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Source: Comparative Parasitology, 71(2) : 93-103

Published By: The Helminthological Society of Washington

URL: https://doi.org/10.1654/4136

Comp. Parasitol.
71(2), 2004, pp. 93–103

A Patch Hath Smaller Patches: Delineating Ecological Neighborhoods for Parasites

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ABSTRACT: Use of the host individual as a boundary for parasite populations and communities provides an unambiguous spatial unit that is useful for pattern description, but this framework precludes consideration of the host landscape and within-host population dynamics. Recognizing host individuals as spatially and temporally complex landscapes requires modified concepts of parasite populations and communities. An outline of the currently accepted hierarchies of parasite populations and communities is provided on the basis of ecological neighborhoods that are delineated by discrete habitat patches or functional dynamics (or both), as opposed to host individuals. This parasite-based framework accommodates consideration of both within- and among-host dynamics and facilitates investigation into the mechanisms by which these 2 levels of investigation interact.

KEY WORDS: parasite, ecology, neighborhood, scale, population, community, dynamics.

The appropriate extent and grain (sensu Wiens, 1989) of any ecological investigation must encompass both a time scale appropriate to the process being investigated and a spatial extent determined by an organism's sphere of influence on the process during that time period (Addicott et al., 1987). This longstanding concept (von Uexküll, 1921; Hutchinson, 1953) is formalized by Addicott et al. (1987) as an "ecological neighborhood." Viewing parasitism as an interaction between an organism and its habitat (Leukhart, 1879 and Filipchenko, 1937, as cited in Dogiel, 1964; Zelmer, 1998) facilitates unique tests of current ecological theory, especially metapopulation (Levins, 1969, 1970; Hanski, 1994, 1996) and metacommunity theory (Hubbell, 2001), and affords extrapolation from host–parasite systems to more general ecological patterns and processes. Hosts represent well-defined and almost perfectly replicated habitats that harbor intrinsically hierarchical populations and communities of parasites (Esch and Fernandez, 1993), facilitating the type of multiscale, among-system contrasts of matched habitats that are exceptionally difficult in other natural systems. Unfortunately, the convenience of the unambiguous boundary of the host individual (Aho and Bush, 1993) has led to the arbitrary designation of host individuals and populations as appropriate ecological neighborhoods. Although the vagaries of adopting arbitrary temporal and spatial sampling units have been well documented in population and community investigations in free-living systems (Brown and Kodric-Brown, 1977; Connell and Sousa, 1983; Connor et al., 1983; Cunningham, 1986; Addicott et al., 1987), the potential effects of similar practices on current interpretations of the ecology of parasitic species have not been subjected to thorough examination.

Constraining the infrapopulation concept to individuals of a species in an individual host at a particular time (Margolis et al., 1982; Bush et al., 1997) rather than focusing on the actual ecological unit of an interacting parasite population is convenient for describing patterns of parasite distributions and abundance but ignores how the host landscape might affect the processes responsible for producing those ecological patterns. For parasites compartmentalized into reasonably distinct subpopulations within a host individual, either by stage (e.g., the exerythrocytic stages of *Plasmodium* spp.) or by physiological requirements (e.g., localization of *Trypanosoma cruzi* in cardiac or smooth muscle), the changes occurring within each subpopulation and the connectivity among subpopulations must be evaluated to understand the within-host dynamics of a single species and better understand the among-host dynamics.

For example, African trypanosomes infect a wide variety of mammalian hosts (Ashcroft, 1959; Ashcroft et al., 1959) and insect (*Glossina* spp.) vectors (Molyneux and Ashford, 1983; Leak, 1999), undergoing a series of dynamic population changes within the mammalian hosts (Molyneux and Ashford, 1983). Peak parasitemia is reached 5 to 7 d after inoculation, at which point all available extracellular sites and,

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perhaps, selected intracellular sites (e.g., brain tissue) are occupied by trypanosomes (Ormerod and Venkatesan, 1971; Jenni et al., 1983; Stoppini et al., 2000). At this point, growth of the trypanosome population is checked by density (or quorum) sensing and subsequent transformation of trypanosomes into a nondividing stage. Ultimately, the host immune response clears the bulk of the trypanosome population. What remains is a minor population of antigenically distinct trypanosomes that reproduce and repopulate the host, repeating the cycle of infection. Depending on the host involved and the species of trypanosome, these cyclic fluctuations in parasitemia can continue for weeks or years. This simplified description of African trypanosome in vivo ecology is based on monitoring of parasitemia at the level of the host individual. The actual patterns and processes of these population dynamics are far more complex.

