Spatial behavioral responses to the spread of an infectious disease can suppress Turing and Turing–Hopf patterning of the disease

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Abstract

Reducing risky behaviour and/or avoiding sites where the risk of infection is perceived as higher - i.e. social and spatial distancing - represent the two main forms of non–pharmaceutical behavioral responses of humans to the threats of infectious diseases. Here we investigate, within a reaction-diffusion setting, a family of new models for an endemic SIR (susceptible-infective-removed) infectious disease for which no vaccine is available and individuals' responses to the infection threat are entirely based on changes in either their social behavior or in their mobility behavior, that is avoiding to visit sites with a high infection prevalence.

First, we derive general conditions for the onset of Turing patterns for a general class of spatially inhomogeneous SIR models with a prevalence-dependent contact rate and constant recruitment. Then, we characterize our main family of models where the behavioural response also includes a spatial component, and show the condition bringing to the mitigation, or even the destruction, of Turing patterns. **The same conditions allows the transition from Turing-Hopf spatiotemporal patterns to pure Hopf temporal patterns**. The same is also done for two SIS models. These results bring an inference of interest: the reduction of spatial clustering typically observed during the course of an epidemics might be related to a combination of agents' spontaneous social and spatial distancing.

To validate our theoretical results and further explore other spatio–temporal impact of the proposed spatial behavioral responses, numerical simulations of a SIR model have been performed.

Keywords: Human Behaviour, Infectious Diseases, Spatial, Social distancing, nonlinear Cross–Diffusion, Turing bifurcation**, Turing–Hopf instability**.

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1 Introduction

The effects of spatial mobility and spatial diffusion on the spread of infectious diseases have been investigated in many specific models described by different mathematical tools ranging from simple deterministic, spatially implicit, ODE models, to spatially explicit reaction-diffusion PDE models, up to fully stochastic models, ranging from network up to IMB models, and a wide body of results is now available [1–6]. Though some recent models are highly sophisticated and include a huge amount of structural details on the underlying population, as is the case e.g., of the highly realistic IBM models used for pandemic prediction [7–9] they suffer the general shortcoming of most mathematical epidemiology literature, namely the fact they treat humans as passive actors keeping the same behavior regardless of the state of the epidemics in the population considered. This fact, possibly already untrue in the pre-scientific period, is fully denied in the current days by a large body of evidence [10, 11]. **Important contemporary example are constituted by the recent Ebola epidemics [12–14] and H1N1 flu epidemics [15–17] . However, analysis of Spanish flu data have shown that even one century ago the spread and control of that infamous pandemics were deeply influenced by important effects related to spontaneous and forced changes of behaviour [18–20]. This was shown both for Europe [18, 19] and in USA [20].** This dramatic change of perspective in the relation between humans and infectious diseases has led, during the last 15 years, to the development of the behavioral epidemiology of infectious diseases (BE), a new branch of mathematical epidemiology (see [10, 11] and references therein) using a range of multidisciplinary tools to investigate how humans can adapt their behavior to respond to the threats brought by infections.
However, given that a large part of the behavioural epidemiology research carried out so far has been based on simple models, little work has been done yet to incorporate the agents' behavioral within spatially structured epidemiological models, especially with regard to the area of epidemic models within reaction-diffusion PDE settings. In this area the few attempts to include - mostly indirectly - behavioral components, have followed two main separate directions.

The first one is represented by those efforts including nonlinear cross diffusion terms initiated by [21, 22], where susceptible individuals are assumed to be repelled away by the gradient of the function representing the (spatial) prevalence of infective individuals. This area has seen a number of more recent contributions [23–26].

