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Effective sizes of macroparasite populations: a conceptual model

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Effective population size (N_e) is a crucial parameter in evolutionary biology because it controls genetic drift and the response to selection. Thus, N_e influences evolutionary processes in parasites, such as speciation, host-race formation, local host adaptation and the evolution of drug resistance. However, N_e is a parameter that is ignored almost completely in parasitology. Our goal is to provide a conceptual framework that facilitates future studies of the N_e of macroparasites. The key feature of macroparasite populations is that breeders are subdivided into infrapopulations. We use a model of subdivided breeders to show how some basic demographic factors that control N_e in all species could be estimated for macroparasites. An important conclusion is that several features of parasite life cycles probably function in concert to reduce N_e below that expected in a single free-living population of equivalent census size.

Effective population size

The effective population size (N_e) (see Glossary) has a large influence on the overall level of genetic diversity in populations and on the fate of alleles under selection. For example, if $N_e s \gg 1$ (s = selection coefficient), change in allelic frequency is determined primarily by selection rather than random genetic drift [1]. Therefore, selection for drug-resistant alleles and adaptation to local hosts might be more efficient in parasite populations with a large N_e. Despite the importance of N_e, we are not aware of attempts to estimate the N_e in parasites using demographic methods (Box 1) and there is little published speculation on what ecological features should influence the N_e of parasites [2–6].

The complex life cycles and ecology of many macroparasites (Box 2) make it challenging to predict N_e in natural populations of parasites. Therefore, a framework that links ecological attributes of parasites to demographic determinants of N_e would be useful. Our goal is to facilitate studies on the N_e of macroparasite populations by showing how some basic demographic factors that control N_e in all species might be estimated for macroparasites. In the conceptual model presented, we outline the parameters to be estimated, assess the feasibility of obtaining such estimates and identify crucial areas for future research.

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Conceptual model

Several ecological concepts regarding macroparasites (Box 2) are relevant to the framework because they highlight potential ecological and epidemiological factors that affect N_e. In particular, the infrapopulation concept [7] and the transmission dynamics of many macroparasites influence our choice of model to estimate N_e. Infrapopulations in definitive hosts define the breeding groups within, but not between, which mating can occur (Box 2). Either eggs or larvae are passed into the external environment, so progeny from different infrapopulations are mixed each generation (see Figure I in Box 1). Progeny that survive to maturity are, again, separated among hosts. This transient separation of breeders into infrapopulations is repeated each generation. Here, we wish to estimate the N_e of the component population (all the infrapopulations in definitive hosts).

For systems in which breeders are subdivided into groups, N_e can be estimated using Equation 1:

$$N_e = \frac{1}{\sum_{i=1}^{n} \left(\frac{X_i^2}{N_{bi}}\right)} \quad (1)$$

where N_{bi} is the effective number of breeders in infrapopulation i, and X_i is the proportional contribution of progeny from the ith infrapopulation to the mixed pool that makes up the next generation [8]. N_b is analogous to N_e except it refers to the effective number for a subset of

Glossary

Abundance: the number of individuals of a particular parasite either in or on an individual host, regardless of whether the host is infected [7].
Component population: all individuals of a parasite species in a specified life-history phase (e.g. mature adults) at a particular place and time [7].
Definitive host: the host either in or on which a parasite sexually reproduces.
Deme: a cohesive genetic (sub)population that has a recurrence of generations such that random genetic drift can occur over successive generations (i.e. an evolving unit).
Effective population size (N_e): the inbreeding effective size, which is defined as the size of an ideal population that has the same rate of inbreeding as the population of interest. Generally, N_e is smaller than the number of individuals in the population (N) because some parents contribute many more offspring to the next generation than others. (For other definitions of N_e, see Ref. [1]).
Genetic drift: the change in allele frequencies over time caused by sampling error associated with sampling gametes from one generation to the next. Demes with smaller N_e values have greater rates of drift.
Infrapopulation: all individuals of a parasite species that are in or on an individual host at a particular time [7].
Intensity: the number of individuals of a particular parasite that are either in or on a single infected host [7].
Macroparasite: multicellular parasites such as nematodes, platyhelminths, acanthocephalons, pentastomes and arthropods.

