Introduction

Historical context

The study of phase transitions—changes in the states of matter—was a leading area of research in the 19th and 20th centuries. Physicists categorized these state changes as being either first- or second-order. First-order or discontinuous transitions are characterized by an abrupt change of phase when a control variable, such as temperature, is smoothly and monotonically varied across the transition point, causing, for example, ice to melt, and water to vaporize. Reversing the direction of the temperature change reverses the transition, causing steam to abruptly condense into liquid water, and water to freeze into a crystalline solid. But for first-order transitions the particular state of matter can depend on the history of the control variable. Thus, in the absence of nucleation centers, pure water can remain liquid when cooled below its normal ice–water transition point, or when heated above its normal water–steam point. This state dependence on history is called hysteresis.

In contrast, second-order or continuous phase transitions show a smooth change of state with no evidence of hysteresis. For example, when a ferromagnet in a zero magnetic field is heated so that its temperature crosses a critical temperature (the Curie point), its magnetic state smoothly changes from aligned (ferromagnetic) to random (paramagnetic).

Early studies focused on so-called equilibrium transitions in which the behavior of state variables, such as gas pressure, temperature, and volume, is governed by a thermodynamic equation of steady state whose mathematical form is determined by the locations of the local minima attractors within a free-energy potential landscape.

Experiments indicated that phase transitions exhibit a set of universal properties—notably power-law divergence of bulk parameters such as heat capacity, susceptibility, compressibility—as the critical point is approached. The quest to understand the origin of these unifying principles led to advances such as such the Kadanoff and Fisher scaling laws, and culminated in the development of renormalisation group theory. These theoretical advances also introduced the notion of an order parameter, assigned a non-zero value in the more ordered (e.g., ferromagnetic) phase.

In the 1960s, the pioneering work of the Brussels group led by Nicolis and Prigogine revealed another type of transition—the pattern-forming phase transitions exhibited by particular types of chemical reaction in fluids. Another fundamental advance at this time was Haken’s treatment of the laser as a self-organizing tran-
sition from uncorrelated light fields into directed photon emissions that are coherent in time and space. The fluid and laser transitions both belong to the family of nonequilibrium phase transitions, so called because the underlying reactions require a continuous flux of reactants and energy, so are far from thermodynamic equilibrium and cannot be described in terms of a free-energy potential function. Such phase transitions are of a spatiotemporal kind, characterized by spontaneous spatial pattern formation (the original homogeneous steady-state becomes destabilized by a Turing instability) and temporal oscillations (destabilization via a Hopf instability). The identification of an order parameter for such transitions remains unclear, with the amplitude of the critical, slow mode that emerges at the transition point being a promising candidate.

**Book overview**

In this book, we put forward the perhaps controversial idea that phase transitions can and do occur in the brain. Like all “living” biological components, the brain never operates in closed thermodynamic equilibrium, and yet we find that on approach to a neural change of state (e.g., moving from wake to anesthetic sleep, or from slow-sleep into REM sleep), its bulk electrical signals can display divergent correlated fluctuations that are tantalizingly similar to first- and second-order thermodynamic phase transitions. Further, we argue that the emergence of spatiotemporal patterns in the brain (e.g., epileptic seizure, alpha and gamma oscillations, the ultraslow oscillations of BOLD fMRI patterns) provides strong evidence of nonequilibrium transitions in brain state.

This idea for this book arose from discussions at the CNS*2007 Computational Neuroscience Meeting held in Toronto, Ontario in July 2007. Joseph Burns, then Senior Editor for Life Sciences, Springer, suggested to ASR and MSR that they construct a book proposal for a contributed volume of chapters written by senior researchers in computational brain modeling. *Phase Transitions in the Brain* was chosen as the unifying foundation for the book, and this proved to be an attractive theme that was enthusiastically adopted by the coterie of invited authors.

Brain activity can be modeled either by a discrete *network of active nodes*, or by a *mean-field continuum*—both approaches are illustrated in this book. In the network approach, each node could be a conductance-based spiking neuron, or an idealized neuron, or could represent a cluster of neurons, with the biological fidelity (and mathematical complexity) of each node being determined by the purpose and scale of the model. The topology of the connections between nodes is another modeling choice, and can be, for example, all-to-all, random, small-world, or distance-dependent. Chapters 4, 5, and 7 illustrate the network-based approach to brain modeling.

