fact that there are actually three levels of broken symmetry in vertebrates such as ourselves. These involve planes which define the anterior & posterior regions (top-bottom), dorsal & ventral (front-back) domains, and the left/right arrangement. Thanks to very striking experimental observations over the last few years, we now know that the breaking of left-right symmetry can often be traced to fluid flows in a small region of the embryo, driven by tilted beating cilia (flexible hair-like appendages some 10 microns long). These observations have helped establish that physical phenomena amenable to quantitative mathematical description, such as advection-diffusion processes, underlie these important biological functions.

The present paper by Soriano, Colombo, and Ott addresses a comparatively much simpler problem of symmetry-breaking: that found in the famous organism *Hydra*. This fresh-water animal ranges from a few to tens of millimetres in length, with a foot at one end and, at the other end, a mouth surrounded by a number of tentacles armed with stinging cells which inject neurotoxins into prey (see figure).



Hydra have an especially simple symmetry: radial. They also possess remarkable regenerative capabilities. If a disk of tissue is excised from the body column of the adult organism, cut into fragments, and the cells from one fragment are completely dissociated from one another, then reaggregated, that cluster will develop into a normal adult. To do this, it rounds up to form a hollow sphere, breaks spherical symmetry by forming an axis, and then develops on to the adult form. It is known that determination of the axis is controlled by a small group of the first few cells restored during regeneration. That region is the locus of expression of a key gene known as *Wnt*.

The paper by Soriano, et al. investigated a hypothesis which dates back to C. Child in 1929, namely that a gradient of metabolic activity should determine the axis position. In contrast to many previous unsuccessful attempts to verify that hypothesis using temperature gradients (which would spatially alter metabolic activity through activated processes), the present work has succeeded. They key result, though, is that such a gradient has that axis-defining effect only during a particular period in regeneration. That period is one in which the ball of cells undergoes high-amplitude, low-frequency oscillations, ending about 20 hours after the start of regeneration. It is at that end-point that the axis is irreversibly defined.

Interestingly, the authors' studies of spatial variations in gene expression show that the probability distribution of clusters of active cells exhibits a power law just at 20 hours after regeneration begins, with characteristic sizes on either side of that moment. There, the expression pattern appears fractal. Since a system near a critical point becomes increasingly susceptible to external perturbations, it is reasonable to identify this special time as one in which a state of (self-organized) criticality has emerged.

No detailed model yet exists which can explain the quantitative aspects of these observations, but there are some features which appear in various models of self-organized criticality. As the authors point out, though, it is the specific biological features of this system, including differential cell adhesion, which will likely be key to a microscopic theory.

Time for theorists to get to work!