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Box 1. Demographic determinants of N_e in the subdivided-breeders model

The effective size (N_e), rather than the census size of a population (N), determines the rate of random genetic drift. Typically, N_e is smaller than N because of uneven sex ratios and non-binomial variance in VRS among individuals. The effective size of a component population is a function of the effective number of breeders (N_{bi}) in each infrapopulation (Figure I; see also Equation 1 in main text). Equation I:

$$N_{bi} = \frac{N_i\mu_{ki} - 1}{\mu_{ki} - 1 + \frac{\sigma^2_{ki}}{\mu_{ki}}} \quad \text{(I)}$$

can be used to estimate the N_{bi} of an infrapopulation for monoecious species, where N_i is the census number of parents in infrapopulation i, and μ_{ki} and σ^2_{ki} are the mean and variance of the number of progeny per parent within host i. The ratio σ^2_{ki}/μ_{ki} can be considered an index for the direction that N_{bi} deviates from N_i such that when this ratio $>1-1/N_i$, $N_{bi}<N_i$, and vice versa [35]. In dioecious species, Equation I is calculated separately for males (N_{bmi}) and females (N_{bfi}). The total N_{bi} for the infrapopulation is then calculated from Equation II:

$$\frac{1}{N_{bi}} = \frac{1}{4N_{bmi}} + \frac{1}{4N_{bfi}} \quad \text{(II)}$$

which takes into account uneven sex ratios.

Ideally, demographic estimates of N_b are based on the enumeration of parents and offspring at the sexually mature stage of development [29,30]. Unfortunately, enumeration of the number of adult offspring produced per adult parent is impossible for most macroparasites in natural populations because sampling is often destructive. In many situations, the μ_{ki} and σ^2_{ki} of an infrapopulation can still be estimated, based on counts of number of either eggs or larvae per parent. However, the high-reproductive output of many macroparasites necessitates adjustments of μ_{ki} and σ^2_{ki} because it is possible that $\sigma^2_{ki} \gg \mu_{ki}$ when μ_{ki} is large [29,30]. One possible adjustment is to assume that survival of progeny to adulthood is random and to standardize μ_{ki} to 2 for each infrapopulation [29,30]. This adjustment estimates the reduction in N_{bi}/N_i caused by demographic processes that occurred before the life stage of enumeration [30].

We do not discuss other factors that effect N_e such as fluctuating population sizes and overlapping generations (see Ref. [36] for consequences and formulas). For example, long-term N_e is closer to the harmonic mean of the per-generation N_e than to the arithmetic mean. Thus, long-term N_e is affected most strongly by generations with small N_e. Also, inbreeding, which might be common among parasites (e.g. selfing platyhelminths), can reduce N_e [37,38]. (See Ref. [39] for a recent theoretical treatment of how selfing can reduce N_e.)

