First-order phase transitions in outbreaks of co-infectious diseases and the extended general epidemic process

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Abstract – In co-infections, positive feedback between multiple diseases can accelerate outbreaks. In a recent letter Chen, Ghanbarnejad, Cai, and Grassberger (CGCG) introduced a spatially homogeneous mean-field model system for such co-infections, and studied this system numerically with focus on the possible existence of discontinuous phase transitions. We show that their model coincides in mean-field theory with the homogenous limit of the extended general epidemic process (EGEP). Studying the latter analytically, we argue that the discontinuous transition observed by CGCG is basically a spinodal phase transition and not a first-order transition with phase coexistence. We derive the conditions for this spinodal transition along with predictions for important quantities such as the magnitude of the discontinuity. We also shed light on a true first-order transition with phase coexistence by discussing the EGEP with spatial inhomogeneities.

Introduction. – The recent outbreak of ebola in Africa is the latest reminder of the devastation that epidemic infectious diseases have caused throughout the history of mankind. Theoretical studies of the dynamics of epidemic processes may lead to clues for developing effective countermeasures. Such studies have focused in the past mainly on the dynamics of a single disease. Recently, however, the case of cooperative diseases, where positive feedback between multiple infections can lead to more violent progressions, has gained increasing attention (see publications cited in [1]). One of the most fundamental and interesting questions is whether cooperation in co-infections can change the outbreak from being a continuous (“second-order”) to a discontinuous (“first-order”) phase transition because the amount of time one has to enact countermeasures depends critically on the transition type. As the favorability of conditions passes the transition point, the epidemic grows continuously in a second-order transition, whereas it can take over a population explosively in a first-order transition.

Recently, Chen, Ghanbarnejad, Cai, and Grassberger (CGCG) [1], introduced a mean-field model of cooperative co-infection in a spatial homogeneous (“well-stirred”) situation by generalizing the “susceptible-infected-removed” (SIR) model [2]. Assuming the symmetry between two diseases, CGCG derived a set of ordinary differential equations describing the reactions of their model which then was integrated numerically to find out the properties of the final steady states where all disease activity has died out. As one of their main results, CGCG report that their numerical results indicate the presence of a first-order phase transition. Note though, that in non-equilibrium systems, the notion of a first-order transition is not unique, and different definitions are being used in the literature. The most stringent definition that is closest in spirit to an equilibrium first-order transition in the sense of the traditional Ehrenfest classification is one that requires the coexistence between phases at a non-equilibrium transition, too. However, the term first-order transition is also often being used for discontinuous non-equilibrium transitions without phase coexistence, e.g. for a discontinuous transition at a spinodal point. Perhaps somewhat judiciously, we adopt here the stringent definition and refer to a discontinuous transition only as a first-order transition when there is phase coexistence and we refer to a discontinuous transition at a spinodal point as a spinodal transition.

In a non-equilibrium steady state one does not have a “tool” such as a free-energy potential to properly capture a first-order transition with a spatially homogeneous model, and hence one has to resort to other approaches.
For example, one can discuss the first-order transition in terms of the drift velocity of a moving interface between both phases (provided that this interface is well defined in the sense that it is not a too rugged fractal), as we will do in the present paper. This velocity has to be zero at the transition point [3].

Here, we will argue that CGCG’s model coincides in mean-field theory with the spatially homogeneous limit of the extended general epidemic process (EGEP) that we, Janssen, Müller and Stenull (JMS) [4], introduced some 10 years ago to discuss tricritical and first-order behavior in percolation processes. Recently, the EGEP has been studied numerically by Bizhani, Paczusky and Grassberger [5]. This numerical study has verified the existence of first-order transitions in spatial dimensions larger than two as predicted by JMS.

Given the recent results by CGCG, we think that it is in order to revisit the EGEP. After briefly reviewing the EGEP, we study the homogenous mean-field theory that applies to both the CGCG model and the EGEP. The set of differential equations defining the EGEP can be reduced to an equation of motion for the removed (dead or immune) individuals. The temporal behavior of the process and the properties of the ultimate final steady states can then be understood simply by discussing the analytical behavior of the production rate for the fraction of the removed constituents, without the need for numerical integrations. It turns out that the discontinuous transition found by CGCG is a spinodal transition.

