Fronts and fluctuations at a critical surface

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The theory of first and second order phase transitions is a well-established part of statistical physics, and its generalization to out-of-equilibrium problems, like glassy behavior and percolation-like transitions, has also received a lot of attention during the last decades. However, most of these works focused on the case where the control variable (like temperature) is homogenous in space. Only recently has the equilibrium properties of thermodynamic systems with a spatially varying temperature that takes its critical value only in a localized region begun to be studied [2].

Coincidentally, an out-of-equilibrium process with the same spatial characteristics was suggested as the underlying mechanism behind one of the most fundamental processes in biology, Drosophila gap genes along the anterior-posterior axis of Drosophila embryos. Measuring the expression levels of the maternal morphogens and not bifurcational.

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The only reliable indicator turns out to be the fluctuation statistics. These take a Gaussian form in equilibrium continuous (“second order”) transition, with a characteristic fluctuation spectrum at the crossing point. Doing that, one realizes that the second scenario, the bistable front model, better captures the features of the morphogenetic process considered in [1].

Qualitatively speaking, the bistable scenario is the analog of a simple first order transition system, although (as we shall see below) one should make a distinction between its equilibrium and out-of-equilibrium properties. Imagine a water-ice mixture in three dimensions, say, where the temperature depends on $x$ and $T(x=0) = T_m$, where $T_m$ is the melting temperature. In the right half-space water invades ice and in the left ice grains grow in water, so the ice-water front will be trapped around $x = 0$. Due to thermal or other fluctuations the front will move back and forth in a region determined by $x_t$, leading to a characteristic fluctuation spectrum at $x = 0$; below we will distinguish between the instantaneous shape of the front and its average over time and will analyze the distribution of fluctuations.

The bifurcation model, which is the one considered in [1], is slightly more complicated. This model is a nonequilibrium continuous (“second order”) transition, with a transcritical bifurcation at $x = 0$. To imitate the gene expression case one needs two competing fields. A generic
set of PDEs that yields the required behavior is
\[
\frac{\partial a(x,t)}{\partial t} = D\nabla^2 a + a - \frac{a^2 + [1 + C(x)]ab}{K} + \zeta_a(x,t),
\]
\[
\frac{\partial b(x,t)}{\partial t} = D\nabla^2 b + b - \frac{b^2 + [1 - C(x)]ab}{K} + \zeta_b(x,t).
\]

Where \(a\) and \(b\) are the expression levels of the corresponding genes \(A\) and \(B\), \(C(x)\) is the background field (maternal morphogenes) that switches sign at zero and \(\zeta\) is, say, white noise.

In the absence of noise, \(\zeta = 0\), in the regime \(C(x) > 0\) the fixed point (FP) of this system is \(a = 0, b = 1\) while if \(C(x) < 0\) the FP is \(a = 1, b = 0\). The diffusion term, however, couples the left and the right regions, and the expression level must be a smooth function of \(x\) that approaches the FPs at large \(|x|\) and takes the symmetric value \(a = b = 1/2\) at the crossing point.

An appropriate and quite generic choice of the external field profile is \(C(x) = \tanh(x/x_1)\), where \(x_1\) sets the scale of the external field gradient. Plugging \(b = 1 - a\) into Eqs. \(1\) one finds in the deterministic limit (from here on we normalize \(K\) to unity), \(a = D\nabla^2 a - C(x)a(1-a)\); expanding \(C\) at \(x \ll x_1\) the equation for the stable front is then
\[
a''(y) - ya(y)[1-a(y)] = 0, \tag{2}
\]
where \(y = x(Dx_1)^{-1/3}\) and spatial derivatives are taken with respect to \(y\).

Eq. \(2\) describes a deterministic, spatial voter model with selection \(3\), where the value of \(y\) determines the preference towards one of the "alleles" (opinions). The front width is proportional to \([Dx_1]^{1/3}\); its shape and the fluctuation spectrum at the front will be determined below.