In the continuum approach, the brain is described in terms of *populations* of excitatory and inhibitory neurons that interact via chemical synapses over both short and long ranges. Differential (or integro-differential) forms are derived to give the equations of motion for spatially-averaged (i.e., *mean-field*) activity subject to external
(subcortical drive) and internal (neurotransmitter) influences. Although the authors of chapters 3, 6, and 8–12 all use a mean-field philosophy, their model details can and often do differ in subtle but important ways. Some of these distinctions will be outlined below.

We now give a brief summary of each of the 12 chapters. With the exception of Chaps 1 and 12 (by the editors), the chapters are organized alphabetically by author.

In Chap. 1, Alistair Steyn-Ross and colleagues examine theoretical and experimental evidence for phase transitions in single neurons (onset of spiking), and in neural populations (induction of anesthesia, SWS–REM sleep cycling, transition from wake to sleep). The type-I and II spiking-neuron models due to H.R. Wilson are biophysical simplifications of the conductance-based Hodgkin–Huxley “gold standard”. A spiking instability can be induced by increasing the dc stimulus current entering the neuron. By adding a subtle white-noise “tickle” to the dc bias, the nearness to spiking transition can be quantified by allowing the neuron to explore its near-equilibrium state space, exercising what Jirsa and Ghosh (Chap. 4) call its dynamic repertoire. The subthreshold fluctuations grow in amplitude while becoming critically slowed (type I) or critically resonant (type II) as the bifurcation point is approached. Similar critical changes in fluctuation statistics are seen in the EEG activity recorded from patients undergoing, then recovering from, anesthesia; and in the brain activity of mammals (cat, fetal sheep, human) transiting from slow-wave to REM sleep. Near the point of falling asleep, the phase transition conjecture predicts a nonlinear increase in neural “irritability” (susceptibility to small stimulus); this critical effect may explain the puzzling, yet commonly experienced whole-body hypnic jerk at sleep onset.

We argue that there appears to be ample evidence of phase transition-like behavior in the brain. But can we quantify these qualitative state changes by extracting the critical exponents underlying the power-law growth of the fluctuations in cortical activity? Given the inherently nonstationary nature of the signal at the point of transition, this would be a highly challenging ambition. In Chap. 2, Andreas Galka and colleagues present a possible way forward. These authors describes a state-of-the art generalized autoregressive conditional heteroscedastic (GARCH) method, first used in financial modeling, which allows the dynamical noise covariance to change with time. They apply this GARCH technique to three distinct dynamical state transitions captured by EEG recordings: induction of general anesthesia in a human patient, emergence of epileptic seizure in a human, and transition from slow-wave to REM sleep in a fetal sheep. They demonstrate that the GARCH variance can accurately locate the point of phase transition without any prior information on the timing of the nonstationary event.

In Chap. 3, Axel Hutt investigates a 1-D continuum model of the cortex that is expressed in terms of a single neural population whose effective membrane voltage \( V \) is written as the signed summation of the excitatory and inhibitory postsynaptic potentials that combine at the soma: \( V = V^e - V^i \). Using Mexican-hat axonal distribution functions, he is able to establish analytic conditions for the existence of stationary (Turing) and oscillatory (Hopf and traveling wave) instabilities. The sta-
bility of the Turing bifurcation in the presence of noise is investigated. Close to the instability point, a linear analysis predicts critical fluctuations, that is, the emergence of long-lived zero-wavenumber fluctuations of large variance. When the system becomes unstable, a nonlinear stability analysis shows that the presence of global noise can restore stability to the homogeneous state by suppressing the stochastic Turing instability. The fact that noise can both stimulate and suppress formation of spatiotemporal activity patterns in the cortex may have significant implications for information processing in the brain.

In Chap. 4, Viktor Jirsa and Anandamohan Ghosh emphasize the fundamental importance of random noise in allowing an excitable system to explore and exercise the repertoire of dynamic behaviors that can be accessed from its resting, equilibrium state. This idea is illustrated first in simple bifurcation (saddle–node and Hopf) models, and then applied to a network simulation of a brain at background rest. The simulation utilizes a biologically realistic primate (macaque) connectivity matrix with 38 nodes, and includes time delays via signal propagation between brain areas, and intrinsic noise. The authors argue that the working point of the brain during wakeful rest is often close to the critical boundary between stable and unstable regions. From the network simulation results they are able to identify the correlated and anticorrelated subnetworks that are active during the ultra-slow BOLD signal oscillations, and demonstrate excellent agreement with experimental observations. The authors offer some insights into the rich default-mode dynamics of the idling brain, suggesting that undirected, spontaneous thoughts can only arise because of the presence of noise (else the rest-state would be truly at rest), but that the response to this random stimulus is tuned by the brain’s deterministic “skeleton” (anatomical connectivity, time-delay structure, internal dynamics) delicately poised close to an instability.

