A patched Ross-Macdonald malaria model with movement by hosts and vectors: implications for control

Patrick De Leenheer

Oregon State University, USA, deleenhp@oregonstate.edu

Keywords: malaria transmission, patched Ross-Macdonald model, control

Malaria is a mosquito-borne disease caused by Plasmodium parasites, and is responsible for hundreds of thousands of deaths every year worldwide. As transmission to humans occurs exclusively through mosquito bites and parasites do not have an environmental reservoir, transmission is dependent upon interactions between human and mosquito populations. These interactions can be very complex, and mosquitoes [8] and humans [13, 16, 17] move between areas while carrying parasites, facilitating parasite spread.

Human and mosquito populations are often spatially clustered [10], causing malaria risk to be heterogeneous across spatial scales [7, 4]. Host mediated parasite movement on these landscapes drives source-sink parasite dynamics which elimination programs must account for [5], 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 [5]. As transmission foci enable parasite persistence in sinks, they have been proposed as prime targets for control efforts [5, 12]. Conceptually, regional malaria elimination can then be achieved by reducing transmission within all transmission foci to below self-sustaining levels [11].

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 [17]. 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 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 [14, 15] 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 which was first proposed and analyzed in [6]. The patched nature of this model allows us to better capture spatial heterogeneity in mosquito and human populations. Since mobility patterns are included as well, we need to specify how exactly vectors and humans move, and here we have adopted the so-called Lagrangian approach, see [6] 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, 3, 6], and are not restricted to malaria. More recently, more sophisticated patch 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 [9]. The main contributions of this minicourse are:

1. **To review the global dynamics of a patched Ross-Macdonald model**, which was first investigated in [6]. 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.

2. **To 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. **To 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 a single host 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 hosts. 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.

Bibliography

[1] J. Arino, and P. van den Driessche, *Mathematical Population Studies.* A multi-city epidemic model, Mathematical Population Studies, 10, 175-193, 2003.

[2] J. Arino, J.R. Davis, D. Hartley, R. Jordan, J.M. Miller, and P. van den Driessche, *Mathematical Medicine and Biology.* A multi-species epidemic model with spatial dynamics, 22, 129-142, 2005.

[3] P. Auger, E. Kouokam, G. Sallet, M. Tchuente, and B. Tsanou, *Mathematical Biosciences.* The Ross-Macdonald model in a patchy environment, 216, 123-131, 2008.

[4] P. Bejon, T.N. Williams, C. Nyundo, S.I. Hay, D. Benz, P.W. Gething, M. Otiende, J. Peshu, M. Bashraheil, B. Greenhouse, T. Bousema, E. Bauni, K. Marsh, D.L. Smith, and S. Borrmann, *eLife 1-19, doi:10.7554/eLife.02130.* A micro-epidemiological analysis of febrile malaria in Coastal Kenya showing hotspots within hotspots, 2014.

[5] T. Bousema, J.T. Griffin, R.W. Sauerwein, D.L. Smith, T.S. Churcher, W. Takken, A. Ghani, C. Drakeley, and R. Gosling, *PLOS Medicine.* Hitting hotspots: Spatial targeting of malaria for control and elimination, 9, e1001165, 2012.

[6] C. Cosner, J.C. Beier, R.S. Cantrell, D. Impoinvil, L. Kapitanski, M.D. Potts, A. Troyo, and S. Ruan, *Journal of Theoretical Biology.* The effects of human movement on the persistence of vector-borne diseases, 258, 550-560, 2009.

[7] A.K. Githeko, J.M. Ayisi, P.K. Odada, F.K. Atieli, B.A. Ndenga, J.I. Githure, and G. Yan, *Malaria Journal.* Topography and malaria transmission heterogeneity in western Kenya highlands: prospects for focal vector control, 5, 107, 2006.

[8] G.F. Killeen, B.G.J. Knols, and W. Gu, *Lancet Infectious Diseases.* Taking malaria transmission out of the bottle: implications of mosquito dispersal for vector-control interventions, 3, 297-303, 2003.

[9] C.A. Manore, K.S. Hickmann, J.M. Hyman, I.M. Foppa, J.K. Davis, D.M. Wesson, and C.N. Mores, *arXiv:1405.2258v1.* A network-patch methodology for adapting agent-based models for directly transmitted disease to mosquito-borne disease.

[10] C.M. Mbogo, J.M. Mwangangi, J. Nzovu, W. Gu, G. Yan, J.T. Gunter, C. Swalm, J. Keating, J.L. Regens, J.I. Shililu, J.I. Githure and J.C. Beier, *American Journal of Tropical Medicine and Hygiene.* Spatial and temporal heterogeneity of Anopheles mosquitoes and Plasmodium falciparum transmission along the Kenyan coast, 68, 734-742, 2003.

[11] B. Moonen, J.M. Cohen, R.W. Snow, L. Slutsker, C. Drakeley, D.L. Smith, R.R. Abeyasinghe, M.H. Rodriguez, R. Maharaj, M.Tanner, and G. Targett, *Lancet.* Operation strategies to achieve and maintain malaria elimination, 376, 1692-1603, 2010.

[12] S.H. Paull, S. Song, K.M. McClure, L.C. Sackett, A.M. Kilpatrick, and P.T.J. Johnson, *Frontiers of Ecology and Environment.* From superspreaders to disease hotspots: linking transmission across hosts and space, 10, 75-82, 2012.

[13] R.M. Prothero, *International Journal of Epidemiology.* Disease and mobility: a neglected factor in epidemiology, 6, 259-267, 1977.

[14] D.L. Smith, and F.E. McKenzie, *Malaria Journal.* Statics and dynamics of malaria infection in Anopheles mosquitoes, 3,13, 2004.

[15] D.L. Smith, K.E. Battle, S.I. Hay, C.M. Barker, T.W. Scott, and F.E. McKenzie, *PLoS Pathogens.* Ross, Macdonald, and a Theory for the Dynamics and Control of Mosquito-Transmitted Pathogens, 8, e1002588, 2012.

[16] S.T. Stoddard, A.C. Morrison, G.M. Vazquez-Prokopec, V.P. Soldan, T.J. Kochel, U. Kitron, J.P. Elder, and T.W. Scott, *PLOS Neglected Tropical Diseases.* The role of human movement in the transmission of vector-borne pathogens, 3, e481, 2009.

[17] A.J. Tatem, and D.L. Smith, *Proceedings of the National Academy of Sciences.* International population movements and regional Plasmodium falciparum malaria elimination strategies, 107, 12222-12227, 2010.