Isolation of trypanosomes from sites other than the blood has demonstrated that both abundance and surface variant antigens (variant antigen types or VATs) differ among trypanosome subpopulations within a single host individual (Seed and Effron, 1973; Seed et al., 1984). In addition to the genotypic differences that occur among the VAT subpopulations, 2 distinct stages occur within the mammalian host. The ''long slender'' stage divides rapidly to populate the host but has limited infectivity for the insect vector. In contrast, the ''short stumpy'' stage does not divide but is infective to the insect vector. Thus, there are stage-structured, genetically disparate subpopulations (VATs) of trypanosomes, with apparently independent dynamics, occupying distinctly different foci within the host habitat at any given time. The complexity and dynamics of the mechanisms revealed when the grain of investigation is focused on ecological neighborhoods of trypanosome infrapopulations are obscured when infections are considered only at the host level.

Empirical evidence suggests that the phenomenon of multiple neighborhoods within a single host can be applied across a broad range of parasitic taxa. It has long been recognized that high rates of mutation can produce genetically distinct subpopulations of viruses and bacteria within host individuals (Eggers and Tamm, 1965; Holland et al., 1982; Sedivy et al., 1987; Dominingo and Holland, 1988; Eigen and Biebricher, 1988; Smith and Palese, 1988; Steinhauer et al., 1989; de la Torre and Holland, 1990; de la Torre et al., 1990) and that significant ecological and immunological interactions can occur among these coexisting strains (Berchieri and Barrow, 1990; Sernicola et al., 1999; Barrow and Page, 2000; Lipsitch et al., 2000). The potential for similar metapopulation dynamics among the protozoa is not restricted to the trypanosomes (Read and Taylor, 2001). Species of *Plasmodium* also demonstrate variable antigenic types (Brown and Brown, 1965; McLean et al., 1982; Hommel et al., 1983; Handunetti et al., 1987; Fandeur et al., 1995) in addition to the within-host genetic diversity that arises as a product of sexual reproduction and continual colonization (Daubersies et al., 1996; Mercereua-Puijanon, 1996; Bruce and Day, 2003) with dramatic effects on the outcome of infection (Hargreaves et al., 1975; Snounou et al., 1989). It is likely that similar dynamics also occur in metazoan parasite systems where stages are separated spatially within a single host (e.g., schistosomes and ascarids) or reproduce within a host (e.g., digenean parthenitae and taeniid metacestodes).

The importance of genetically variable (Saag et al., 1988; Parry et al., 1990; Wolfs et al., 1990; Nowak et al., 1991; de Boer and Boerlijst, 1994; Mittler et al., 1995), spatially structured (Embretson, Zupancic, Ribas et al., 1993; Pantaleo et al., 1993) subpopulations and refugia (Embretson, Zupancic, Beneke et al., 1993; Antia et al., 1996; Pilyugin et al., 1997) in promoting the persistence of viral and bacterial infections also has been demonstrated on theoretical grounds. Although most theoretical considerations of within-host dynamics explicitly (Mittler et al., 1996; Pilyugin et al., 1997; Austin et al., 1998) or implicitly (Bonhoeffer and Nowak, 1994; Antia et al., 1996; Antia and Lipsitch, 1997; Hoshen et al., 2000) assume the host environment to be a ''well-mixed bucket'' (Mittler et al., 1996), there are significant limitations on the explanatory power of models that do not incorporate a compartmentalized host model (Antia and Halloran, 1996). The host organism represents a complex landscape of habitats (Smith and Holt, 1996) and demands a framework that considers populations at a scale smaller than the host individual. Such a framework requires a neighborhood approach to the concept of an infrapopulation (sensu Margolis et al., 1982; Bush et al., 1997) to accommodate investigation of the dynamics of parasitic infections.