The second direction is represented by those works considering nonlinear incidence rates [27–33], and which extended to reaction-diffusion settings the pioneering paper by Capasso and Serio [34] and of later researches [35–37]. The works [27–33] focused on the search for the conditions leading to the onset of Turing bifurcations [2,3,5,38] and of Turing-Hopf instabilities [39]. Turing bifurcations are not only a hallmark of system complexity but represent in epidemiology the ability of infectious diseases to spatially clustering [27]. Turing–Hopf instability [5], being characterized by both a temporal and a spatial symmetry breaking instead represent a higher degree of complexity, often an evidence of spatiotemporal chaos [40]. And chaotic time–series are very frequent in epidemiology of childhood infectious diseases [41]. Very importantly, beside classical models where continous or regular lattice spaces were considered, many recent epidemiological works have been conducted on network–based structures [11, 42–46].

Though the adoption of nonlinear contact rates is indeed a main avenue to incorporate the agents' behaviour responses (see [10, 11] and references therein) in no one of previous paper explicit mention of behavioural hypotheses was actually made.
In this work we introduce, within a reaction-diffusion setting, a family of new models for an endemic

SIR (susceptible-infective-removed) infectious disease for which no vaccine (or pharmaceutical treatment either) is available and individuals' responses to the infection threat are entirely based on changes in either their social behavior, or in their mobility behavior, as in [21, 22]. The underlying intuition is that - once awareness of the infection has been acquired - aware individuals respond to the infection through by increasing their "'social distancing"' i.e., reducing their contact and transmission rates, and/or by increasing "'spatial distancing"' i.e., avoiding to visit those spatial sites where the local infective prevalence is perceived as relatively larger, as in [21, 22]. Arguably, combinations of "'social"' and "'spatial"' distancing have represented the two key forms of humans' behavioral responses to the threats of infectious diseases in mankind history before the advent of pharmaceutical interventions such as vaccination and treatments, **as reviewed in** [11, 47]. **Important historical examples are the social and spatial distancing enacted during various plague epidemics, as documented in [48] and in fundamental literary works [49]. For example, the *Decameron* by Giovanni Boccaccio, the *Diary* by Samuel Pepys and various works by William Shakespeare.** Moreover, in the absence of pharmaceutical interventions, both forms of distancing remain two main options even in modern societies as documented e.g., by the dramatic decline of travels to Far-East during the SARS crisis - as an example of avoidance of movements towards area perceived as "'high risk"' [50]. **Similar large–scale phenomena were also evidenced , although to a lesser exent, during the H1N1 flu epidemics** [51].

In particular our model for behaviour is "'simple"' i.e., we do not include a specific layer for modeling the acquisition of awareness. Therefore, our formulation of social behaviour change is implicit i.e, it is based on a phenomenological relation between the contact (or transmission rate) and the infective prevalence.
Our analysis focuses, from both the biophysics and the public health viewpoints, on a specific problem of epidemiological relevance: the suppression of Turing patterns induced by the spatial behavioural reaction modelled by (2). To achieve this aim, we analyse the proposed family of models in a hierarchical manner. First, we analyse a general spatially homogenous SIR model with a general prevalence-dependent contact rate. Then we re-analyse the model by including the spatial structure under the classical hypotheses on diffusion and derive general conditions for the onset of Turing pattern around the endemic equilibrium. Finally, we include in our family of models also a spatial component in the behavioural reponse, and provide the conditions ensuring the mitigation, or even the destruction, of Turing patterns. Indeed, a further motivation for the present work based on a general family of models was that all the above cited contributions using nonlinear infection rates [27–33] exhibited - despite their specificity - many similarities, especially in the derivation of the onset of Turing patterns.
The manuscript is organised as follows. Section 2 provides a review of the literature on epidemiological models in reaction diffusion settings including behavioral effects. Section 3 presents and analyses a family of models for an endemic infectious diseases with spontaneous agents' behaviour responses in the absence of spatial structure. The analysis of the basic spatial version of the model is reported in section four. In section five the full model also including spatial distancing is reported. Sections six and seven extend the analysis to the case of an SIS (susceptible-infective-susceptible) infection. **In section 8 we numerically investigate a SIR model in order to verify and fine–tune our theoretical results and obtain further results**. Concluding remarks follow.