It appears to be instructive to contrast the bifurcation model \(2\) with the other generic scenario, a bistable system. Let us consider the simplest model of a bistable system with a crossing point, described by a spatially inhomogeneous Ginzburg-Landau (GL) Equation:
\[
\dot{\phi}(x,t) = D\nabla^2 \phi(x,t) + \phi(x,t)[1 - \phi(x,t)] - C(x)]. \tag{3}
\]

When \(C\) is a constant, \(\phi\) admits three spatially homogeneous FPs, two stable FPs at \(\phi = 0\) and \(\phi = 1\) and an unstable FP at \(C\), the \(\phi = 1\) invades the zero phase if \(C < 1/2\) and zero invades if \(C > 1/2\). \(C = 1/2\) is the melting point, or the stall point of the GL front; at the melting point, when the system evolves from inhomogeneous initial conditions like \(\phi = 0\) for \(x < 0\) and \(\phi = 1\) for \(x > 0\), it relaxes to the stable front solution, \(\phi_0 = [\tanh(x/\sqrt{4D}) + 1]/2\). Accordingly, even when \(C\) is \(x\) dependent, as in the case \(C(x) = \tanh(x/x_1)\) considered above, as long as the intrinsic width of the front \(\sqrt{4D}\) is much smaller then \(x_1\), the shape and the width of the front will be essentially independent of the external field (see Figure \(1\)). Although both scenarios support a stable front, the dependence of its width on the external parameters is different: in a bifurcation system this width scales like \(D^{1/3}\) and depends on the width of the crossing region \(x_1\), while in a bistable system the width scales like \(D^{1/2}\) and is independent of \(x_1\) when \(x_1\) is large.

However, when a front is observed, as in the experiment discussed by \(1\), and one would like to determine the underlying mechanism, the utility of diagnostic tools based on static properties of the front is quite limited. In experiments it is quite difficult to change \(D\) or \(x_1\) to do that, the dynamics on the molecular level should be manipulated - so one cannot measure the dependency of the front width on \(D\). Worse than that, it turns out that the front shape is almost identical in both cases. In the bifurcation model \(\phi_0 = 1/2 + x/\sqrt{16D}\) close to \(x = 0\), meaning that the front satisfies, to first order in \(x\) and \(\phi\), \(D\nabla^2 \phi(x) + (x/Q)\phi(x)[1 - \phi(x)] = 0\), i.e., it is equivalent, up to a constant, to the bifurcation front solution \(2\), so the differences between \(\phi_0(x)\) and the solution of Eq. \(2\) (denoted hereon as \(a_0(x)\)) are extremely small, as demonstrated in Figure \(1\). Without measuring the diffusion constant of the underlying morphogenesis molecular agents, or monitoring the front profile to a very high degree of accuracy, one cannot use static properties to distinguish between the two possible scenarios.

Not only the static properties of the front are practically useless as an indicator of the underlying mechanism,
the same is true for some dynamical aspects of the dynamics. In [1], for example, the location of the crossing point was identified (assuming an underlying bifurcation scenario) by a peak in the anticorrelations between the densities of \(a\) and \(b\), and the existence of a slow and fast manifold was demonstrated by a scatter plot of the fluctuations, showing that the sum \(a + b\) is kept almost fixed through time but the differences \(a - b\) fluctuate strongly. Indeed, the same features are also a characteristic of a bistable scenario. To show that, we have developed a two-species model that supports bistability (in the one species case [3] the features demonstrated in [1] are embarrassingly trivial, since the field \(\phi\) should be interpreted such that \(a \equiv \phi\) and \(b \equiv 1 - \phi\), so the sum is fixed and the anticorrelations are guaranteed in advance).

To construct a simple two species bistable model we define \(S(x,t) = a(x,t) + b(x,t)\) and \(Q(x,t) = a(x,t) - b(x,t)\), and the local dynamics satisfies

\[
\dot{S} = S(\alpha - S) \quad \dot{Q} = (Q - C(x))(S^2 - Q^2)
\]

so the stable FP's correspond to \(S = \alpha\) and \(Q = \pm \alpha\) and for constant \(C\) there is an unstable FP at \(Q = C\). Both reactants \(a\) and \(b\) diffuse with a diffusion constant \(D\). As shown before, the bistable front has an intrinsic width and its shape is independent of the external field parameter \(x_i\), as long as \(x_i \gg \sqrt{8D}\). Accordingly we simulate this system with antiperiodic boundary conditions and without an external field. The correlation function of \(a\) and \(b\), together with a scatter plot of the fluctuations at the crossing point, are depicted in Figure 2, showing that both models have very similar qualitative behavior.

