Critical response

Collective organization and dynamics lie behind some of the most sophisticated phenomena of living systems, including genetic regulation and the dynamics of immunity, as well as brain function and intelligence. In virtually all species, and in ways we barely understand, interactions among many elementary components produce special kinds of coherent, collective order. What are its general principles?

No doubt there may be many. But for several decades, physicists have been fascinated by one provocative idea — the notion that many biological systems may reflect a functionally useful balance between order and disorder, between stability and instability. The motivating metaphor arises from the theory of phase transitions and critical phenomena, and from the special behaviour of systems poised near the edge of a phase transition. Organization close to criticality could provide biological systems with a subtle balance, making them at once robust to environmental perturbations, yet also flexibly poised to adapt to changing conditions. Critical organization would, researchers have also argued, provide a platform for optimal computing capabilities, a wide range of possible dynamical responses, and extreme sensitivity to external stimuli.

This conjecture has stirred great excitement — and also controversy, as physicists have not always shown respect for prior thinking in other fields. Yet, as Miguel Muñoz describes in a recent review (preprint at https://arxiv.org/abs/1712.04499), the case for the broad relevance of the notion of criticality has grown stronger over the years, especially as recent advances in high-throughput genomics, neuroscience and big data technologies have provided more precise detail on biological fluctuations and dynamics.

That biological systems should at least crudely resemble critical systems may be obvious. They cannot be too stable to respond adaptively to changes around them, nor can they be too variable, changing more or less randomly and without correlation to their environment. The simultaneous integrity and adaptability required in biology implies some kind of balance of stability and instability. If the hypothesis of criticality has scientific meaning, it must go beyond this easy qualitative view and help us to understand more specific quantitative features of many real biological systems. As Muñoz points out, in many cases it does.

Organization close to criticality may provide biological systems with a subtle balance, making them poised to adapt.

One of the clearest comes from the structure of auditory and other sensory systems. For example, vertebrates can hear and identify the pitch of very weak sounds, and they maintain this capability for signals over many orders of magnitude in strength. A natural tuning to a critical point seems to be involved. Hair cells in vertebrate ears oscillate even in the absence of sound, and hearing results from a resonant response to an input. The oscillations, it turns out, follow a dynamics with a bifurcation controlled by the calcium concentration in hair cells — low concentration yielding damped oscillations and higher concentrations sustained oscillations. Empirical studies find that hair cells regulate calcium to stay very close to the bifurcation point where the oscillatory response is formally infinite. This gives a strong response even to tiny signals of the right frequency. Other sensory systems including vision involve similar critical tuning.

Another example is the neural activity observed in the human brain, as well as in the neural systems of many other animals, even when resting and stimuli are absent. This perpetual electrochemical activity shows relatively quiescent periods interrupted by sporadic brief outbursts of many neurons firing in synchrony. Remarkably, it consumes around a fifth of all the oxygen used by a resting person, and criticality might partly explain its role. Experimental studies show a wealth of neural phenomena suggestive of criticality, including neural avalanches with delicate spatiotemporal correlations across the whole brain. Measurements of neural synchronization also find strong long-range order between different brain regions. This suggests that the resting activity of the nervous system could be tuned to allow a high variability in responses to stimuli or, as Muñoz puts it, a "large dynamical repertoire" useful for ensuring a balance between integration and segregation.

Indeed, high-resolution recordings from human brains even show that healthy conscious activity shows a mathematical signature of persisting instability. Analysis of spatiotemporal patterns of neural activity find eigenvalues in awake individuals that tend to stay close to a threshold of instability, whereas eigenvalues for an anaesthetized brain are significantly stabilized.

These examples lie in higher level biological functions of whole organisms, but many others exist at lower levels. Living cells are of course stable, yet also show rich variability that lets them respond to environmental changes. In a first approximation, cellular states can be seen as dynamical attractors of underlying genetic regulatory networks. Only in the past two decades have biologists had the means to probe the dynamics of such networks in great detail, and biology as a result has moved from single genes to ever more complex circuits of interacting genes. A variety of expression experiments have probed both the network structure of gene interactions, as well as the overall dynamics of expression levels. With fair consistency, they find that regulatory dynamics in real cells has critical features.

Again, this makes sense, as Stuart Kauffman proposed many years ago in *Origins of Order* (Oxford University Press, 1993). Too strongly ordered dynamics would respond to different environmental stimuli in the same way, offering little sensitivity and control, but strongly disordered dynamics could let very weak stimuli wreak inappropriate havoc on cellular function. Critical organization seems a mechanism to provide a balance between the regularity biological function requires, yet persisting sensitivity to environmental clues.

As experimental methods get more precise, signs of criticality are showing up almost everywhere — in anything from fluctuations in cell membranes to morphogenesis, in physiological rhythms, in the replication dynamics of RNA viruses, in the swarming and herding behaviour of insect and animal groups. It appears to identify a useful dynamical regime that biology discovered long before scientists knew of it.

But Muñoz makes a useful point: as the notion of criticality is among our best ideas for describing complexity, perhaps we should be surprised to find it so useful for talking about the most complex systems we know — the living ones. ❐

MARK BUCHANAN