Parasite sources and sinks in a patched Ross–Macdonald malaria model with human and mosquito movement: Implications for control

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Nick W. Ruktanonchai[a], David L. Smith[b], Patrick De Leenheer[c,1,*]

[a] University of Southampton, Southampton, United Kingdom
[b] Institute for Health Metrics and Evaluation, Department of Global Health, University of Washington, Seattle WA
[c] Department of Mathematics and Department of Integrative Biology, Oregon State University, Corvallis, OR, United States

ARTICLE INFO

ABSTRACT

We consider the dynamics of a mosquito-transmitted pathogen in a multi-patch Ross–Macdonald malaria model with mobile human hosts, mobile vectors, and a heterogeneous environment. We show the existence of a globally stable steady state, and a threshold that determines whether a pathogen is either absent from all patches, or endemic and present at some level in all patches. Each patch is characterized by a local basic reproduction number, whose value predicts whether the disease is cleared or not when the patch is isolated: patches are known as "demographic sinks" if they have a local basic reproduction number less than one, and hence would clear the disease if isolated; patches with a basic reproduction number above one would sustain endemic infection in isolation, and become "demographic sources" of parasites when connected to other patches. Sources are also considered focal areas of transmission for the larger landscape, as they export excess parasites to other areas and can sustain parasite populations. We show how to determine the various basic reproduction numbers from steady state estimates in the patched network and knowledge of additional model parameters, hereby identifying parasite sources in the process. This is useful in the context of control of the infection on natural landscapes, because a commonly suggested strategy is to target focal areas, in order to make their corresponding basic reproduction numbers less than one, effectively turning them into sinks. We show that this is indeed a successful control strategy—albeit a conservative and possibly expensive one—in case either the human host, or the vector does not move. However, we also show that when both humans and vectors move, this strategy may fail, depending on the specific movement patterns exhibited by hosts and vectors.

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1. Introduction

Malaria is a mosquito-borne disease caused by *Plasmodium* parasites, and is responsible for hundreds of thousands of deaths every year worldwide. The malaria parasite is found in red blood cells of an infected person, and transmission to humans occurs predominantly through mosquito bites, although according to the CDC [10] "it can also be transmitted through blood transfusion, organ transplant, the shared use of needles or syringes contaminated with blood, or from a mother to her unborn infant before or during delivery (congenital malaria)". Transmission depends on complex interactions between moving mosquito [19], and moving human [26,29,33,34,37] populations to facilitate parasite spread.

Human and mosquito populations are often spatially clustered [23], causing malaria risk to be heterogeneous across spatial scales [6,16]. Host mediated parasite movement on these landscapes drives source-sink parasite dynamics which elimination programs must account for [9], as areas with enough transmission to sustain parasite populations locally will export excess parasites through host movement, known as transmission foci, supporting parasite populations in sink areas, or areas where parasites would not persist otherwise [9]. As transmission foci enable parasite persistence in sinks, they have been proposed as prime targets for control efforts [9,25]. Conceptually, regional malaria elimination can then be achieved by reducing transmission within all transmission foci to below self-sustaining levels [24].

Simply targeting the areas with the highest apparent transmission neglects human and mosquito movement and their role in parasite persistence, however, causing movement processes to potentially undermine elimination efforts [34]. Using a patched Ross–Macdonald model, we identify transmission foci in the context of both human and mosquito movement, and determine whether a

strategy that targets foci exclusively is sufficient for parasite elimination, finding that while this strategy works when either humans or mosquitoes do not move between patches, there are network topologies where parasites persist even if transmission in all focal areas are brought to below sustainable levels.

The celebrated Ross–Macdonald model goes back to the groundbreaking work of Ronald Ross who received the Nobel Prize in Physiology or Medicine in 1902 for elucidating the complex infection cycle of malaria. Ross' model has since then been applied and refined by many authors including Macdonald, see [31,32] for recent reviews. Classical Ross–Macdonald models consider infection dynamics in a single patch, but for all the reasons mentioned above, we extend this here to a patched model, a variant of which was first proposed and analyzed in [17]. Another variant of this model, considered in [28] and reviewed in [3,15,35], includes host movement, but excludes vector movement. More spatial models for malaria transmission have been reviewed in [11,15] where space is treated discretely in the form of distinct patches, and in [12,15] where space is either treated as discrete or as continuous, in the latter case leading to models that take the form of reaction–diffusion equations.

