SIS epidemics with time-dependent rates describing ageing of information spread and mutation of pathogens

P. Van Mieghem*

Delft University of Technology
v1: 15 June 2014
v2: 24 February 2015

Abstract

We present the exact solution of the classical mean-field SIS epidemics on regular graphs with general time-dependent rates. Our solution provides an explanation why fits of measured data on popularity of on-line social networks and of websites based on models with constant rates seem to be so successful. Moreover, we show that oscillatory rates may model mutation behavior in epidemics.

1 Introduction

Most papers on SIS epidemics assume, for simplicity, that the infection rate β and curing rate δ are constant, independent of time. In reality, these rates are not necessary constant during the lifetime of an epidemic. The infection strength can diminish over time. For example, consider information spread on a network (such as Twitter). When the news is "hot", it spreads fast, but after some time, the information ages and looses attraction, so that retweeting fades. Another example of time-varying rates stems from real epidemics, where the virus can mutate over time or where infected hosts increase their resistance against the virus and their immune system slowly recovers to annihilate the virus.

From a modeling point of view, there are not many analytically solvable SIS-like epidemic models, that can incorporate time-dependent rates. Kendall's linear rate birth and death process [1] is, perhaps, the first epidemic model with time-dependent rates that has an analytic solution. Kendall computes the probability that the infected subpopulation has k members. Each infected individual can infect a susceptible member of the population with infection rate $\beta(t)$. At the same time, an infected individual can be cured at rate $\delta(t)$ and leave the infected subpopulation. Solving the exact SIS Markovian epidemics with time-dependent rates is currently intractable, even on the complete graph. Indeed, the SIS Markovian epidemics on the complete graph can be reduced to a quadratic rate birth and death process as shown in [2]. While a linear rate birth and death process still has an analytic solution (as beautifully shown by Kendall [1]), we are in doubt whether a quadratic rate birth and

*Faculty of Electrical Engineering, Mathematics and Computer Science, P.O Box 5031, 2600 GA Delft, The Netherlands; *email*: P.F.A.VanMieghem@tudelft.nl

death process with general time-dependent rates is solvable (as argued in [3, p. 243]). However, if a mean-field approximation is made, which is very accurate for the complete graph, then an analytic solution is possible as we will show here.

In the N-intertwined mean-field approximation (NIMFA) [4, 5], the governing equation for the probability $v(t)$ of infection in a node at time t in a regular graph G with degree r equals

$$\frac{dv(t)}{dt} = r\beta(t)\, v(t)\,(1 - v(t)) - \delta(t)\, v(t) \tag{1}$$

where the infection rate $\beta(t)$ and the curing rate $\delta(t)$ are general non-negative real functions of time t. The probability $v(t)$ at time t changes due to two possible actions: (a) if the node is healthy with probability $1 - v(t)$, its r infected neighbors – each neighbor is infected with the same probability $v(t)$ (due to symmetry) – can infect the node with instantaneous rate $\beta(t)$; (b) when the node is infected, which happens with probability $v(t)$, a curing processes with instantaneous rate $\delta(t)$ can heal the node. Since the rates are time-varying, the infection and curing process are independent, inhomogeneous Poisson processes [3]. As shown in [6] for regular graphs, the governing differential equations are precisely the same for NIMFA and the heterogeneous mean-field (HMF) approximation [7] of Pastor-Satorras and Vespignani. Hence, the equation (1) constitutes a general SIS mean-field approximation for regular graphs. An interesting feature of (1) is its independence on the size of the network, which avoids (or ignores) finite-size effects that often complicate studies of phase transitions. Finally, for regular graphs, the NIMFA average fraction of infected nodes $y(t) = v(t)$ and $y(t)$ is coined the order parameter in statistical physics.

Equation (1) with constant rates, $\beta(t) = \beta$ and $\delta(t) = \delta$, has been investigated earlier by Kephart and White [8]. Many variations on and extensions of the epidemic Kephart and White model have been proposed (see e.g. [9]). In fact, the differential equation (1) with constant rates has already appeared in earlier work (see e.g. [10, 11]) and is also known as the logistic differential equation of population growth, first introduced by Verhulst [12] in 1845. Verhulst has deduced (1) for the population size $p(t) = v(t)$ at time t, with $r\beta(t) = m$ (population growth rate) and $r\beta(t) - \delta(t) = n$ ("undetermined coefficient") and has written the solution as

$$t = \int_{p_0}^{p(t)} \frac{ds}{ns - ms^2} = \frac{1}{m} \ln\left(\frac{p(t)\left(\frac{m}{n} - p_0\right)}{p_0\left(\frac{m}{n} - p(t)\right)}\right)$$

which is further interpreted in terms of $\frac{m}{n}$ and compared with demographic data.