Populations and communities can be delineated spatially and functionally depending on whether one is concerned with patterns or processes. Based solely on the description of pattern, a population can be delineated as a temporally and spatially contiguous set of individuals of a particular species. However, understanding the mechanisms that govern the abundance of a species at a particular locality requires consideration of a population as a functioning, interacting unit. Unlike pattern description, the ecological neighbor-

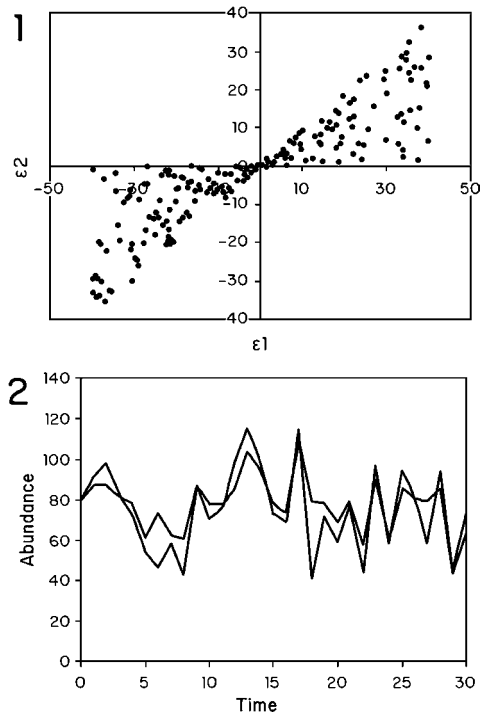
hood of a population is not simply measured but rather is determined by the extent of gene flow and the potential for positive and negative interactions. Recalling the earlier African trypanosome example, the observation that there are genetically and ecologically asynchronous dynamics in different sites within the same host individual suggests that there are discrete populations within a single host.

One obvious solution is to delineate infrapopulations and therefore infracommunities according to the habitat patches occupied by reasonably distinct subpopulations of parasites. The primary goal of the work presented here is to establish just what constitutes an ecological neighborhood for parasitic organisms. Although the work focuses on within-host population and community dynamics, among-host dynamics are addressed, where appropriate, both to clarify ecological concepts and to demonstrate that a functional delineation of populations and communities crosses theoretical boundaries between different levels of ecological investigation.

ECOLOGICAL NEIGHBORHOODS OF PARASITE POPULATIONS

Evaluating the host individual as a relevant scale for parasite infrapopulations requires quantification of infrapopulation dynamics at a grain finer than that circumscribed by the host individual to determine whether spatially disjunct parasitic individuals function as a panmictic infrapopulation or as a set of relatively discrete populations or demes. The connectivity among infrapopulations within a single host individual (i.e., the spatial component of the ecological neighborhood) can be evaluated in a discrete fashion by monitoring genotypes (as described for the VATs of the African trypanosomes). Alternatively, emergent properties of infrapopulations can be used to assess the spatial extent of ecological neighborhoods by evaluating the degree to which the dynamics of the infrapopulations are synchronous.