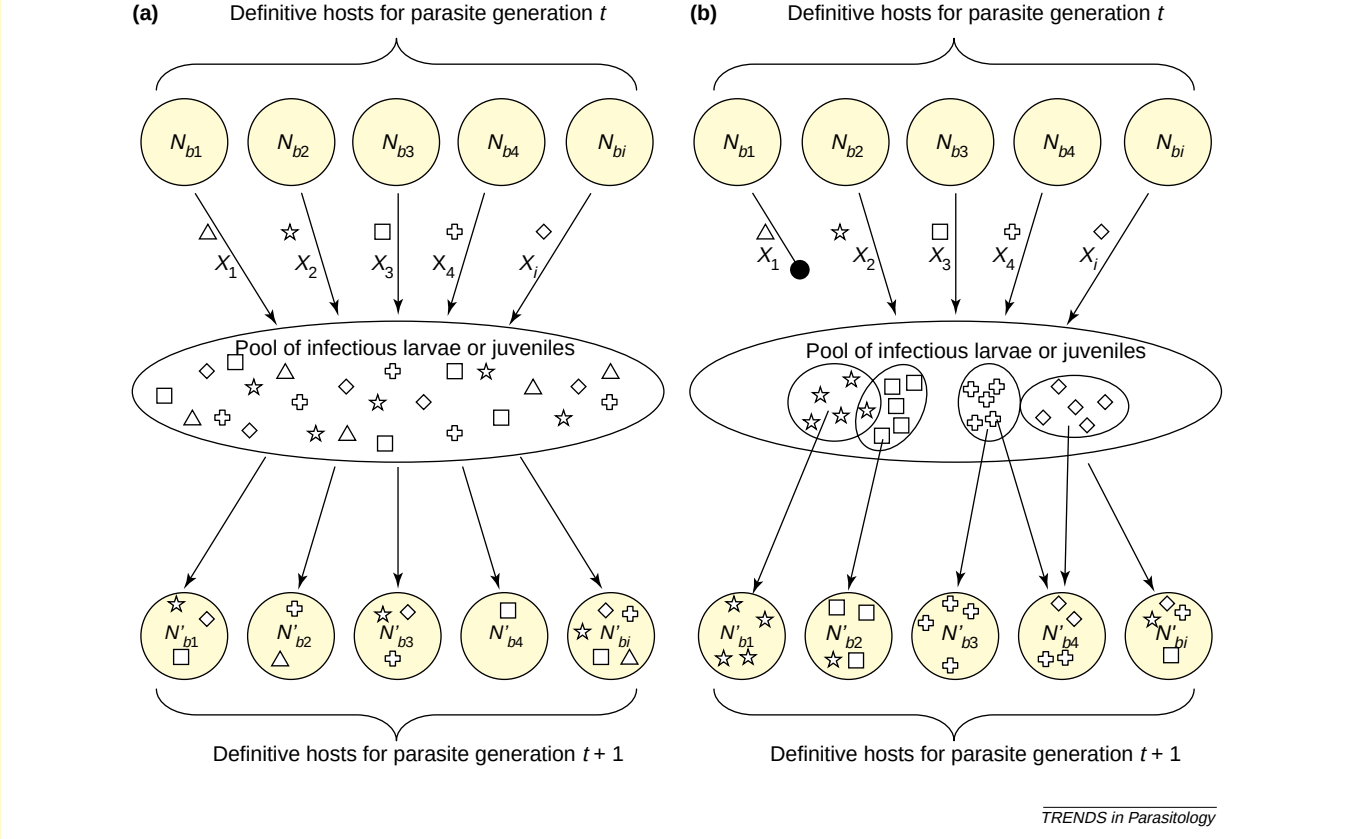

Figure I. Schematic representation of the subdivided-breeders model applied to the component population for a species of macroparasite. **(a)** Circles indicate infected definitive hosts in generations t and $t+1$. Parasite breeders are separated into infrapopulations in both generations. Parents of generation t release propagules into the external environment, which might include intermediate hosts. Offspring are mixed randomly and, at adulthood, are grouped into infrapopulations to start generation $t+1$. Symbols indicate the infrapopulation origin of offspring (e.g. triangles are offspring from parents in host 1). N_{bi} is estimated separately for each infrapopulation based on VRS and sex ratio. X_i values indicate the proportional contribution of progeny from the ith infrapopulation to the mixed pool that makes up the next generation. This schematic illustrates random mixing of progeny from the different infrapopulations. **(b)** Schematic of the subdivided-breeders model that correlates survival and transmission of progeny. $X_1=0$ because either the host dies or offspring are deposited in unsuitable habitat. Correlation between survival and transmission exacerbates variance among infrapopulations in output to the next generation, thus, reducing the effective size of the component population.

Box 2. Ecological characteristics of macroparasites

Often, macroparasite populations are described as a nested hierarchy [7] in which the component population is the sum of all infrapopulations for parasites of a particular life stage. This terminology emphasizes that different ecological processes function on different scales. For example, direct conspecific interactions are limited mainly to within-host dynamics (e.g. matings only happen within, not between, definitive hosts). Thus, the number of parasites in an infrapopulation might be limited by intraspecific competition, whereas transmission dynamics and host-population size might control the number of infrapopulations.