Motivated by the large application range of the differential equation (1), which has to our knowledge previously not been studied in the field of epidemics, we present here a short analysis with most mathematics deferred to the Appendices.

2 General solution of (1)

As shown in Appendix A, the differential equation (1) can be solved exactly, resulting in

$$v(t) = \frac{\exp\left(\int_0^t (r\beta(u) - \delta(u))\, du\right)}{\frac{1}{v_0} + r\int_0^t \beta(s) \exp\left(\int_0^s (r\beta(u) - \delta(u))\, du\right) ds} \tag{2}$$

where v_0 is the initial fraction of infected nodes. The crucial quantity is the net dose

$$\rho(t) = \int_0^t (r\beta(u) - \delta(u))\, du \tag{3}$$

which equals the net average number of infection minus curing events in $[0,t]$ at a particular node in the regular graph. The net dose $\rho(t)$, which also appears as a key quantity in Kendall's [1] model, can be negative as well as positive and can change over time, which complicates a further general analysis (without detailing the specific functions $\beta(u)$ and $\delta(u)$). In terms of the net dose, (2) becomes

$$v(t) = \frac{e^{\rho(t)}}{\frac{1}{v_0} + r\int_0^t \beta(s)\, e^{\rho(s)} ds} \tag{4}$$

Since $\rho'(s) = r\beta(s) - \delta(s)$ and $\int_0^t \rho'(s)\, e^{\rho(s)} ds = e^{\rho(t)} - 1$, we have that

$$r\int_0^t \beta(s)\, e^{\rho(s)} ds = e^{\rho(t)} - 1 + \int_0^t \delta(s)\, e^{\rho(s)} ds$$

so that

$$v(t) = \frac{1}{1 + \left(\frac{1}{v_0} - 1\right) e^{-\rho(t)} + e^{-\rho(t)} \int_0^t \delta(s)\, e^{\rho(s)} ds} \tag{5}$$

Since[1] $0 \leq e^{-\rho(t)} \int_0^t \delta(s)\, e^{\rho(s)} ds \leq e^{-\rho(t)} \max_{s\in[0,t]} e^{\rho(s)} \int_0^t \delta(s)\, ds$, we deduce from (5) the lower bound

$$v(t) \leq \frac{1}{1 + \left(\frac{1}{v_0} - 1\right) e^{-\rho(t)}} \tag{6}$$

and the lower bound

$$v(t) \geq \frac{1}{1 + \left(\frac{1}{v_0} - 1\right) e^{-\rho(t)} + e^{-\rho(t)} \max_{s\in[0,t]} e^{\rho(s)} \int_0^t \delta(s)\, ds} \tag{7}$$

Since the lowest possible value of $e^{-\rho(t)} \max_{s\in[0,t]} e^{\rho(s)}$ is one, which occurs if $\rho(t) = \max_{s\in[0,t]} \rho(s)$, for example, if $\rho(t)$ is increasing for all t, the highest possible lower bound is achieved[2]

$$v(t) \geq \frac{1}{1 + \left(\frac{1}{v_0} - 1\right) e^{-\rho(t)} + \int_0^t \delta(s)\, ds} \tag{8}$$

[1] The mean value theorem [13, p. 65] states that, if $\phi(x) \geq 0$ and $f(x)$ is continuous, there exists a number $a \leq \xi \leq b$ such that

$$\int_a^b f(x)\, \phi(x)\, dx = f(\xi) \int_a^b \phi(x)\, dx$$

Application of the mean value theorem yields, with $0 \leq \xi \leq t$,

$$e^{-\rho(t)} \int_0^t \delta(s)\, e^{\rho(s)} ds = e^{-\rho(t)+\rho(\xi)} \int_0^t \delta(s)\, ds$$

[2] Alternatively, after partial integration, we obtain

$$e^{-\rho(t)} \int_0^t \delta(s)\, e^{\rho(s)} ds = \int_0^t \delta(s) - e^{-\rho(t)} \int_0^t ds e^{\rho(s)} \rho'(s) \int_0^s \delta(u)\, du$$

and

$$v(t) = \frac{1}{1 + \int_0^t \delta(s) + e^{-\rho(t)} \left(\frac{1}{v_0} - 1 - \int_0^t ds e^{\rho(s)} \rho'(s) \int_0^s \delta(u)\, du\right)}$$

which illustrates that, if $\int_0^t ds e^{\rho(s)} \rho'(s) \int_0^s \delta(u)\, du \geq 0$, the largest possible lower bound (8) is reached and this happens, e.g. if $\rho'(s) \geq 0$ for $s \in [0,t]$.