However, the sharp-eyed observer may notice a subtle qualitative difference between the scatter plots of fluctuation amplitudes. In the bifurcation model simulations the points appear to have higher density in the middle (around \([0.5,0.5]\), which is the steady state value of the front at the crossing point), while the simulation of the bifurcation model yields higher concentration of fluctuations close to the two extremes \(a = 0, b = 1\) and \(a = 1, b = 0\). This is not an accident, and provides a crucial hint: the two mechanisms, bifurcation and bistability, admit qualitatively different fluctuation statistics.

In the bistable scenario, due to the absence of the external gradient, the noise causes the front to move back and forth freely around the crossing point, so at \(x = 0\) the system is almost always either at the \(\phi = 1\) state or the \(\phi = 0\) state, leading to a fluctuation spectrum with two peaks at zero and one and a dip at \(1/2\). The bifurcation mechanism, on the other hand, yields only a single peak around the steady state value \(a_0(0) = b(0) = 1/2\).

To quantify this, we consider first the fluctuations around the steady state front of the bifurcation model, \(a_0(x) + \delta(x,t)\) in the presence of an external white noise. Linearizing Eq. (2) to the first order in \(\delta\), and taking into account the front shape close to the crossing point, \(a_0(x) \sim 1/2 + c_1 x/(Dx_i)^{1/3}\), where \(c_1\) is an \(O(1)\) constant, one obtains a dynamical equation for the fluctuations of the bifurcation model:

\[
\dot{\delta}(x,t) = D \nabla^2 \delta(x,t) - \kappa x^2 \delta(x,t) + \zeta(x,t)
\]

where \(\kappa = c_1 (Dx_i)^{4/3}\) and \(\zeta\) is a white noise, \((\zeta(x,t) = 0\) and \(\zeta(x,t) \zeta(x',t') = \delta(x-x')\delta(t-t')\) where \(\delta\) is the Heaviside function. In terms of normalized quantum harmonic oscillator wavefunctions, \(\delta(x,t) = \sum \beta_m(t) \psi_m(x)\), and using their orthonormality properties one obtains,

\[
\beta_m(t) = -\Gamma_m \beta_m(t) + \eta(t),
\]

with \(\Gamma_m = 2\sqrt{D\kappa}(m + 1/2)\) and \(\eta(t)\) is, again, white noise. Every coefficient \(\beta_m\) is subject to an Ornstein-Uhlenbeck process and its probability distribution function is given by a Gaussian with zero mean and variance \(\Delta/\Gamma_m\). An immediate result is that \(\delta\) itself is a zero mean Gaussian, i.e., that the fluctuation density histogram is a Gaussian centered at \(a_0(x = 0) = 1/2\). Indeed one can do even better and calculate the variance of this Gaussian,

\[
Var(\delta) = \sum_{m \text{ even}} \psi_m^2(0)Var(\Gamma_m)
\]

In a bistable system the situation is completely different. As explained above, as long as \(x_i\) is significantly
larger than the internal width of the front, one can replace the external field (with exponentially small corrections in a finite system) by antiparallel boundary conditions at \( \pm \infty \), and the fluctuations admit a zero (Goldstone) mode since the location of the front is translationaly invariant. Accordingly, one finds the crossing point either in the \( a \) phase or in the \( b \) phase, with fluctuations due to the effect of noise on any of these phases. As a result the histogram of fluctuations amplitude, instead of being a Gaussian around 1/2, has two peaks that correspond to the two attractive fixed points of the system. These features are demonstrated in Figure 3 where the strong qualitative difference, allowing for easy discrimination between the two scenarios, is manifest. On the other hand, when \( x_t \) is much smaller than the natural width of the front, even the bistable system loses its translational invariance property, the front is trapped by the external field and cannot change significantly its spatial location, and the resulting fluctuation spectrum is peaked at 1/2. In such a case we cannot offer a simple method to distinguish between the two alternatives mechanisms.