The EGEP. – We briefly review the EGEP to provide background information and to establish notation. The standard GEP [6–9], assumed to take place on a \(d\)-dimensional lattice, is described with help of the reaction scheme

\[
\begin{align*}
S(r) + X(r') & \underset{\kappa}{\rightarrow} X(r) + X(r'), \\
X(r) & \underset{\lambda}{\rightarrow} Z(r),
\end{align*}
\]

with reaction rates \(\kappa\) and \(\lambda\). \(S\), \(X\), and \(Z\) respectively denote susceptible, infected, and removed individuals on nearest-neighbor sites \(r\) and \(r'\) of a \(d\)-dimensional lattice. A susceptible individual may be infected by an infected neighbor with rate \(\kappa\) (reaction (1a)). By this mechanism the disease (henceforth also called the agent) spreads diffusively. Infected individuals are removed with a rate \(\lambda\) (reaction (1b)). JMS extended the GEP reaction scheme by introducing weak (or touched) individuals \(Y\). Instead of being infected right away by an agent, any susceptible individual may be weakened with a reaction rate \(\mu\) by such an encounter. When the disease passes by anew, a weakened individual is more susceptible to attracting the disease and gets sick with a rate \(\nu > \kappa\). Therefore, the EGEP is described by the additional reactions

\[
\begin{align*}
S(r) + X(r') & \underset{\mu}{\rightarrow} Y(r) + X(r'), \\
Y(r) + X(r') & \underset{\nu}{\rightarrow} X(r) + X(r').
\end{align*}
\]

Note that these two reactions introduce a kind of cooperation through repeated encounters of agents which then can lead to instabilities.

Denoting by \(s\), \(w\), \(n\), \(m\) the fractions of the total population of the constituents \(S\), \(Y\), \(X\), and \(Z\), respectively, the reaction equations read

\[
\begin{align*}
\dot{s}(t, r) &= -(\kappa + \mu) s(t, r) n(t, r), \\
\dot{w}(t, r) &= (\mu s(t, r) - \nu m(t, r)) n(t, r), \\
\dot{n}(t, r) &= (\kappa s(t, r) + \nu w(t, r)) n(t, r) - \lambda n(t, r), \\
\dot{m}(t, r) &= \lambda n(t, r),
\end{align*}
\]

where

\[
\dot{n}(t, r) = \frac{1}{2d} \sum_{r'} n(t, r') = \frac{1}{\lambda} \frac{\partial}{\partial t} \bar{m}(t, r).
\]

Here, \(\sum_{r'} n(t, r')\) denotes summation over the 2\(d\) nearest neighbors of site \(r\). Note, that in the homogeneous limit, the first three reaction equations of the scheme (3) are identical to the reaction equations of CGCG. At each lattice site there is the additional constraint

\[
s + w + n + m = 1.
\]

Equations (3a) and (3b) are readily integrated. Using the initial conditions \(s(0, r) = s_0(r), w(0, r) = w_0(r), m(0, r) = 0\), we obtain

\[
s(t, r) = s_0(r) \exp(-\rho \bar{m}(t, r))
\]

and

\[
w(r, t) = w_0(r) \exp(-\nu \bar{m}(t, r))
\]

where we have defined \(\rho = \kappa + \mu\). The time scale \(\lambda\) has been set to unity for simplicity. Equation (3d) together with the constraint (5) finally leads to the mean-field equation of motion for the removed individuals of the EGEP:

\[
\dot{m}(t, r) = 1 - m(t, r) - w_0(r) \exp(-\nu \bar{m}(t, r))
\]

\[
- s_0(r) \left( \frac{\nu - \kappa}{\nu - \rho} \exp(-\rho \bar{m}(t, r)) - \frac{\rho - \kappa}{\nu - \rho} \exp(-\nu \bar{m}(t, r)) \right).
\]

Homogeneity and spinodal transition. – First we consider the spatially homogeneous case. We use the initial values \(s_0 = 1 - \varepsilon, w_0 = \nu c\), implying \(n_0 = (1 - r) \varepsilon\). To establish contact with the notation of CGCG, we set \(\rho = 2\alpha, \kappa = \alpha \delta, \nu = \alpha c\), where \(c\) is a measure of cooperativity. For convenience, we include the factor \(\alpha\)
We make the simplifying replacements $\frac{\varepsilon}{K} = \alpha$ as we can because we are interested in small $\varepsilon$, $\varepsilon \sim 10^{-3}$ or so. Using the CGCG-value $\delta = 1$ (in addition CGCG use $r = 1/2$), the equation of motion reads

$$\frac{\dot{m}}{\alpha} = R(m) = G(m, c) - \frac{m}{\alpha} + \varepsilon \left(1 - re^{-cm}\right), \quad (10a)$$

$$G(m, c) = \left\{1 - \frac{c - 1}{c - 2} e^{-2m} + \frac{1}{c - 2} e^{-cm}\right\}. \quad (10b)$$

This differential equation can be solved by a simple integration. Using $m = 0$ for $t = 0$, we obtain the inverse function

$$t = I(m) := \int_0^m \frac{dm'}{\alpha R(m')} \quad (11)$$

of $m(t)$. From this result, one can readily extract analytical prediction for the time-dependent quantities in the numerical study of CGCG.