These bounds (6) and (7) help to evaluate some limit cases. If $\lim_{t\to\infty}\rho\left(t\right)=\rho_{\infty}\to-\infty$, then the upper bound (6) shows that the steady-state infection probability $v_{\infty}=0$. Also, if ρ_{∞} is finite, then v_{∞} is always smaller than 1, but larger than zero. On the other hand, if $\rho_{\infty}\to\infty$, so that $\lim_{t\to\infty}e^{-\rho(t)}\max_{s\in[t_0,t]}e^{\rho(s)}=1$, the lower bound (7) becomes

$$v_{\infty}\geq\frac{1}{1+\int_{0}^{\infty}\delta\left(s\right)ds}$$

If, in addition to $\rho_{\infty}\to\infty$, $\int_{0}^{\infty}\delta\left(s\right)ds$ is finite, then $v_{\infty}>0$, implying that there is always a non-zero fraction of nodes infected. On the other hand, if $\int_{0}^{\infty}\delta\left(s\right)ds\to\infty$, then $v_{\infty}\geq0$ and the steady state can still be infection free. Given that $\rho_{\infty}=\int_{0}^{\infty}r\beta\left(s\right)ds-\int_{0}^{\infty}\delta\left(s\right)ds\to\infty$, this conclusion is quite remarkable, because infinitely many more infection events can still be annihilated. In other words, even if there is (infinitely) more "infection power" than "curing power", the epidemics can still disappear eventually. In some sense, this imbalance is a reflection of the asymmetry in the governing equation (1), namely $v\left(t\right)\left(1-v\left(t\right)\right)$ for $r\beta$ versus $v\left(t\right)$ for δ.

If $\lim_{t\to\infty}\beta\left(t\right)=\beta_{\infty}$ and $\lim_{t\to\infty}\delta\left(t\right)=\delta_{\infty}$ exist, then the steady state can also be deduced from the differential equation (1), leading to

$$0=r\beta_{\infty}v_{\infty}\left(1-v_{\infty}\right)-\delta_{\infty}v_{\infty}$$

that has the trivial solution $v_{\infty}=0$ and, with $\tau_{\infty}=\frac{\beta_{\infty}}{\delta_{\infty}}$, the non-trivial one

$$v_{\infty}=1-\frac{1}{r\tau_{\infty}}$$

which resembles the classical NIMFA steady state for a regular graph. Extremal values of $v\left(t\right)$ are investigated in Appendix B.

2.1 Linear scaling of quantities

In measurements, a linear scaling of time $t=\gamma u$ or $q\left(t\right)=sv\left(t\right)$ is often useful. For example, usually, the number of infected nodes $q\left(t\right)=Nv\left(t\right)$ is measured, rather than the average fraction of infected nodes or the probability of infection $v\left(t\right)$. The time scaling (in units of either hours, minutes or seconds), $t=\gamma u$, is relatively easily incorporated in the differential equation (1),

$$\frac{dv\left(\gamma u\right)}{\gamma du}=r\beta\left(\gamma u\right)v\left(\gamma u\right)\left(1-v\left(\gamma u\right)\right)-\delta\left(\gamma u\right)v\left(\gamma u\right)$$

Defining $v^{*}\left(u\right)=v\left(\gamma u\right)$ and similarly, $\beta^{*}\left(u\right)=\beta\left(\gamma u\right)$ and $\delta^{*}\left(u\right)=\delta\left(\gamma u\right)$, we arrive at

$$\frac{dv^{*}\left(u\right)}{du}=r\gamma\beta^{*}\left(u\right)v^{*}\left(u\right)\left(1-v^{*}\left(u\right)\right)-\gamma\delta^{*}\left(u\right)v^{*}\left(u\right)$$

By comparing with the orginal differential equation (1), we conclude that the linear time transformation $t=\gamma u$, transforms the rate functions $\beta\left(t\right)\to\gamma\beta\left(\gamma u\right)$ and $\delta\left(t\right)\to\gamma\delta\left(\gamma u\right)$, which physically makes sense because a rate is expressed as an average number of events per unit time.