Often, macroparasites have different population dynamics from microparasites (viruses, bacteria and protozoans) [40]. For example, they tend to release either eggs or larvae into the external environment and, generally, do not multiply within/on their definitive host. The complexity of transmission patterns for many macroparasites (especially in aquatic systems and for parasites with multiple intermediate hosts) makes a stable recurrence of generations for a single infrapopulation seem implausible. Thus, the question of whether the component population or the infrapopulation is the relevant unit of evolution (i.e. a deme) has been raised repeatedly [3,41,42]. In reality there is probably a continuum. If offspring are well mixed, then the transmission process only separates adult breeders into infrapopulations each generation but does not result in recurrent generations within individual infrapopulations. At the other end of the continuum, if offspring re-infect their natal host (e.g. lice and pinworms) or if offspring are transmitted as a clump from host to host over several generations, the component population behaves more like a traditional subdivided population with infrapopulations as demes. In our model, correlated transmission (incomplete mixing) is important because it increases the reproductive success of some infrapopulations over others. Thus, correlated transmission exacerbates variance in the μ_{Bki} values among infrapopulations.

Distribution data (i.e. the mean abundance and its variance) are paramount in parasite ecology and epidemiology for understanding transmission patterns and developing models of population dynamics [40,43,44]. Usually, the distribution of macroparasites among definitive hosts is highly aggregated [45,46]. Therefore, most hosts in a population harbor few or no parasites, whereas a few hosts are infected with many, if not the majority, of the parasites in the component population. Aggregation exposes parasites to different degrees of crowding and is often discussed in relation to the regulation of either host or parasite populations [40,43,44].

Density-dependent effects (crowding) on parasite growth, fecundity and survival have also received considerable attention in parasitology [19,40,44,47,48]. Experimental [49] and field [50] data show that as intensity increases, parasite *per capita* fecundity decreases (Figure I). Sometimes crowding effects might not be apparent until a threshold intensity is reached [15,48]. It is common to have a large variance in *per capita* fecundity at low intensities [26] (Figure I). For our purposes, a key prediction is that crowding should have a huge effect on the σ^2_{ki}/μ_{ki} ratio (see Box 1) within infrapopulations, but empirical data are needed.