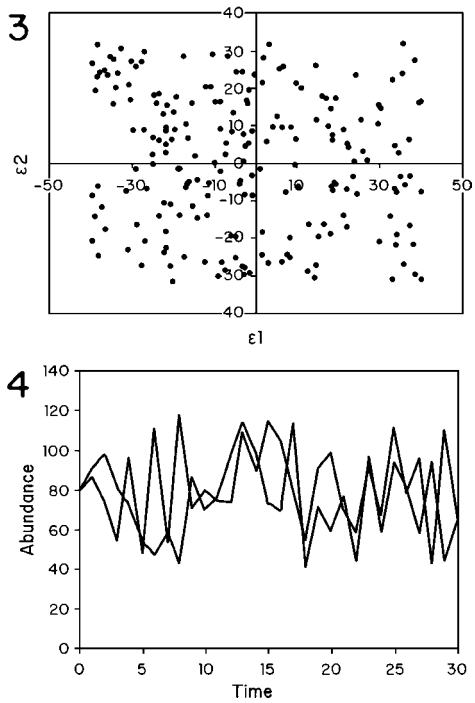
Moran (1953) postulated that the correlation between the changes in abundance of spatially separated populations with similar population growth rates is equivalent to the correlation between the stochastic variations in their environments. Thus, spatially separated groups of individuals of a single species of parasite demonstrating synchronous within-host dynamics (Figs. 1, 2) either are responding to the same scale of environmental changes (Moran, 1953; Royama, 1992; Ranta et al., 1995; Haydon and Steen, 1997) or are interconnected by sufficient dispersal to allow the sum of the infrapopulations to



Figures 1, 2. Synchronous population dynamics for 2 populations produced by a discrete logistic growth model with an intrinsic rate of increase of 0.5 individuals per unit time and a carrying capacity of 80 individuals. At each time step, a stochastic event (ε1) alters the abundance of the first population by –40 to 40 individuals. This random change is multiplied by a random number between 0 and 1 to determine the change in the second population (ε2). **1.** Correlation between stochastic events affecting the 2 populations. **2.** Resultant synchronous population dynamics.

experience the "average" host environment (Holmes et al., 1994; Molofsky, 1994; Bascompte and Solé, 1998; Kendall et al., 2000). In either case, the biology of the situation suggests that delineating the infrapopulation at the level of the host individual is justified. In contrast, asynchronous dynamics (Figs. 3, 4) are indicative of either disparate population growth rates or a response to stochastic environmental changes at a grain finer than that delineated by the host individual. One could reasonably conclude that such asynchronous, spatially disjunct infrapopulations were behaving as functionally distinct infrapopulations, but patterns require cautious interpretation because the interaction between host immune responses and parasite density dependence can produce complete asynchrony among serotypes within a single host (Bruce and Day, 2003).

The host individual might not be the smallest



Figures 3, 4. Asynchronous population dynamics for 2 populations produced by a discrete logistic growth model with an intrinsic rate of increase of 0.5 individuals per unit time and a carrying capacity of 80 individuals. At each time step, a stochastic event (ε1) alters the abundance of the first population by –40 to 40 individuals, and an independent stochastic event (ε2) alters the abundance of the second population by –40 to 40 individuals. **3.** Uncorrelated stochastic events affecting the 2 populations. **4.** Resultant asynchronous population dynamics.

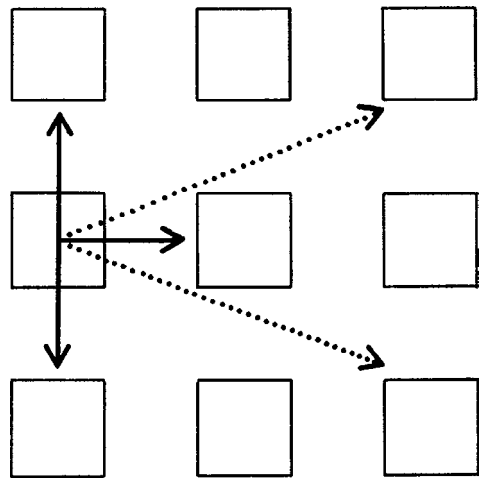


Figure 5. Two-dimensional representation of direct transmission of a parasite between individuals (squares) in a host population. Solid arrows represent transmission probabilities that would be high in hosts with low vagility. Broken arrows represent transmission probabilities that only would be high in hosts with high vagility.

relevant habitat unit of a parasite infrapopulation; nonetheless, it does provide an unambiguous boundary (Bush et al., 1997). For parasites exhibiting disjunct within-host dynamics, the host individual constitutes an ecological neighborhood for investigations of metapopulation dynamics. Essentially, a metapopulation of free-living organisms can be considered in 2-dimensional space as a distribution of organisms within suitable habitat patches that are surrounded by unsuitable habitat but interconnected by dispersal (Levins, 1969, 1970; Hanski, 1994, 1996). This model is appropriate for the within-host dynamics of parasites that reproduce in stage-independent, disjunct habitats within a host individual and for parasites with direct transmission, where host individuals comprise the patches of suitable habitat (Fig. 5).