The other scaling $q\left(t\right)=sv\left(t\right)$ is a little more involved. After multiplying both sides of the differential equation (1) by s, we observe that

$$\frac{d\left(sv\left(t\right)\right)}{dt}=\left\{r\beta\left(t\right)-\delta\left(t\right)\right\}\left(sv\left(t\right)\right)-\frac{r}{s}\beta\left(t\right)\left(sv\left(t\right)\right)^{2}$$

resulting, by letting $q(t) = sv(t)$, in the differential equation

$$\frac{dq(t)}{dt} = \{r\beta(t) - \delta(t)\} q(t) - \frac{r}{s}\beta(t) q^2(t)$$

which is slightly different from (1). Its solution follows from the Appendix A, where the function $h(t) = \frac{r}{s}\beta(t) q^2(t)$ instead of $h(t) = r\beta(t) v^2(t)$, as

$$q(t) = \frac{e^{\rho(t)}}{\frac{1}{q_0} + \frac{r}{s}\int_0^t \beta(s) e^{\rho(s)} ds} \tag{9}$$

with the net dose $\rho(t)$ still unchanged and precisely equal to (3), thus without scaling $r \to \frac{r}{s}$. Another way to see the result (9) of the scaling $q(t) = sv(t)$ follows by multiplying both sides of (4) by s and using $q(t) = sv(t)$ and $q(0) = q_0 = sv_0$,

$$q(t) = \frac{v(t)}{\frac{1}{s}} = \frac{e^{\rho(t)}}{\frac{1}{sv_0} + \frac{r}{s}\int_0^t \beta(s) e^{\rho(s)} ds}$$

In conclusion, a scaling $q(t) = sv(t)$ only changes the degree $r \to \frac{r}{s}$ in (9), but leaves the net dose $\rho(t)$ in (3) unchanged.

2.2 Examples

When the rates vary as a power in t, i.e. $\beta(t) = \beta t^b$ and $\delta(t) = \delta t^d$, then

$$\rho(t) = \int_0^t \left(r\beta u^b - \delta u^d\right) du = \frac{r\beta}{b+1} t^{b+1} - \frac{\delta}{d+1} t^{d+1}$$

where both $b > -1$ and $d > -1$ must be positive (else $\rho(t)$ does not exist). Only if the powers are equal, $b = d > -1$, we can evaluate the integral in (2), leading to

$$r\int_0^t \beta(s) \exp\left(\int_0^s (r\beta(u) - \delta(u)) du\right) ds = \frac{r\beta}{r\beta - \delta}\left\{\exp\left((r\beta - \delta)\frac{t^{b+1}}{b+1}\right) - 1\right\}$$

and (2) becomes

$$v(t) = \frac{1}{\left(\frac{1}{v_0} - \frac{1}{1-\frac{1}{r\tau}}\right) \exp\left(-(r\tau - 1)\frac{\left(\frac{t}{\frac{1}{\delta^{b+1}}}\right)^{b+1}}{b+1}\right) + \frac{1}{1-\frac{1}{r\tau}}} \tag{10}$$

which generalizes the Kephart and White solution, that corresponds to $b = 0$, to any real power $b > -1$. We observe that the exponent b is merely a form factor that does not essentially change the physical interpretation, only the speed towards the steady state. Also, the time unit is most conveniently expressed in terms of $\delta^{\frac{1}{b+1}}$, i.e. $t^* = \frac{t}{\frac{1}{\delta^{b+1}}}$. When $0 > b > -1$, the rates decrease over time and are very high for small t.

A more intriguing behavior is generated for oscillatory rates. We confine here[3] to $r\beta(t) = e^{at}\cos^2\omega_\beta t$ and $\delta(t) = e^{at}\cos^2\omega_\delta t$, for which the instantaneous effective infection rate $\tau(t) = \frac{\beta(t)}{\delta(t)} =$

[3] There is a wealth of oscillatory functions such as $\cos(\omega t^\gamma + \varphi)$, $\cos(\omega(\log t)^\gamma + \varphi)$ and Bessel functions $J_p(t)$. In fact, the real (or imaginary) part $\mathrm{Re}\, f(x + it)$ of most analytic functions $f(z)$ that are real on the real axis; e.g. the real part of the Gamma function $\Gamma(z)$ and of the Riemann Zeta function $\zeta(z)$.