In Chap. 5, Marcus Kaiser and Jennifer Simonotto picture the cortex as a complex neural network whose overall level of activity is delicately balanced between the unhealthy extremes of quenched silence, and runaway excitation of the entire network—as seen in the transition to the epileptic state. How is the desired state of persistent, yet contained, network activation sustained, and what prevents uncontrolled spreading of activity to ignite the entire network? The authors argue that, in addition to neuronal inhibition via inhibitory interneurons, network architecture plays a crucial role. In particular, their simulations demonstrate that a network composed of hierarchical clusters—with denser connectivity within clusters than between clusters—provides a form of topological inhibition that tends to suppress runaway spreading, even in the absence of inhibitory units. This topological protection against transition into epilepsy arises because of the sparser connectivity between clusters, while the higher density of connections within clusters allows sustained levels of activity. Non-hierarchical topologies, such as small-world and random networks, are shown to be not only less protective against global spreading, but also more susceptible to quenching. Since the anatomy of the brain displays a modular, hierarchical architecture (from microcircuits at the lowest level, to cortical areas then brain areas at the global level), these network insights are likely to have biological significance.
In Chap. 6, David Liley and colleagues focus attention on the alpha rhythm (8–13 Hz activity) ubiquitous in human brain EEG. They present the constitutive partial differential equations for a 2-D continuum model of a cortex driven by noisy extracortical sources. With appropriate changes to the cortical parameters, the model can exhibit linear noise-driven dynamics, and nonlinear deterministic (chaotic and limit-cycle) oscillations. The authors demonstrate that the cortical model can undergo Hopf and wave bifurcations in both the alpha and gamma (∼40 Hz) bands, and that the transition from subthreshold alpha to limit-cycle gamma can be achieved by reducing the strength of the inhibitory postsynaptic potential. They argue that a marginally stable alpha rhythm could provide a “readiness” substrate for neural activity, enabling rapid transitions to the higher frequency cortical oscillations required for information processing.

In Chap. 7, Hans Liljenström presents a range of network models, of varying complexity, designed to investigate phase transitions in mesoscale brain dynamics, arguing that this intermediate scale, lying somewhere between micro (ion channels and single neurons) and macro (whole brain), provides a bridge between neural and mental processes. His network models include a three-layer paleocortex (olfactory cortex and hippocampus) of nonspiking nodes; a five-layer neocortex of either conductance-based or simplified spiking neurons; and a monolayer grid of spiking neurons. By modulating an appropriate control parameter, each network model exhibits a characteristic phase transition behavior; thus an increase in intrinsic noise can cause the paleocortex to form spatiotemporal patterns of activity; an electrical stimulus applied to the neocortex can generate seizure-like oscillations; and a reduction in ion-channel conductance can cause a dramatic slowing in EEG dynamics similar to that seen during the induction of general anesthesia.

In Chap. 8, Peter Robinson and colleagues outline a philosophy for the construction of continuum models for the brain, and correct some misconceptions about mean-field theory and its applications. The authors present two biophysically-motivated mean-field models. The first model describes the EEG signals generated by the neuronal interactions between the cortex and thalamus, and the second is focused on the slow interactions between brainstem and hypothalamic structures that control the wake–sleep diurnal cycle. Loop resonances in the corticothalamic model produces EEG spectral peaks at the alpha and beta frequencies. By varying loop gains and synaptic strengths, four distinct saddle–node and Hopf bifurcations to limit-cycle oscillations (slow spike–wave, 3-Hz theta, 10-Hz alpha, 10–15-Hz spindle) are identified. These neurodynamic phase transitions may correspond to the genesis of seizure activity. Their sleep–wake model is based on mutual inhibition between wake-active (MA) and sleep-active (VLPO) brainstem nuclei, resulting in a flip-flop dynamics that is controlled by the circadian (C) and homeostatic (H) drives. The model predicts first-order phase transitions between sleep and wake, with state stability enhanced by a hysteresis separation between transition points.

In Chap. 9, Jamie Sleigh and colleagues investigate the phase transition between slow-wave and REM sleep, comparing continuum-modeling predictions against ECoG activity recorded from sleep-cycling rats. They argue that the primary effect of the cortical change into the REM state is a progressive linear increase in
cholinergic excitation of the cortex which they model in terms of an increase of neuron resting voltage $V^{\text{rest}}_e$, coupled with a simultaneous decrease in $\lambda$, the strength of the excitatory postsynaptic potential (EPSP). The distribution of equilibrium soma voltages, plotted as a function of resting voltage and EPSP gain, defines a sleep manifold featuring multiple steady states and a region of instability that extends beyond the fold, into the upper (active) and lower (quiescent) cortical states. The upper-branch displays a Hopf bifurcation to $\sim 8$-Hz limit-cycle oscillations; this dynamic instability may explain the theta-band oscillations observed in ECoG recordings of rats transiting from SWS into REM sleep. The authors are able to demonstrate good agreement between modeled and measured spectrograms across the transition event.