Models that include mobility need to specify how exactly vectors and humans move, and here we have adopted the so-called Lagrangian approach, see [11] and references therein. A salient feature of the Lagrangian model is that all individuals are declared to be residents of a specific patch, but that they can spend parts of their time in other patches, where they might infect others, or pick up the infection. This is in contrast to the more popular Eulerian approach, where individuals are not assigned to a particular patch, but instead simply move around between the various patches at certain prescribed rates. Examples of the Eulerian approach can be found in various contexts related to the spread of infectious diseases such as in [1,2,5,11], and are not restricted to malaria. Our methods can be used to study similar patched Ross–Macdonald models based on the Eulerian approach, but to keep our analysis concise, we restrict ourselves to models based on the less frequently used Lagrangian approach. More sophisticated patch models have been proposed more recently. These models have been coupled to agent-based models to incorporate movement of the individual agents (both vectors and humans) in response to other environmental triggers such as temperature or rainfall, revealing fascinating patterns in the numerical simulations of these hybrid systems, see [22]. The main contributions of this paper are:

1. **Establish the global dynamics of a patched Ross–Macdonald model**, a variant of which was first investigated in [17] and reviewed in [11]. This model assumes an arbitrary number of patches between which both humans and mosquitoes are allowed to move. These movement patterns are quantified by matrices which express the fractions of time spent by residents of each patch in all other patches. A single real and positive quantity—the spectral radius of a matrix defined in terms of model parameters of all patches, as well as the movement matrices—determines the fate of the infection in the network: When this spectral radius is less than one, the infection is cleared. When it is larger than one, all solutions converge to a unique positive steady state and the infection globally persists in all the patches.
   Although our proof is based on techniques that are similar to those used in [11] for a closely related model, we have decided to include a concise and self-contained proof in an Appendix here, for two main reasons. First, there are important differences between the modeling assumptions made in [17], and those considered here. Second, our proof relies on specific irreducibility properties of the matrices that encode

vector and host mobility, and these conditions are different from those stated in [11], in a rather subtle way.

2. **Identify local sinks and sources from steady state measurements of infected humans in the network.** Each patch in the patched Ross–Macdonald model has its own transmission characteristics. In fact, to each patch we can associate a basic reproduction number, which would predict infection persistence or clearance in this patch if the patch were isolated. Since control measures are often aimed at lowering the reproduction numbers of those patches with the highest reproduction number values, an obvious first step is to determine, or at least estimate, the basic reproduction numbers of every patch with as little knowledge of model parameter values as possible. We show how to do this, based on the steady state measurements of infected humans in all the patches of the network. It turns out that only a limited number of model parameters is needed to achieve this, and we precisely state which ones these are.

3. **Investigate how the patch reproduction numbers, in conjunction with host and vector mobility patterns, affect disease persistence or clearance in the network.** We first consider the special cases where either only humans, or only mosquitoes move. If all patches are hotspots (respectively, sinks), then no matter what the mobility pattern of the moving host is, the disease persists in (respectively, is cleared from) the network. Thus, the control strategy that makes the reproduction number of every patch less than one, is guaranteed to clear the infection from the network, no matter what the mobility pattern of the moving host is. However, when there is a mix of hotspots and sinks in the network, this control strategy might be too conservative: For some mobility patterns the infection might be cleared without any intervention, although it may persist for others. This also indicates that in this case, an alternative control strategy -namely to intervene in the mobility patterns of the hosts—might be sufficient to clear the infection; and it may even be a cheaper one in certain cases, in particular when imposing travel restrictions is more cost-effective. We end by considering the general scenario in which both humans and mosquitoes move. A striking difference, compared to the cases where only one population moves, is that now the control strategy that makes the basic reproduction numbers less than one in all patches, may fail to clear the infection from the network. Failure or success depends on the mobility patterns of both humans and mosquitoes. Similarly, it may happen that in a network consisting of only sources, the infection is cleared by itself, without any control intervention at all. These results indicate that controlling a malaria infection in a network depends in a subtle way on the interplay between local transmission characteristics in the patches on the one hand, and the movement patterns of both hosts on the other.

The rest of this paper is organized as follows. In Section 2 we introduce the patched Ross–Macdonald model and discuss its global behavior. Two Appendices contain the proof of this result. In Section 2 we also propose a solution to the problem of determining the local reproduction numbers of all the patches based on steady state measurements. In Section 3 we investigate how patch characteristics, together with mobility patterns of vectors and human hosts, affect disease clearance or persistence in the network. Implications for control strategies aimed at clearing the infection from the network are considered here as well. Finally, we conclude this paper with some remarks in Section 4.