2 Spatial epidemiological models with behavioral responses: a review of the literature

Milner and coworkers introduced [21,22] a modification of the spatial version of Kermack and McKendrick SIR model [1] where they added to the "'classical"' term repelling individuals (irrespective of their epidemiological state) away from crowded areas, a truly behavioral term repelling susceptible individuals from sites characterized by large prevalence of infective individuals. Consequently they modeled the spatial flux of susceptible individuals including the gradient of infectives [21, 22]

$$J_S = -aS\nabla N - cS\nabla I \tag{1}$$

where $a > 0$ and $c > 0$.
Here we assume that only the second phenomenon is enacted as spatial component of behavioural response of the healthy subjects to which one has to add the diffusive flow of the susceptible:

$$J_S = -cS\nabla I - D_S\nabla S \tag{2}$$

Given a compartmental population model u fluxes of the type

$$J_i = -\sum_{j=1}^{n} D_{i,j}^{(0)}\nabla u_j - u_i \sum_{j\neq i} D_{i,j}\nabla u_j, \tag{3}$$

where $D_{i,j} > 0$ and $D_{i,j}^{(0)} > 0$, first introduced in mathematical epidemiology by Capasso and coworkers [52] are termed in the literature non linear cross–diffusion fluxes.
At the best of our knowledge the current mathematical epidemiology literature has only focused on problems of existence, uniqueness and positiveness of the solution of the resulting dynamical systems. For example, in [23] Bendhamane and Langlais provided existence results for nonnegative solutions of a special SIR epidemic model characterised by nonlinear cross–diffusion for all the three epidemic classes and by absence of births (but presence of death). However, no justification was given for the presence of nonlinear cross diffusion.
The following nonlinear cross diffusion flux in the susceptible:

$$J_S = -a(S, I)\nabla S - c(S, I)\nabla I$$

(2) was introduced first by Berres and Ruiz–Baier in [24] (see also [25, 26]), who also gave an implicit behavioural description of the flux, in the context of a specific SI model. They investigated two specific cases: $c(S, I) = c_0 > 0$ (i.e. classical linar cross-diffusion) and $c(S, I) = c_0 SI(c_1 - S - I)_+$ with $c_1 > 0$. The focus of their investigation was on defining new numerical methods and, from the modeling viewpoint, on the cross-diffusion driven onset of spatial patterns.
Finally, it is important to stress that in ecology and eco–epidemiology recently were proposed models where an opposite behavioural effect is included: a population (for example of predators or of male animals) that follows a second population (for example of preys or female animals) [53–55]. This would correspond, in the simple framework of our model to the case of $c < 0$. By adopting (with abuse of meaning) a terminology of theoretical cellular biology [56] **our model describe a chemorepulsion-like phenomenon, whereas models** [53–55] **are chemotaxis-like model. Two opposite phenomena. Moreover, in our model the chemorepulsion–like behaviour is due to reduce the contagion of the disease, whereas in** [53–55] **the chemotaxis–like behaviour is due to disease–unrelated bio–phenomena.**

In the forthcoming sections we propose a general family of models combining nonlinear cross diffusion - mimicking a behaviour–related reduced mobility of at risk individuals, with an appropriate functional specification of the infection incidence, mimicking social-distancing - to represent the overall behavioral response to the infection threat in a situation where no vaccination or treatments are available.

3 A general family of SIR models for behaviour change: the space-homogeneous case

Our general formulation considers an SIR-type infection which is endemic in a stationary population and for which neither prevention through vaccination nor pharmaceutical control measures are available. To make our presentation as smooth as possible we depart from the space–homogeneous case in the absence of any behavioural responses.