Turning back to the work of Krotov, et al. [1], the results from the experiment they analyzed clearly show a crossing regime with anticorrelations between \( a \) and \( b \) with fast and slow manifold, however, as we explained here, this cannot reveal the nature of the dynamics governs the system. The only simple qualitative indicator is the histogram of the amplitude of the fluctuations, and their results (Fig 3C of [1]) clearly show a double peak structure, meaning that the underlying dynamics is evidently bistable, equivalent to a first order transition with an external field (primary maternal morphogenes) that changes the “temperature” such that the melting temperature marks the crossing point. This appears to rule out the bifurcational interpretation suggested in [1].

Finally, in the context of the bistable model we would like to stress the difference between two possible definitions of a front separating two phases. The analysis followed Eq. 3 regards the instantaneous shape of a front, i.e., the typical shape of a snapshot of the crossover region. In contrast one may define the time averaged, or the "equilibrium" front, wherein that the a density, say, is averaged at \( x \) over a long time span and the resulting front is the profile of \( \langle a(x) \rangle \), where \( (...) \) represents the time, or equivalently the thermodynamic, average.

The width of an equilibrium front under smoothly varying external field was analyzed by [2] in the context of a 2d \( q \)-state Potts model, these authors found that for \( q \geq 4 \) when the system has a first-order transition, the width of the front \( \langle a(x) \rangle \) scales as \( x_t^{1/3} \). To understand and generalize their result, let us consider an equilibrium system at the transition point. Starting from a homogeneous \( A \) state, \( B \) phase droplets with the same bulk energy are nucleated and shrink only due to the surface tension. As a result, the larger the droplet, the more stable it is; monitoring the phase at a certain point \( x \) for long time one finds \( \langle a(x) \rangle = 1/2 \), independent of the location of the measurement. Considering a randomly moving front, like the one described above, one arrives at the same conclusion.

What limits the size of these droplets, hence determining the width of the equilibrium front, is the external field gradient. If phase \( A \) invades the region \( x > 0 \) (where phase \( B \) is preferred) by a compact semisphere of radius \( A \), the bulk energy cost \( U \) of such a droplet is

\[
U \propto \int_0^R (R^2 - x^2)^{d-1} x dx \sim \frac{R^{d+1}}{x_t},
\]

meaning that the width of the equilibrium front scales like \( x_t^{1/(d+1)} \) (the scaling \( x_t^{1/3} \) when \( d = 2 \), was found in [2]). Accordingly, the width of the equilibrium front does depend on \( x_t \), as opposed to the instantaneous front. In any case, the hallmark of a bistable system is the double peak of the fluctuation spectrum, not the shape of the front.

The problem considered here, a front pinned by smooth spatial gradient of an external field, appears to be quite generic. Beyond the experimental results that were considered in [1], it may be relevant to the effects of environmental gradient on the genetic heterozygosity of a population (see, e.g., [4]) and on the species richness, gene transfer and speciation in ecological communities along such a gradient (known as an ecotone or ecoline) [5-6]. In particular, the distinction between a stable, bifurcational front and the wandering front characterizing a bistable scenario may be very relevant to the rate of gene flow and to the chance of ecotonal species to survive. Further studies of these phenomena, and in particular an appropriate classification of front dynamics using fluctuation

![FIG. 3: Fluctuations statistics: a histogram (unnormalized) of \( a(t) \) values at the crossing point for the bifurcation (red line with filled circles) and bistable (blue) models. In both cases noise leads to deviations from the steady state value \( a = 0.5 \), however in the bifurcation case these deviations are distributed normally around the average while the bistable system distribution is bimodal. Simulation parameters are identical to those specified in the caption of Figure 2](image-url)
statistics, may shed a new light on many fundamental processes both in physics and in the life sciences.

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