For parasite species with complex life cycles, the model is more complex. Instead of a 2-dimensional distribution of host patches, host distributions are envisioned as a vertical series of horizontal planes (i.e., host distributions are "stacked"; upon one another [Fig. 6]). Each horizontal plane represents a host species or group of species in which the individuals of a given parasite species share a particular ontological sequence determined by the nature of the habitat (i.e., they are individuals of the same stage or set of stages). Thus, the individual parasites inhabiting a single horizontal plane constitute a component population (sensu Bush et al., 1997) of parasites. The same model, with each horizontal plane representing a specific habitat type (e.g., organs or tissues), applies to within-host dynamics when spatial structuring of a parasite species is stage-dependent.

Conventional 2-dimensional metapopulation models assume horizontal dispersal between patches. In a 3-dimensional parasite metapopulation model, among-patch transmission occurs only in the vertical plane (i.e., from one component population to the next). Spatial structuring of the model becomes a question of which hosts on a horizontal plane can be infected by propagules generated on the plane immediately below. Given the focal nature of parasite transmission (Audrey, 1958; Pavlovsky, 1966), spatial structuring of this model is determined by the vagility of the hosts on either of the 2 planes and the infective stages of the parasites. If the motility of both host species and the infective stage of the parasite are restricted, transmission probabilities will be high only for transmission of propagules from a host to the

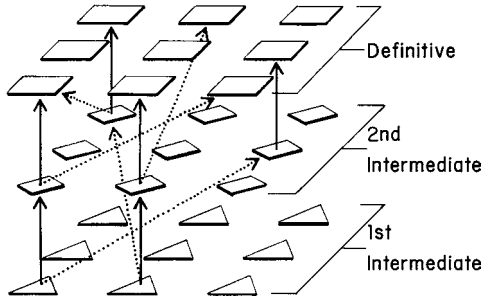


Figure 6. Three-dimensional representation of transmission of a parasite with a 3-host life cycle. Each shape represents a host individual, and each horizontal plane of shapes represents a host population. Solid arrows represent transmission probabilities that would be high when both species of host on planes connected by transmission and the dispersing stages of the parasites exhibit low vagility. Broken arrows represent transmission probabilities that only would be high when hosts on 1 or both connected planes, or the dispersing stages of the parasites, exhibit high vagility.

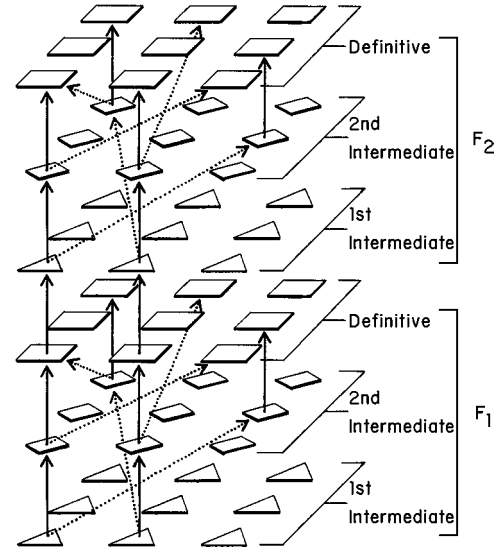


Figure 7. Three-dimensional noncyclic model of transmission of a parasite with a 3-host life cycle and nonoverlapping generations. Each shape represents a host individual, and each horizontal plane of shapes represents a host population. Solid arrows represent transmission probabilities that would be high when both species of host on planes connected by transmission and the dispersing stages of the parasites exhibit low vagility. Broken arrows represent transmission probabilities that only would be high when hosts on 1 or both connected planes, or the dispersing stages of the parasites, exhibit high vagility.

neighboring host on the horizontal plane directly above (solid transmission arrows of Fig. 6). When host vagility on either of the 2 interacting planes is high or the motility of the dispersing stage of the parasite connecting the 2 planes is high, the spatial structure decreases and probabilities of infecting any host in the next higher plane increase as a function of the increased probability of spatial overlap between the 2 hosts (broken transmission arrows of Fig. 6).