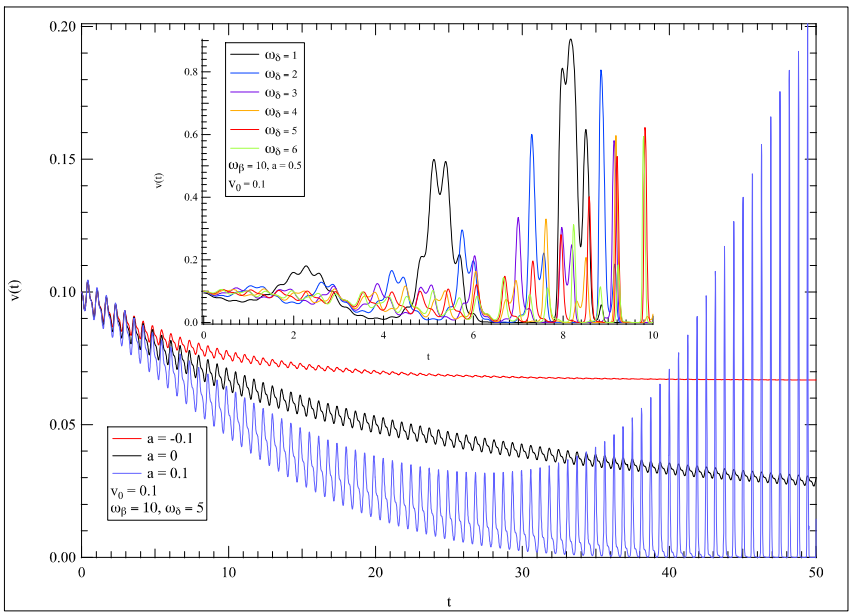

Figure 1: The fraction of infected nodes $v\,(t)$ versus time t for oscillatory infection and curing rates with parameters $\omega_\beta = 10$, $\omega_\delta = 5$ and three exponential arguments $a = -0.1, 0, 0.1$. The initial fraction of infected nodes was $v_0 = 0.1$. The inset shows the effect of changes in the frequencies $\omega_\delta = (1, 2, 3, 4, 5, 6)$, while $\omega_\beta = 10$ and $a = 0.5$. The higher $\frac{\omega_\beta}{\omega_d}$, the more bursty $v\,(t)$ varies over time t.

$\frac{1}{r}\left(\frac{\cos\omega_\beta t}{\cos\omega_\delta t}\right)^2$ can tend to infinity when $\frac{\omega_\beta}{\omega_\delta}$ is not an odd integer. The net dose

$$\rho\,(t) = e^{at}\left(\frac{a^2\cos(2\omega_\beta t) + a^2 + 2a\omega_\beta\sin(2\omega_\beta t) + 4\omega_\beta^2}{2\left(a^3 + 4a\omega_\beta^2\right)} - \frac{a^2\cos(2\omega_\delta t) + a^2 + 2a\omega_\delta\sin(2\omega_\delta t) + 4\omega_\delta^2}{2\left(a^3 + 4a\omega_\delta^2\right)}\right)$$

oscillates between $-e^{at}$ and e^{at}. As illustrated in Fig. 1, the average fraction of infected nodes exhibits a rich oscillatory behavior with similar features as in the simple pathogen mutation model of Girvan *et al.* [14].

3 Applications and conclusion

In a study on the growth and death of websites, Ribeiro [15] has modeled measured data based on a variant of (10) with $b = 0$. Although the rates in his model were constant, interestingly, Ribeiro was able to fit the data well. When replacing the integrals over $[0, t]$ in $\rho\,(t)$ by constants (that act as fit parameters) and noting that the sensitivity (15) of the integral in (5) is weak as shown in Appendix C, (2) reduces roughly to the constant rate case (i.e. (10) with $b = 0$). Hence, Ribeiro's fit function also appears valid for time-dependent growth and decay of websites, which may explain the success of fitting the measured data of websites.

Gleeson *et al.* [16] investigated the popularity of memes in Twitter. When competition between memes is ignored, their model is based on the differential equation (1) with constant rates, $\beta\,(t) = \beta$

and $\delta(t) = \delta$. Even with this constant rate model, Gleeson *et al.* [16] found a relatively good match with Twitter data. Just as in Ribeiro's study, our analysis here support the wider validity of their model.

In summary, we have derived the general solution (2, 5) of the differential equation (1), which only gives a first-order description of many spreading phenomena, because the underlying network is largely simplified and a mean-field approximation is made. In spite of these shortcomings, the model (2, 5) seems capable to explain the success of fit models with constant rates of measured processes possessing time-dependent rate functions. Also, the effect of mutation can be modeled (in contrast to the constant-rate logistic function).