3.1 General SIR models for behaviour change: the space-homogeneous case without behavioural response

Let S_*, I_*, R_* denoted the numbers of individuals who at time t are susceptible, infectious, and recovered respectively. Our formulation reads as follows:

$$\frac{d}{dt}S_* = \zeta - \mu S_* - C_*(S_*, I_*) \tag{4}$$

$$\frac{d}{dt}I_* = C_*(S_*, I_*) - (\nu + \mu)I_* \tag{5}$$

$$\frac{d}{dt}R_* = \nu I_* - \mu R_* \tag{6}$$

where $\nu > 0$ is the (constant) recovery rate, $\mu > 0$ is the (constant) mortality rate, $\zeta > 0$ the (constant) recruitment rate, and finally $C_*(S_*, I_*) > 0$ is the overall infection rate, also termed the infection incidence rate.
The overall population $N = S + I + R$ obeys

$$\frac{d}{dt}N = \zeta - \mu N$$

In what follows we assume that the the population has achieved its steady state

$$N_{ss} = \frac{\zeta}{\mu}$$

and normalize the state variables and the infection rate as follows

$$(S, I, R) = \frac{1}{N_{ss}}(S_*, I_*, R_*)$$

$$C(S, I) = \frac{1}{N_{ss}}(N_{ss}S, N_{ss}I).$$

Given that $R = 1 - S_{ss} - I_{ss}$ we can disregard the R variable obtaining the system:

$$\frac{d}{dt}S = \mu(1 - S) - C(S, I) \tag{7}$$

$$\frac{d}{dt}I = C(S, I) - (\nu + \mu)I \tag{8}$$

As regards the (normalized) infection rate $C(S,I)$, we assume it is a continuous function with the following properties: i) no flux from the susceptible to infectious exists in absence of infectious (no epidemics) or of susceptible (theoretical removal by quarantine or vaccination of all the healthy population)

$$C(S,0) = C(0,S) = 0;$$

ii)the larger is the infectious prevalence the larger is the infection rate

$$\partial_I C(S,I) > 0;$$

ii)the larger is S the larger is the infection rate

$$\partial_S C(S,I) > 0.$$

3.2 General SIR models for behaviour change: the space-homogeneous case with behaviour response

To include the behavioral component we next suppose that the population is able to enact measures to reduce the risk to acquire the infection. In the practice individuals can achieve this by reducing their social contact rate (i.e., the average number of social contacts per unit of time) and/or by reducing the transmission probability per single social contact. In our general formulation, which does not specify these parameters in an explicit manner, the risk reduction will be represented by a suitable continuous and decreasing function of prevalence $\phi(I)$ multiplying the incidence rate. The transmission model has to be modified as follows:

$$\frac{d}{dt}S = \mu(1-S) - \phi(I)C(S,I) \tag{9}$$

$$\frac{d}{dt}I = \phi(I)C(S,I) - (\nu+\mu)I \tag{10}$$

$$\tag{11}$$

where the function $\phi(I)$, $0leq\phi(I)leq1$ is such that: i) no risk reduction is observed at very low prevalence levels:

$$\phi(0) = 1$$

ii)the function is decreasing:

$$\phi'(I) < 0.$$

Henceforward we will call the incidence rate in absence of behavioural reponse, $C(S,I)$, the baseline, or *normal*incidence rate (NIR), while we we will call the incidence rate

$$\Psi(S,I) = \phi(I)C(S,I)$$

the behavioral incidence rate (BIR).
Note that the introduction of the behavioural response impacts on infection transmission because the sign of $\partial_I\Psi$is no more determined a priori. This happens in situations where I is sufficiently large so that the decrease of ϕ is able to compensate the increase of C thus giving $\partial_I\Psi < 0$.
Model (9)-(10) always admits a disease free equilibrium $DFE = (1,0)$. Setting

$$(S,I) = (1-x,y)$$

with $0 < x << 1$ and $0 < y << 1$ and writing

$$\Psi(1-x,y) \approx ay^p$$

the equation for I at the DFE reads:

$$y' = ay^p - (\mu+\nu)y,$$

implying that for $p < 1$ then the DFE is not stable, for $p > 1$ then the DFE is always stable. Note that for $p = 1$ the condition for the LAS of the DFE is

$$\frac{a}{\mu+\nu} < 1.$$

which allows to give the parameter $a/\mu+\nu$ the interpretation of basic reproduction number (BRN) of the infection considered, allowed by the fact that in this case parameter a represents the growth rate of incidence per unit time in the situation where the population is essentially wholly susceptible. From the differential inequality:

