

Fundamental processes in the evolutionary ecology of Lyme borreliosis

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Abstract | The evolutionary ecology of many emerging infectious diseases, particularly vector-borne zoonoses, is poorly understood. Here, we aim to develop a biological, process-based framework for vector-borne zoonoses, using *Borrelia burgdorferi sensu lato* (s.l.), the causative agent of Lyme borreliosis in humans, as an example. We explore the fundamental biological processes that operate in this zoonosis and put forward hypotheses on how extrinsic cues and intrinsic dynamics shape *B. burgdorferi* s.l. populations. Additionally, we highlight possible epidemiological parallels between *B. burgdorferi* s.l. and other vector-borne zoonotic pathogens, including West Nile virus.

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Evolutionary ecology is an amalgamation of evolutionary biology and ecology, which considers evolutionary relationships and genetic changes in species or populations as well as their interactions with each other and with the environment. Two questions are central to the scientific debate in evolutionary ecology: how do population fluctuations arise and how is diversity generated and maintained^{1,2}? Despite different terminology, the same fundamental questions are at the centre of contemporary infectious disease epidemiology³.

The prevailing trend towards the development of unifying frameworks for understanding infectious disease dynamics recently culminated in the development of a concept known as 'phylogenetics', a framework to describe how the genetic variation of a pathogen is influenced by epidemiology, the dynamics of host immunity, host and pathogen population survival, and the phylogeny of the pathogen⁴. For a few pathogens (for example, HIV, influenza virus, dengue virus and measles virus), the work leading to the development of this framework has resolved several crucial issues, including the mechanisms involved in the evolution of diversity^{4,5}.

Gog and Grenfell coined the term 'strain space' for directly transmitted pathogens, and the geometry of this space is described by two processes: host immunity and the rate of genetic change of the pathogen⁶. Many emerging infectious diseases are transmitted by vectors, mainly ticks and insects⁷, and for these diseases, vector-related processes could further define the strain space^{8,9}. Therefore, it is essential to understand vector-related

processes to decide to what extent the principles that are common to directly transmitted pathogens can be extrapolated to vector-borne pathogens¹⁰.

Current models of vector-borne zoonoses are theoretical, except for models that aim to capture the spatial-temporal distribution of these zoonoses using statistical, pattern-matching approaches⁹⁻¹¹. Although statistical models can shed light on biological processes if used correctly, models based on biological processes are thought to be more powerful in illuminating the underlying key biological mechanisms that generate the observed spatial-temporal distribution patterns¹⁰. Such models should be able to identify geographical and climatic variables a priori that can be used to predict pathogen and disease occurrence in both time and space. The scientific community has now realized that the development and parameterization of biological, process-based models of vector-borne diseases is a timely, feasible and important task that is necessary to predict, prevent and control disease^{4,10,12}.

Mathematical modelling of multi-strain, multi-host pathogens remains a major challenge^{12,13}. As shown recently for directly transmitted pathogens, however, comparing the transmission dynamics of different systems can be a powerful means to explore the roles of different biological processes in shaping pathogen populations³. Here, we aim to set out the framework needed to develop biological, process-based models of vector-borne zoonoses, using *Borrelia burgdorferi sensu lato* (s.l.), the spirochaete agent of Lyme borreliosis, as an example. By