Here, however, we are mainly interested in the final steady state with $n(t \to \infty) = 0$, where all activity has died out. This state is determined by the $m = m_\infty := m(t \to \infty)$ that solves the equation $R(m_\infty) = 0$. To simplify the discussion of our analytical results and their comparison to the numerics of CGCG, we switch from $m$ as our order parameter to the fraction of converted susceptibles

$$K = 1 - s = 1 - s_0 \exp \left(-2m\right) \quad (12)$$

as used by CGCG. Note that this mapping from $m$ to $K$ is one-to-one. Figure 1 displays a collection of curves of $K = K_\infty := K(t \to \infty)$ as functions of $\alpha$ with parameter $c$ for $r = 1/2$ and small $\varepsilon$, $\varepsilon = 5 \times 10^{-3}$ and $\varepsilon = 10^{-4}$. Comparing fig. 1 with fig. 2 of ref. [1], we note that the numerical curves of CGCG are implied in our analytical curves.

We think that it is worthwhile to discuss the order parameter curves in more detail. Figure 2 shows a schematic sketch of a generic order parameter curve for some given $c$. Only those parts of the curve that have a positive gradient are locally stable. The part between the spinodal points $s$ and $u$ is an unstable branch. In the hatched part of the figure, the rate $R(m)$ is negative and therefore non-physical in the homogeneous case. Let us suppose that we want to follow a process with a given set of parameters from its beginning to its end. Every such process starts with $m = 0$, i.e., $K = \varepsilon$, and its order parameter is the final $K = K_\infty$. Each process with fixed $c$ and $\alpha$ corresponds to an upward directed vertical line in fig. 2. If $\alpha < \alpha_{sp}$, the upper part of the curve is inaccessible to the process and its final $K$ lies on the lower branch. If $\alpha > \alpha_{sp}$, the final $K$ lies on the upper branch. Thus, the order parameter jumps right at the spinodal point $u$, where the parameter $\alpha$ takes the value $\alpha_{sp}$. This jump is in perfect agreement with the discontinuities produced by the numeric integration procedure of CGCG. Note that the numerical curves shown in fig. 2 of ref. [1] and our analytical curves can literally be superimposed, including the jumps. CGCG interpret these discontinuities as first-order phase transitions with thresholds $\alpha = \alpha(c)$. We learn here, though, that they are transitions at a spinodal point, the point where the lower locally stable part of the curve becomes unstable. Since the reactions are completely irreversible, the upper spinodal point $s$ with corresponding $\alpha = \alpha_s$ is irrelevant, and no hysteresis appears. $\alpha_{tr}$ pertains to the EGEP when spatial inhomogeneity is permitted, see further below, where we will argue that true first-order transition appears in the EGEP at values $\alpha = \alpha_{tr}(c)$ in the interval between $1/2 < \alpha < 1$ even in the limit $\varepsilon \to 0$ where all the $\alpha_{sp}(c)$ tend to 1.

In addition to the order parameter curves, all the other numerical results by CGCG absolutely agree with and in fact can be extracted from the analytical results presented in ref. [4] including the mean-field behavior near the tricritical point $c = 2$, $\alpha = 1$ and the critical line $c < 2$, $\alpha = 1$. We note that the limit $c \to \infty$ leads back to the ordinary GEP with a continuous transition now at $\alpha = 1/2$.

Beyond these established results, we think it is interesting to calculate the range of values of the cooperativity $c$ over which the discontinuous behavior seen in the numerics of CGCG exists. The end points of this range are defined by the inflection point with vertical tangent of the order parameter curves. Hence, to determine these
are, in general, functions of the spatial position. Because of this, we seek the solutions of the diffusion equation

\[ \frac{\partial M}{\partial t} = \nabla \cdot (D \nabla M) \]

where \( D \) is some combination of constants and the prime \( G' \) denotes the derivative of \( G \) with respect to \( m \). Note that according to eq. (8), \( R \) and \( G \) depend on the initial distribution of the susceptibles and agents, and, therefore, are, in general, functions of the spatial position. Because we are interested in the final steady state determined by \( \hat{m} = 0 \), we focus on the steady-state condition

\[ \lambda \nabla^2 m + V'(m) = 0, \]

where \( V(m; \alpha, c) \) is a “potential” defined by the integral

\[ V(m; \alpha, c) = \int_0^m \frac{d\eta'}{G'(\eta')}, \]