$$\frac{d}{dt} = \Psi(S,I) - (\nu+\mu)I \leq \Psi(1-I,I) - (\nu+\mu)I,$$

it follows that if for $I > 0$

$$\Psi(1-I,I) < (\nu+\mu)I$$

then the DFE is Globally stable.
As regards the existence of endemic equilibria $EE = (S_e, I_e) > (0,0)$, from $(S+I)' = 0$ it follows that

$$S = 1 - (1+\rho)I,$$

where $\rho = (\nu/\mu) >> 1$. As a consequence, $I' = 0$ implies that:

$$\Psi(1-(1+\rho)I, I) = (\nu+\mu)I \tag{12}$$

Equation (12) is generic, and it can have none, one or more than one (typically two) positive solutions. In other words, the system can have none, one or multiple endemic equilibria.
The Jacobian matrix J at an endemic equilibrium is such that

$$J_{11} = -\mu - \partial_S\Psi(S_e, I_e)$$

$$J_{12} = -\partial_I\Psi(S_e, I_e)$$

$$J_{21} = \partial_S\Psi(S_e, I_e)$$

$$J_{22} = \partial_I\Psi(S_e, I_e) - (\mu+\nu)$$

In the following, for the sake of notational simplicty we will write $\partial_S\Psi$ and $\partial_S\Psi$ instead of, respectively, $\partial_S\Psi(S_e, I_e)$ and $\partial_I\Psi(S_e, I_e)$.
From the characteristic polynomial

$$\lambda^2 - (J_{11}+J_{22})\lambda + J_{11}J_{22} - J_{12}J_{21}$$

the standard conditions for the local stability are: i) $-(J_{11}+J_{22}) > 0$, i.e.

$$2\mu + \nu + \partial_S\Psi - \partial_I\Psi > 0 \tag{13}$$

and $J_{11}J_{22} - J_{12}J_{21} > 0$, i.e.

$$\mu(\mu + \nu - \partial_I \Psi) + (\mu + \nu)\partial_S \Psi > 0 \tag{14}$$

If at an endemic equilibrium point EE the previous conditions are not fulfilled, then the EE is unstable. The global behaviour of the system can be quite complex, and needs to consider specific examples of $\Psi(S, I)$. In other words we ought to renounce to work at level of the entire family of models to move to the study of specific subcases. There is nonetheless one important case where the analysis remains fully general which is the case where the EE is unique and the DFE is unstable. In this case Yakubovich theorem [57] implies that the solutions of the system will be oscillating (either periodically or aperiodically: the type of oscillations depends on the specific model and it cannot be predicted analytically).
Since we want both to keep our analysis at level of meta-models and to focus on spatial patterning, in this work we will not proceed further in the investigation of specific subcases.

4 The spatially structured case with behaviour change and Turing patterns

In this section we will consider the baseline spatial version of the model of the previous section where the agents' behavioral responses do not involve their mobility patterns i.e., individuals keep the same mobility regardless of their epidemiological status. The model then reads as follows:

$$\partial_t S = D_S \Delta S + \mu(1 - S) - \Psi(S, I) \tag{15}$$

$$\partial_t I = D_I \Delta I + \Psi(S, I) - (\nu + \mu) I \tag{16}$$

$$\partial_n I|_{\partial\Omega} = \partial_n S|_{\partial\Omega} = 0 \tag{17}$$

Many complex phenomena can of course arise, but here we are mainly interested to the onset of Turing patterning around *a spatially homogeneous locally stable endemic equilibrium EE*. By linearizing spatio–temporally around the endemic equilibrium, and applying the Fourier's transform one gets the following spatio–temporal jacobian matrix [3]

$$J_{ST}(k) = J(EE) + Diag(-D_S k^2, -D_I k^2)$$

whose characteristic polynomial reads

$$\lambda^2 + a_1(k)\lambda + a_0(k) = 0$$

where

$$a_1(k) = (D_S + D_I)k^2 - (J_{11} + J_{22}) > 0$$

$$a_0(k) = D_S D_I k^4 - (D_I J_{11} + D_S J_{22})k^2 + (J_{11}J_{22} - J_{12}J_{21})$$