Acknowledgement. We are grateful to Rob Kooij and Odo Diekmann for pointing out that our solution (2) is a special case of a non-linear Bernoulli differential equation[4]. Odo has informed us about the literature in mathematical physics or applied mathematics on the "logistic" differential equation (1) and the delayed logistic variant. The work is supported by EU project CONGAS (Grant No. FP7-ICT-2011-8-317672).

References

[1] D. G. Kendall. On the generalized birth-and-death process. *Annals of Mathematical Statistics*, 19(1):1–15, 1948.

[2] P. Van Mieghem and E. Cator. Epidemics in networks with nodal self-infections and the epidemic threshold. *Physical Review E*, 86(1):016116, July 2012.

[3] P. Van Mieghem. *Performance Analysis of Complex Networks and Systems*. Cambridge University Press, Cambridge, U.K., 2014.

[4] P. Van Mieghem, J. Omic, and R. E. Kooij. Virus spread in networks. *IEEE/ACM Transactions on Networking*, 17(1):1–14, February 2009.

[5] P. Van Mieghem. The N - Intertwined SIS epidemic network model. *Computing*, 93(2):147–169, 2011.

[6] C. Li, R. van de Bovenkamp, and P. Van Mieghem. Susceptible-infected-susceptible model: A comparison of *N*-intertwined and heterogeneous mean-field approximations. *Physical Review E*, 86(2):026116, August 2012.

[7] R. Pastor-Satorras and A. Vespignani. Epidemic dynamics and endemic states in complex networks. *Physical Review E*, 63:066117, 2001.

[8] J. O. Kephart and S. R. White. Direct-graph epidemiological models of computer viruses. *Proceedings of the 1991 IEEE Computer Society Symposium on Research in Security and Privacy*, pages 343–359, May 1991.

[9] R. Pastor-Satorras and A. Vespignani. Epidemic spreading in scale-free networks. *Physical Review Letters*, 86(14):3200–3203, April 2001.

[10] N. T. J. Bailey. *The Mathematical Theory of Infectious Diseases and its Applications*. Charlin Griffin & Company, London, 2nd edition, 1975.

[11] D. J. Daley and J. Gani. *Epidemic modelling: An Introduction*. Cambridge University Press, Cambridge, U.K., 1999.

[12] P. F. Verhulst. Recherches mathématiques sur la loi d'accroissement de la population. *Nouveaux Mémoires de l'Académie Royale des Sciences et des Belles-Lettres de Bruxelles*, XVIII:1–41, 1845.

[13] E. T. Whittaker and G. N. Watson. *A Course of Modern Analysis*. Cambridge University Press, Cambridge, UK, cambridge mathematical library edition, 1996.

[14] M. Girvan, D. S. Callaway, M. E. J. Newman, and S. H. Strogatz. Simple model of epidemics with pathogen mutation. *Physical Review E*, 65(3):031915, 2002.

[4] See e.g. http://mathworld.wolfram.com/BernoulliDifferentialEquation.html

[15] B. Ribeiro. Modeling and predicting the growth and death of membership-based websites. *World Wide Web conference 2014 (WWW14), April 7-11, 2014, Seoul, Korea, also on arxiv1307.1354v3*, 2014.

[16] J. P. Gleeson, J. A. Ward, K. P. O'Sullivan, and W. T. Lee. Competition-induced criticality in a model of meme popularity. *Physical Review Letters*, 112:048701, 2014.

[17] R. P. Feynman and A. R. Hibbs. *Quantum Mechanics and Path Integrals.* Mc-Graw-Hill, New York, 1965.

A Derivation of (2)

We rewrite the differential equation (1) as

$$\frac{dv(t)}{dt} - \{r\beta(t) - \delta(t)\} v(t) = h(t)$$

where

$$h(t) = -r\beta(t) v^2(t)$$

First[5], we focus on the linear differential, homogeneous equation,

$$\frac{dv_h(t)}{dt} - \{r\beta(t) - \delta(t)\} v_h(t) = 0$$

whose general solution is

$$\widetilde{v}_h(t) = cw(t)$$

where c is a constant and

$$w(t) = \exp\left(\int_0^t (r\beta(u) - \delta(u))\, du\right)$$

Next, we assume the existence of a solution of the form $v(t) = c(t) w(t)$, where $c(t)$ is a function to be determined from the differential equation (1). After substitution of $v(t) = c(t) w(t)$ into (1), we obtain