The means of continuing the spatial model through subsequent parasite generations requires transmission from the definitive host component population to the first intermediate host component population and depends on the life span of the hosts and parasites. If the parasite propagules from definitive hosts are likely to encounter a naive first intermediate host component population, the model continues in a noncyclic fashion by adding another series of horizontal planes (component populations), as shown in Figure 7. If there is substantial overlap in parasite generations, a cyclic model of transmission is appropriate (Fig. 8).

The same 3-dimensional models are applied to the within-host dynamics of parasites with stage-dependent spatial structuring if the planes are viewed as specific tissues or organs and the shapes as individuals within an infrapopulation. The same criteria for continuation of generations applies, with parasites whose dynamics allow for minimal overlap of generations at a site within a host following the noncyclic "stack model" (Fig. 7) and parasites with substantial overlap of generations within a host following the cyclic model (Fig. 8).

The concept of a host-delineated parasite neighborhood pools the infective stages of parasites that are vectored or transmitted through trophic interactions with the reproductive stages of the parasite. Thus, the link among host individuals between component populations is not given separate consideration. Identifying all transmissible (infective) infrapopulations within a single host at 1 point in time emphasizes the fact that different infrapopulations within a host individual have very different biological properties by treating infective, dispersing stages at each point in the life cycle as distinct from vegetative and reproductive stages within a host individual. Investigations conducted at the suprapopulation level (Margolis et al., 1982) also might necessitate separate consideration of the dispersing infective stages in which case identification of all of the transmissible infrapopulations within a given component population is recommended as a theoretically useful delineation (Fig. 9).

ECOLOGICAL NEIGHBORHOODS OF PARASITE COMMUNITIES

Communities also can be considered in terms of pattern and process. Determining why a certain

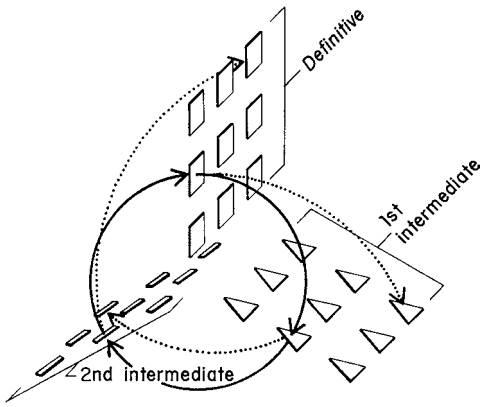


Figure 8. Three-dimensional cyclic model of transmission of a parasite with a 3-host life cycle and overlapping generations. Each shape represents a host individual, and each plane of shapes represents a host population. Solid arrows represent transmission probabilities that would be high when both species of host on planes connected by transmission and the dispersing stages of the parasites exhibit low vagility. Broken arrows represent transmission probabilities that only would be high when hosts on one or both connected planes, or the dispersing stages of the parasites, exhibit high vagility.

assemblage of organisms occurs at a particular locality is fundamentally different from a description of the emergent properties of that community. Thus, the question of whether communities should be delineated spatially (Klopfer, 1969) or in terms of energetic relations (Odum, 1959) is irrelevant: the grain of the investigation (Wiens, 1989) must be dictated by the question. At either level of investigation, the "relevant environment" of the parasites (the *Umwelt* of von Uexküll [1921]) must be given full consideration. It is clear that in many cases the smallest relevant ecological neighborhood for parasitic organisms is not the host individual.