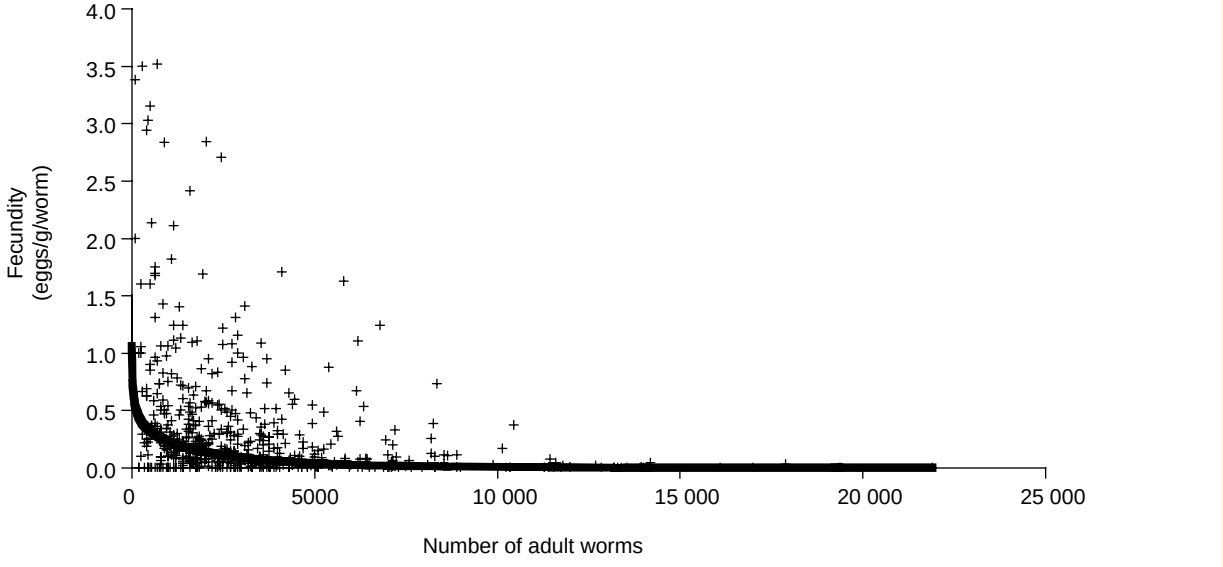

Figure I. The relationship between mean fecundity per worm and the number of adult worms. Fecundity is calculated as the fecal egg count divided by the number of adult worms and is expressed as eggs per gram of feces per adult *Teladorsagia circumcincta* from sheep. Predicted fecundity is shown as a solid line. Note the large variation in per capita fecundity at lower intensities. Reproduced, with permission, from Ref. [50].

the population [9]. Equation 1 (the subdivided-breeders model) has general applicability for systems in which breeders are subdivided into groups [8–10].

The model is applied in two parts. First one needs to estimate the effective number of breeders within each infrapopulation (N_{bi}; Box 1). Then, one must estimate the proportional contribution of progeny from each infrapopulation to the pool of propagules in the next generation (X_i). This model excludes parasites that only parasitize hosts during larval stages (e.g. mermithid nematodes). We assume discrete generations and that the parents are not inbred.

Estimation of N_{bi} for each infrapopulation

To estimate N_{bi}, we need to calculate the mean (μ_{ki}) and variance (σ^2_{ki}) of the number of progeny produced per parent within host i (Box 1). Measuring the individual reproductive output of individual parasites should be feasible, although there are few attempts to obtain such data. Egg counts have been obtained from either individual females or hermaphrodites for some macroparasites [11–13] but, more commonly, body size is used as a surrogate for parasite fecundity [14,15]. An obvious approach that, to our knowledge, has not been applied to parasites is to use molecular markers and standard

Table 1. The impact of subdividing breeders on N_e illustrated by sex-ratio data for *Schistosoma mansoni* infecting *Rattus rattus*

Infrapopulation[a]	N_{mi}[b]	N_{fi}	N_{bi}[c]
1	22	11	29.3
2	22	13	32.7
3	7	7	14
4	1	0	0
5	21	0	0
6	14	0	0
7	17	2	7.16
8	35	0	0
9	5	0	0
10	21	3	10.5
11	7	1	3.5
12	2	2	4
13	3	1	3
14	7	1	3.5
15	19	47	54.1
16	2	1	2.67
17	7	6	12.9
18	4	4	8
19	4	0	0
20	11	3	9.43
21	42	23	59.4
22	35	29	63.4
23	17	5	15.5
24	14	3	9.88
Σ	339	162	343[d]

[a]Data are from the 1986 sample of Ref. [20], which includes 24 infected and 47 uninfected rats.

[b]N_{mi} and N_{fi} are the number of male and female parasites, respectively, in infrapopulation *i*. We have no data on variance in reproduction among individuals, so equate the census numbers of males and females with the effective number of breeders of each sex.

[c]N_{bi} is based on Equation II in Box 1.

[d]N_e is calculated as 343 using the subdivided-breeders model (see Equation 1 in main text) assuming $X_i = N_{bi}/\Sigma N_{bi}$ (i.e. that the contribution of each infrapopulation to the next generation is proportional to its effective size [8]). Ignoring the subdivision of breeders, N_e can be calculated (438) using Equation II in Box 1 from the total number of males (339) and females (162) across all infrapopulations.

methods of kinship analysis to either partition offspring into sibships or assign offspring to parents [16,17].