$$\frac{dc(t)}{dt} = -r\beta(t) c^2(t) w(t)$$

This non-linear first-order differential equation can be rewritten as

$$-\frac{dc}{c^2} = r\beta(t) w(t) dt$$

and, after integration of both sides, we find

$$\frac{1}{c(t)} - \frac{1}{c(0)} = r\int_0^t \beta(s) w(s) ds$$

Hence, the solution for $v(t) = c(t) w(t)$ becomes

$$v(t) = \frac{w(t)}{\frac{1}{c(0)} + r\int_0^t \beta(s) w(s) ds}$$

where the constant $c(0) = v(0) = v_0$. Finally, the solution of the differential equation (1) is (2).We can verify, by substitution, that this solution (2) obeys the differential equation (1).

[5] This solution is inspired by the method of the variation of a constant, which is proven to be successful for any linear differential equation.

B Extremal values for $v(t)$

Next, we rewrite (1) as

$$\frac{dv(t)}{dt} = v(t)\{r\beta(t) - \delta(t) - r\beta(t)v(t)\}$$

If $v(t) > 0$, then the sign of $\frac{dv(t)}{dt}$ depends on the sign of $r\beta(t) - \delta(t) - r\beta(t)v(t)$. In particular, if $1 - \frac{1}{r\tau(t)} \geq v(t) > 0$, then $\frac{dv(t)}{dt} \geq 0$, where $\tau(t) = \frac{\beta(t)}{\delta(t)}$, whereas, if $1 - \frac{1}{r\tau(t)} \leq v(t)$, then $\frac{dv(t)}{dt} \leq 0$. This behavior reflects the stable "attractor"

$$v^*(t) = 1 - \frac{1}{r\tau(t)}$$

because, if the value of $v(t)$ differs from $v^*(t)$ at any time t, the process will tend to direct $v(t)$ towards $v^*(t)$. A consequence is also that $v_\infty = 1 - \frac{1}{r\tau}$ is the steady state when both $\beta(t) = \beta$ and $\delta(t) = \delta$ for all times $t \geq 0$. Hence, if

$$0 < v(t) = v^*(t) = 1 - \frac{1}{r\tau(t)}$$

at some time t and $\tau(t) = \frac{\beta(t)}{\delta(t)} > \frac{1}{r}$ (due to the requirement that $v(t) > 0$), then $\frac{dv(t)}{dt} = 0$, implying that the infection process attains an extremum.

Now, consider

$$\begin{aligned}\frac{d^2v(t)}{dt^2} = {} & \frac{dv(t)}{dt}\{r\beta(t) - \delta(t) - r\beta(t)v(t)\} + \\ & + v(t)\left\{r\beta'(t) - \delta'(t) - r\beta'(t)v(t) - r\beta(t)\frac{dv(t)}{dt}\right\}\end{aligned} \tag{11}$$

In general, it is difficult to determine regimes where $v(t)$ is convex or concave. However, we observe from (11) that, at an extremal point where $\frac{dv(t)}{dt} = 0$, it holds that

$$\frac{d^2v(t)}{dt^2} = v(t)\left\{r\beta'(t) - \delta'(t) - r\beta'(t)v(t)\right\} \tag{12}$$

When both $\beta(t) = \beta$ and $\delta(t) = \delta$ for all times $t \geq 0$, then we find that $\frac{d^2v(t)}{dt^2} = \frac{dv(t)}{dt} = 0$ if $v(t) = 1 - \frac{1}{r\tau}$, which corresponds to the steady state. In the other cases where not both rates are constant, (12) illustrates that, if $v(t) = 1 - \frac{1}{r\tau(t)} > 0$ and

$$\text{if } 1 - \frac{1}{r\frac{\beta'(t)}{\delta'(t)}} \geq 1 - \frac{1}{r\tau(t)} > 0 \quad \text{then } \frac{d^2v(t)}{dt^2} \geq 0$$

implying that $v(t) = 1 - \frac{1}{r\tau(t)} > 0$ corresponds to a minimum, else,

$$\text{if } 1 - \frac{1}{r\frac{\beta'(t)}{\delta'(t)}} \leq 1 - \frac{1}{r\tau(t)} \quad \text{then } \frac{d^2v(t)}{dt^2} \leq 0$$

and $v(t) = 1 - \frac{1}{r\tau(t)} > 0$ is a maximum. Notice that $\frac{d^2v(t)}{dt^2} = \frac{dv(t)}{dt}$, if

$$v(t) = 1 - \frac{1}{r\frac{\beta(t)}{\delta(t)}} = 1 - \frac{1}{r\frac{\beta'(t)}{\delta'(t)}}$$