In a biogeographical sense, a community consists of populations of different species occupying a common space at a particular time (Begon et al., 1996; Fauth et al., 1996), often restricted to specific phylogenetic groups for practical considerations (the assemblages of Fauth et al. [1996]). However, community ecology also is concerned with the emergent properties of communities. To focus attention on what cannot be explained by the sum of the parts, it has been suggested that groups of organisms with similar functional roles (the guilds of Root [1967, 1973] or the local guilds and ensembles of Fauth et al. [1996] [or both]) be the focus of community ecologists (Colwell, 1979; Tudge, 1991; Ricklefs and Miller, 1999). For certain parasitic organisms, such a resource-based neighborhood for community processes will entail delineation of assemblages within the host landscape as opposed to among host individuals.

The ecological neighborhood for investigations into the emergent properties of parasitic communities would include species that have a direct positive or negative effect on spatially and temporally congruent species in equilibrium communities (MacArthur, 1960) (the interactive communities of Holmes and Price [1986]) or those coexisting species that are tracking shared resources in nonequilibrium communities (Wiens, 1984) (a functional subset of the isolationist communities of Holmes and Price [1986]). Thus, a community delineated by emergent properties, theoretically, can contain fewer species than a spatially delineated community within the same geographical boundaries. In equilibrium communities, one expects compensatory changes in the abundances of species with negative interactions, whereas in nonequilibrium communities, species tracking fluctuations in a shared resource should exhibit positive covariation (Schluter, 1984). These expectations facilitate the functional delineation of neighborhoods for community processes by examination of patterns of covariance among candidate species.

Patterns of covariance can be examined using a matrix of abundances (species represented by rows and census times represented by columns) to compare the sum of individual species variances to the variance of their sums (Pielou, 1972; Robson, 1972; Schluter, 1984). The variance of the sums includes the average covariation between pairs of species and is a measure of compensatory fluctuations. The ratio of this variance to the sum of the species variances (V) is a means of quantifying whether species fluctuations are independent ($V = 1$), congruent ($V > 1$), or compensatory ($V < 1$) (Schluter, 1984; Gotelli and Graves, 1996). Monitoring change in V as species are added to the analysis or as the scale of the neighborhood is increased should facilitate a quantitative functional delineation of both equilibrium (compensatory) and nonequilibrium (congruent) communities. It is important for this approach that species or assemblages to be excluded from the covariance analysis be predetermined based on biologically meaningful justifications (Pielou, 1972) and not as the result of "data dredging" (Selvin and Stuart, 1966).

Delineating infracommunities based on assemblages of parasite infrapopulations occupying a specific habitat patch at a particular time facilitates scaling from the level of a single cell to an organ, to an organ system, to the entire host. This delineation encompasses both spatial and functional community