which we have explicitly displayed the dependence on the parameters \( \alpha \) and \( c \). Next, we determine the point \( \alpha_{tr} \) where the disease changes from endemic to pandemic behavior, that is where the spreading, initiated by an completely infected planar slab, begins to evolve but stops in a formerly non-infected region (\( \varepsilon = 0 \)). To this end, we seek a solution of the steady state in the form of an interface between the two phases with order parameters \( m = m_1 \) and \( m = m_2 \) determined by \( R(m_1) = R(m_2) = 0 \) that is planar and perpendicular to the coordinate \( x \). Then the steady-state condition (16) leads to

\[ \frac{d}{dx} \left( \frac{\lambda}{2} m^2 + V(m) \right) = 0 \]

which is analogous in form to a typical equation of motion with “energy” conservation in classical mechanics. Because \( dm/dx \to 0 \) deep in each phase, we have \( V(m_1) = V(m_2) \), which leads to

\[ V(m_2; \alpha, c) - V(m_1; \alpha, c) = \int_{m_1}^{m_2} \frac{d\eta}{G'(\eta)} \]

as the condition of coexistence between the two phases. Note that this coexistence condition (19) is completely analogous to the equal area construction well known from the van der Waals equation in thermostatics. Together with \( R(m_1, \alpha, c) = R(m_2, \alpha, c) = 0 \), this condition uniquely determines the locus \( \alpha = \alpha_{tr}(c) \) and discontinuity \( m_{tr}(c) \) of a true first-order transition. Table 1 compiles values of \( \alpha_{tr}(c) \) and \( m_{tr}(c) \) for \( \varepsilon = 0 \). Note that for \( \varepsilon = 0 \), the spindal point is for all \( c \) at \( \alpha_{sp} = 1 \). The usual integration of the “energy conservation law”, eq. (18), finally leads to the density profile between the two phases.

| \( c \) | 3 | 5 | 15 | 60 | 160 |
|---|---|---|---|---|---|
| \( \alpha_{tr} \) | 0.964 | 0.882 | 0.724 | 0.609 | 0.566 |
| \( m_{tr} \) | 0.251 | 0.337 | 0.274 | 0.152 | 0.095 |

Fig. 3: The range of parameters (hatched area) for which there is a discontinuous transition.

Table 1: Values of the transition point \( \alpha_{tr}(c) \) and the discontinuity \( m_{tr}(c) \) for \( \varepsilon = 0 \).
\[ \tau = 1/\alpha - 1, \quad \sigma = c - 2, \quad \text{and} \quad g = c^2 + 2c - 4. \]

With these approximations, the potential defined in eq. (17) becomes

\[ V(m) = -\frac{\tau}{2}m^2 + \frac{\sigma}{6}m^3 - \frac{g}{24}m^4. \quad (21) \]

Note that our approximation, although certainly not quantitatively correct, comprises all qualitative aspects of the EGEP.

Now, we return to the coexistence condition and its evaluation. Equation (19) in conjunction with the fact that \( m_1 \) and \( m_2 \) are solutions of \( V'(m) \sim R(m) = 0 \) leads to

\[ \frac{\tau_{tr}}{g} = \frac{1}{3} \left( \frac{\sigma}{g} \right)^2, \quad m_1 = 0, \quad m_2 = 2\frac{\sigma}{g}, \quad (22) \]

for the transition point and the order parameters of the two phases. These results imply that the discontinuity \( d_{tr} = m_2 - m_1 \) at the first-order transition is

\[ d_{tr} = 2\frac{\sigma}{g}. \quad (23) \]

From our approximation, eq. (20), we can also extract information about the spinodal transition. Our discussion above (see fig. 2) implies that the rate \( R(m) \) (20) fulfills the conditions \( R(m_3) = R'(m_3) = R(m_4) = 0 \) at the spinodal transition point \( \tau = \tau_{sp} = 0 \), where \( m_3 \) and \( m_4 \) denote the order parameter values at that point. It follows that

\[ m_3 = 0, \quad m_4 = 3\frac{\sigma}{g}. \quad (24) \]

The spinodal discontinuity \( d_{sp} = m_4 - m_3 \) therefore is

\[ d_{sp} = 3\frac{\sigma}{g}. \quad (25) \]

in agreement with our discussion of the spatially homogeneous case.