Thus, since (due to the postulated local stability of the endemic equilibrium) it holds $a_1(k) > 0$ and $a_0(0) > 0$, then the condition to have spatial frequencies that can destabilize EE are the following [3, 27]

$$D_I J_{11} + D_S J_{22} > 0 \tag{18}$$

$$(D_I J_{11} + D_S J_{22})^2 > 4 D_S D_I (J_{11}J_{22} - J_{12}J_{21}) \tag{19}$$

It is easy to show that conditions (18)-(18) can be summarized into the following constraint:

$$D_I J_{11} + D_S J_{22} > 2\sqrt{D_S D_I a_0(0)} \tag{20}$$

Since the r.h.s. of (20) automatically implies the LAS condition (14), otherwise one would have an imaginary number, it follows that (20) must only be complemented by (13).
Despite the fact we are considering a family of models, the above conditions provide interpretable and useful information. For example by rewriting (20) as follows:

$$D_S\left(\partial_I\Psi - (\mu+\nu)\right) > D_I(\mu + \partial_S\Psi) + 2\sqrt{D_S D_I a_0(0)} \tag{21}$$

we obtain two results: i) if $\partial_I\Psi \leq (\mu+\nu)$ then no Turing patterns can occur; ii) since from (13) ($J_{22} < -J_{11}$), it holds that

$$\partial_I\Psi - (\mu+\nu) < \mu + \partial_S\Psi \Rightarrow \partial_I\Psi - (\mu+\nu) = (\mu + \partial_S\Psi)(1-F^2)$$

then one can rewrite (21) in the following form:

$$D_S > \frac{D_I}{1-F^2} + \alpha_0^2 \tag{22}$$

i.e. the Turing pattern can only occur for diffusion coefficients of susceptible individuals that are larger than the diffusion coefficients of the Infectious, which is what we obviously expect in normal conditions. By resorting to specific subcases of function $\Psi(S,I)$ one can study the ensuing specific type of patterns by the method of the amplitude equation [3, 58].

5 Spatial distancing and its impact on spatial patterning

Model (15)-(16), although including the individuals' behavioural response - i.e., what we nowadays term "'social-distancing"' - in the presence of spatial movements, is incomplete as it lacks a spatial component in the behavioral response, what we previously termed "'spatial distancing"'. We therefore now amend model (15)-(16) by adding to the *spatial* flow ψ of susceptible subjects a component that goes in direction opposite to the gradient of the spatial density of infectious individuals. This yields:

$$\psi = -D\nabla S - \bar{A}S\nabla I,$$

where $\bar{A} > 0$. This modeling of spatial behavioural response is remindful of the phenomenon of chemorepulsion, which is the opposite of chemotaxis. The resulting model reads:

$$\partial_t S = D_S\Delta S + div(\bar{A}S\nabla I) + \mu(1-S) - \Psi(S,I) \tag{23}$$

$$\partial_t I = D_I\Delta I + \Psi(S,I) - (\nu+\mu)I \tag{24}$$

$$\partial_n I|_{\partial\Omega} = \partial_n S|_{\partial\Omega} = 0 \tag{25}$$

After linearizing around a space–homogenous stable but spatially–patterned endemic state, and applying the Fourier transform, we obtain the following spatio-temporal jacobian matrix:

$$J^*_{ST} = \begin{bmatrix} J_{11} - D_S k^2 & J_{12} - Ak^2 \\ J_{21} & J_{22} - D_I k^2 \end{bmatrix} \tag{26}$$

where $A = \bar{A}S_{EE}$. The characteristic polynomial associated to J^*_{ST} is

$$\lambda^2 + b_1(k)\lambda + b_0(k) = 0$$