In Chap. 10, Marcus Wilson and colleagues present a thorough investigation of the dynamical properties of the mean-field sleep model alluded to in Chap. 1.4, and tuned for rat sleep-cycling in Chap. 9. A linear stability analysis predicts that the homogeneous steady-state cortex will be destabilized by a sufficient reduction in $\gamma_i$, the rate-constant for the inhibitory postsynaptic potential (IPSP). This prediction is verified by numerical simulations on a 2-D grid for a range of $(\lambda, V^{\text{rest}}_e)$ sleep-manifold coordinates; these simulations show a range of supercritical and subcortical Hopf bifurcations to slow ($\sim 1$-Hz), spatially-symmetric, whole-of-cortex limit-cycle oscillations which the authors identify with seizure. If the homogeneous cortex is stimulated with a brief, spatially-localized impulse, traveling-wave instabilities—reminiscent of K-complexes and delta-waves of slow-wave sleep—can also be evoked.

In Chap. 11, Jim Wright describes a closely detailed continuum model of the cortex that attempts to capture, via a hierarchy of nested integral convolutions, the contributions from multiple scales of neural activity, integrating up from the microscale (ion channels and receptors), to the mesoscale (cortical macrocolumns), and the centimetric macroscale sensed by EEG electrodes. His model includes the effects of ion-channel conformation, receptor adaptation, reversal potentials, and back-propagation of action potentials. Numerical simulations of a 2-D cortex demonstrate that, at a critical level of input flux, the homogeneous cortex undergoes a phase transition into autonomous gamma oscillations. The nature and strength of this bifurcation is controlled by both local (excitatory–inhibitory balance) and global (excitatory tone) flux sources. The author discusses possible implications of gamma synchrony and traveling waves on the recall and processing of information by the brain.

Although the Chap. 12 continuum model of Moira Steyn-Ross and colleagues shares features with the models of Wright (Chap. 11), Robinson et al. (Chap. 8), and Liley et al. (Chap. 4), it differentiates itself with the inclusion of electrical synapses or gap junctions. Inhibitory gap-junction diffusion is found to modulate the onset of Turing and Hopf instabilities, leading to the appearance of spatiotemporal patterns and waves. The authors show that the nature of the feedback between soma and dendrite strongly influences the dynamics of the cortex. If the soma responds slowly to dendritic input, Turing and low-frequency Hopf bifurcations are predicted, but if the soma response is fast, a gamma-band wave instability emerges. These mutually
exclusive extremes may correspond respectively to the awake brain states of *idling rest* (discussed in Chap. 4) and *active cognition* (Chap. 11).

**Final comments**

The brain can sustain an extremely rich diversity of brain states, some of which are unhealthy and pathological. Of the universe of states available to the brain, these chapters have focused attention on just a small subset—anesthetized, slow-wave sleeping, REM sleeping, awake, idle daydreaming, active thinking, epileptic seizing. Transitions between these gross states can be driven by a range of “control” parameters such as altered neurotransmitter and neuromodulator concentrations, gap-junction diffusion, synaptic efficiency, electrical stimulus. Phase transitions in matter arise because of changes in the nature of the bonding between atomic constituents. Perhaps for the brain, one analog of “atomic bonding” might be the strength of coupling between different neural populations, with stronger coupling leading to enhanced synchrony and qualitatively distinct neural states.

The phase transition approach to brain modeling seems to provide natural explanations for some of the counterintuitive fluctuation divergences seen on approach to state change, such as the EEG power surge seen during induction of general anesthesia, and during the natural progression from slow-wave sleep into REM sleep. But as yet, there is no general theory of neural phase transitions. The noise-evoked fluctuation statistics from single-neuron models might provide some guidance, with critical slowing at a saddle–node annihilation, and critical ringing at a Hopf bifurcation, corresponding to increased correlation times and correlation lengths.

Left open and unanswered are many challenging and intriguing questions: How do single-neuron transitions scale up to influence the behavior and response of neural populations and brain areas? Are critical fluctuations “biologically useful”? Might they have a role in the facilitation—or suppression—of phase transitions? What are the general principles that underlie neural changes of state? Can we find universal scaling laws for brain phase transitions?

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