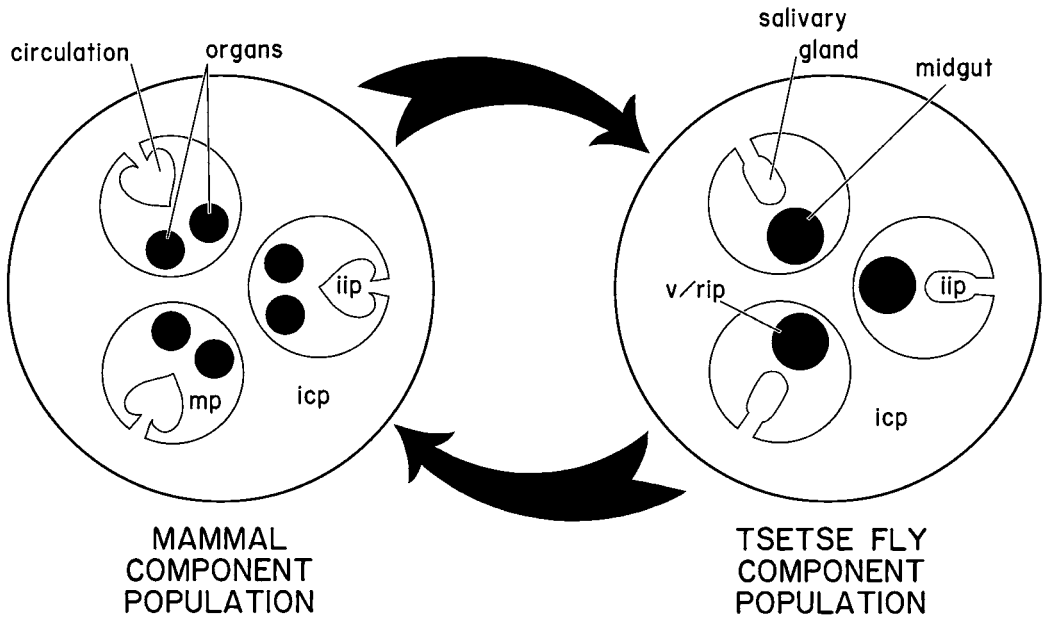


Figure 9. A diagrammatic representation of an African trypanosome suprapopulation. The largest circles delineate the mammal and tsetse component populations. The 3 circles circumscribed by each component population represent host individuals, each of which contains a metapopulation of trypanosomes (mp) comprising the trypanosome infrapopulations in the various organ systems. The heart represents the parasites occupying the host mammal's circulatory system, which constitutes the infective infrapopulation (iip). The space within the large circles representing the component populations connects the infective infrapopulations within each host, thereby representing the infective component population (icp). The midgut of the tsetse fly host represents the vegetative–reproductive infrapopulation (v/rip) within that host.

definitions, necessitating a clear and biologically meaningful demarcation of the ecological neighborhood of the community under investigation. The unambiguous host boundary of Bush et al. (1997) is maintained, but free-living stages within a particular subset of the abiotic environment (i.e., a habitat patch within a locality) also are described as an infracommunity rather than as a component community as suggested by Bush et al. (1997).

The ecological neighborhood of a component community must encompass the interactions of component populations of different species that overlap in habitat use at 1 point in time. This differentiates the free-living stages in a patch (an infracommunity) from the sum of those patches (a component community). The source community (sensu Bush et al., 1993) for a host individual, whether the infective stages are free-living or within the confines of an intermediate host, is included within the infracommunity neighborhood, whereas a host population recruits from a neighborhood that encompasses the component community. The sum of these component communities at a particular locality makes up the neighborhood of the parasite supracommunity, which can be more restrictively defined as a collection of the suprapopulations of different species occupying a particular locality at a particular time.

CONCLUDING REMARKS

As suggested by Bush et al. (1997), the most important aspect of an ecological investigation is the unambiguous definition of the parameters of that investigation. Rather than attempt to subdivide parasite populations and communities into their smallest discernable units or depend on units of sampling convenience and geometry, herein we have described a biologically meaningful framework to delineate parasite populations and communities that is broadly applicable to the empirical population biology and community ecology of both micro- and macroparasites.

Infrapopulation and infracommunity dynamics are poorly understood and until recently have not been the focus of a great deal of research. Such investigations must proceed with the understanding that hosts do not represent a single, stable habitat. Studies of infrapopulation and infracommunity dynamics

must elucidate the degree to which the spatially and temporally complex host landscape affects infrapopulation–infracommunity and metapopulation–metacommunity dynamics within host individuals. Host-based delineation of the ecological neighborhoods encompassing parasite population and community processes cannot be applied to investigations of in vivo dynamics and can bias investigations of parasite populations and communities at larger scales. Modification of current ecological concepts to accommodate both within-host and among-host dynamics is necessary not only for the formulation of clear questions regarding in vivo dynamics but also to provide a parasite-based framework for parasite ecology in general.

ACKNOWLEDGMENTS

The ideas presented herein originated from discussions with numerous students and colleagues and were culled from a much broader pool of vague notions with the helpful suggestions of Mary Everhart, Mike Barger, John Janovy, Jr., Dennis J. Richardson, and especially Rich Clopton.

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