Having discussed steady-state and coexistence properties, we would like to conclude by mentioning that approximate analytical results for the time dependence of the order parameter are available. In ref. [4], we have studied if and under which conditions a percolating interface can emerge and spreads from a plane-like source, i.e., an entire infected slab in the region \(-x/a \gg 1\). Indeed, the reaction-diffusion equation (15) has such a traveling front solution. With the notation used here, this solution reads

\[ m(x, t) = A \left\{ 1 - \tanh[b(x - vt)] \right\}, \quad (26) \]

where

\[ A = \frac{3}{4} \left( \sqrt{\frac{\sigma}{g}} - \frac{8\tau}{3g} + \frac{\sigma}{g} \right), \quad b = \sqrt{\frac{g}{12\lambda}}, \quad (27a) \]

\[ v = \frac{3\alpha}{4} \sqrt{3g\lambda} \left( \sqrt{\frac{\sigma}{g}} - \frac{8\tau}{3g} - \frac{\sigma}{3g} \right), \quad (27b) \]

The positivity of \( \dot{m} \) requires that \( v \geq 0 \). At the first-order transition, \( v \) vanishes, whereas at the spinodal point \( \tau = 0 \) it is

\[ v_{sp} = 3\alpha \sqrt{\lambda/2} \frac{\sigma}{g} > 0 \quad (28) \]

which shows that there is no phase coexistence at this point. The percolating front of the disease propagates with a finite velocity (explosively) under spinodal conditions. Near the first-order transition, \( \tau \leq \tau_{tr} \), the velocity behaves as \( v \sim (\tau_{tr} - \tau) \), which implies a depinning transition with a mean-field exponent \( \beta = 1 \).

Concluding remarks. – The present letter serves three purposes. First, it comments on the recent letter by CGCG. It demonstrates that the jumps in the numerical curves by CGCG have to be interpreted basically as a spinodal rather than a true first-order phase transition with phase coexistence. Second, it derives the conditions for having a true first-order transition within the underlying model system and it provides various results for physical observables at this transition such as the magnitude of the order parameter discontinuity, etc. Third, it contributes to the basic understanding of discontinuous percolation transitions, an area of statistical physics that has recently enjoyed expanding activity [10].

To avoid any potentially lingering confusion, we would like to stress here that first-order and spinodal transitions in non-equilibrium systems are both discontinuous phase transitions. Both display a discontinuity of the same order parameter at the transition; however, both start with different initial states. The following important difference between them arises if one admits inhomogeneous states: At a first-order transition, one has 2 distinct phases coexisting in the final steady state with a stationary interface between them. At a spinodal transition, a spatially homogeneous initial state undergoes a discontinuous transition to a new homogeneous final state, and an initial point-like seed of the contagion would spread out infinitely far with finite velocity.

It is worth emphasizing further the interesting connection between disease spreading and a depinning transition that emerged above. When assuming a \((d-1)\)-dimensional planar slab of infected individuals as the initial state of the EGEP, the mean-field picture that we saw was the following: Below the threshold \( \alpha_{tr} \), the front of the epidemic process progresses diffusively until it stops before a macroscopically large area has become infected. Right at \( \alpha_{tr} \), the front progresses diffusively. When the process stops, a macroscopically large area has become infected with an interface between the infected and non-infected regions that is shaped, on average, as described above. This final state is what we have been alluding to as phase coexistence. Above \( \alpha_{tr} \), the front progresses ballistically, and the infection takes over the entire system.

The qualitative change in the dynamics of the interface right at \( \alpha_{tr} \) clearly has the character of a critical depinning transition.
In this letter, we have restricted our discussion to mean-field theory. In a future publication [11], we will derive a field-theoretic interface model for the EGEP, and we will discuss the first-order transition and the accompanying continuous depinning transition of the percolating front of the contagion beyond mean-field theory. Giving up the mean-field condition, the CGCG model and the EGEP behave differently. The CGCG model corresponds to two cooperatively coupled ordinary GEPs [12], which leads to a hybrid transition with both first-order and universal second-order phase transition aspects and a very rich phenomenology. The EGEP, on the other hand, corresponds to only one GEP cooperating with itself, and it leads to a phase diagram with a line of true first-order transitions with phase coexistence as the threshold of spreading that is separated from a line of continuous ordinary percolation transitions by a tricritical point. The critical depinning transition accompanying the discontinuous transition has a rough interface which seems to belong to the universality class of critically pinned interfaces in isotropic random media [5].

Recently, there has been considerable interest in the literature in hybrid phase transitions that show both first-order and second-order behavior [10]. Though we have not yet studied any of these systems in detail, we note here the intriguing possibility that such hybrid transitions, in particular in random and interdependent networks without short loops (locally tree-like and, therefore, with generic mean-field behavior) [13–18], are often associated with spinodal transitions [19–21].

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