implying that

$$\frac{\beta(t)}{\delta(t)} = \frac{\beta'(t)}{\delta'(t)}$$

which is equivalent to

$$\frac{\delta'(t)}{\delta(t)} = \frac{\beta'(t)}{\beta(t)}$$

Hence, if the logarithmic derivatives $\frac{d\ln\beta(t)}{dt} = \frac{d\ln\delta(t)}{dt}$ are equal at some time t, then $v(t)$ corresponds to an inflection point, else, if $\frac{d\ln\beta(t)}{dt} < \frac{d\ln\delta(t)}{dt}$, then $v(t)$ is minimal; otherwise, if $\frac{d\ln\beta(t)}{dt} > \frac{d\ln\delta(t)}{dt}$, then $v(t)$ is maximal.

C Variational calculus

The expression (5) suggests us to consider the effect of rates $\beta(t)$ and $\delta(t)$ on the infection probability $v(t)$ (or prevalence, since $y(t) = v(t)$ for regular graphs). We focus on

$$V[\beta,\delta] = v^{-1}(t) = 1 + \left(\frac{1}{v_0} - 1\right) e^{-\rho(t)} + e^{-\rho(t)} \int_0^t \delta(s)\, e^{\rho(s)} ds \tag{13}$$

and we study how V changes when the function $\beta(t)$ is slightly changed. We use functional derivatives (see [17, p. 170]). We consider, for any $x \in [0,t]$,

$$V[\beta(x) + \eta(x), \delta(x)] = V[\beta(x), \delta(x)] + \int \frac{\delta V}{\delta\beta(x)} \eta(x)\, dx + o(\eta(x))$$

where $\eta(x)$ is a small perturbation function. First,

$$\int \frac{\delta e^{\rho(t)}}{\delta\beta(x)} \eta(x)\, dx = \exp\left(\int_0^t (r\beta(u) + r\eta(u) - \delta(u))\, du\right) - \exp\left(\int_0^t (r\beta(u) - \delta(u))\, du\right)$$

Now,

$$\begin{aligned}\exp\left(\int_0^t (r\beta(u) + r\eta(u) - \delta(u))\, du\right) &= \exp\left(\int_0^t (r\beta(u) - \delta(u))\, du\right) \exp\left(r\int_0^t \eta(u)\, du\right) \\ &= \exp\left(\int_0^t (r\beta(u) - \delta(u))\, du\right)\left(1 + r\int_0^t \eta(x)\, dx\right)\end{aligned}$$

to first order in η. Thus,

$$\int \frac{\delta e^{\rho(t)}}{\delta\beta(x)} \eta(x)\, dx = \int_0^t r \exp\left(\int_0^t (r\beta(u) - \delta(u))\, du\right) \eta(x)\, dx$$

so that we arrive, for $x \in [0,t]$, at

$$\frac{\delta e^{\rho(t)}}{\delta\beta(x)} = r \exp\left(\int_0^t (r\beta(u) - \delta(u))\, du\right) = r e^{\rho(t)} \tag{14}$$

Next,

$$\frac{\delta}{\delta\beta(x)}\left(e^{-\rho(t)} \int_0^t \delta(s)\, e^{\rho(s)} ds\right) = \frac{\delta e^{-\rho(t)}}{\delta\beta(x)} \int_0^t \delta(s)\, e^{\rho(s)} ds + e^{-\rho(t)} \int_0^t \delta(s) \frac{\delta e^{\rho(s)}}{\delta\beta(x)} ds$$

and invoking (14)

$$\frac{\delta}{\delta\beta\left(x\right)}\left(e^{-\rho(t)}\int_{0}^{t}\delta\left(s\right)e^{\rho(s)}ds\right)=-re^{-\rho(t)}\int_{0}^{t}\delta\left(s\right)e^{\rho(s)}ds+re^{-\rho(t)}\int_{0}^{t}\delta\left(s\right)e^{\rho(s)}ds=0 \tag{15}$$

which illustrates that the sensitivity of $e^{-\rho(t)}\int_{0}^{t}\delta\left(s\right)e^{\rho(s)}ds$ on changes in the infection rate β is negligibly small. Finally, we obtain

$$\frac{\delta V}{\delta\beta\left(x\right)}=-r\left(\frac{1}{v_{0}}-1\right)e^{-\rho(t)}$$

This form shows that, merely the first term in (13) is sensitive to changes in the infection rate β.