Sex ratio is estimated more easily for infrapopulations than σ^2_{ki} is. Biased sex ratios are reported commonly for component populations of macroparasites [18,19]. However, because mating opportunities are restricted to within/on a host (Box 2), the sex ratio of each infrapopulation is important for calculating N_e. For example, consider the data from [20] (Table 1). If we ignore the subdivision of adults into infrapopulations and calculate N_e (see Equation II in Box 1) using the total numbers of males and females in the component population, we get $N_e/N = 0.87$, where N is the census size of the component population. Using the subdivided-breeders model (Equation 1), we get $N_e/N = 0.68$ (Table 1). Thus, there is a pronounced sex-ratio effect on N_e because of separation of individuals among hosts. In part, this occurs because some infrapopulations have individuals of only one sex (Table 1), which results in N_{bi} values of zero.

Effects of parasite abundance distributions on N_{bi}

The distribution of parasites among their hosts (Box 2) should influence the N_e of the component population. In free-living organisms, the ratio of effective size:census size, N_e/N, decreases as population density increases [21]. Experimental data indicate this reduction is caused by an increase in σ^2_{ki}/μ_{ki} (Box 1) as population size increases [22]. Thus, for parasites we might expect that an increase in infrapopulation intensity (i.e. crowding; Box 2) will increase σ^2_{ki}/μ_{ki}. Furthermore, a highly aggregated population should expose a larger fraction of the population to crowded conditions. However, there is almost no data on the effects of crowding on variation in reproductive success (VRS) (Box 1) in parasites. From studies on density-dependence in parasites, we see that that the *per capita* fecundity of an infrapopulation (μ_{ki}) usually decreases with increasing intensity (Box 2). However, σ^2_{ki} cannot be calculated from many of these studies, because fecundity is not measured for individual worms. A few studies show that inequalities in reproductive success (expressed as Gini coefficients) in an infrapopulation can either increase or decrease with intensity [11,12,14], but the relationship of intensity to σ^2_{ki}/μ_{ki} is not discernable from these data.

The effects of aggregation on sex ratio are understood better. The mating-probability model for monogamous parasites [23] provides a good approximation of the effects of intensity and aggregation on infrapopulation sex ratio. The probability of mated female worms, which is necessarily equal to mated male worms in the monogamous model, increases as either intensity or aggregation increases. Some studies find that the sex ratio approaches unity with increasing intensity [20,24], whereas others find no correlation [25]. Thus, a highly aggregated abundance distribution might enhance N_e by its effect on sex ratio.

Estimation of X_i *for each infrapopulation*

Here, we discuss the proportional contribution of offspring from each infrapopulation to the next generation (X_i). The X_i of an infrapopulation is calculated by dividing the number of offspring from host *i* by the total number of offspring from all infrapopulations. Measures of total infrapopulation output are obtained routinely for macroparasites in crowding studies (Box 2).

In the sex-ratio example above, we assumed the contributions from the infrapopulations are proportional to their effective sizes ($X_i = N_{bi}/\Sigma N_{bi}$). In this situation, N_e equals the sum of the individual N_{bi} values ($N_e = \Sigma N_{bi}$). This latter relationship is true when the average number of offspring per effective breeder within host *i* (i.e. μ_{Bki} rather than μ_{ki}, which is based on the census count) is equal for all infrapopulations (Figure 1a). However, if $X_i \neq N_{bi}/\sum N_{bi}$, then N_e will be smaller than ΣN_{bi} [8].

It seems unlikely that all infrapopulations have the same average number of offspring per effective breeder (μ_{Bki}). For example, large differences in *per capita* fecundity are observed often at similar intensities [26] (see Figure I in Box 2), which indicates that infrapopulations almost certainly do not contribute proportionally to their N_{bi} in many parasite systems. It should be stressed that random variation in productivity among infrapopulations can substantially reduce N_e below ΣN_{bi} [9]. Such a reduction can occur even in the absence of a correlation between μ_{Bki} and N_{bi} (Figure 1b). From data on crowding effects (Box 2), it seems plausible that μ_{Bki} might have a density-dependent relationship with N_{bi}, but this depends on the relationship between N_{bi} and N_i and, thus, needs

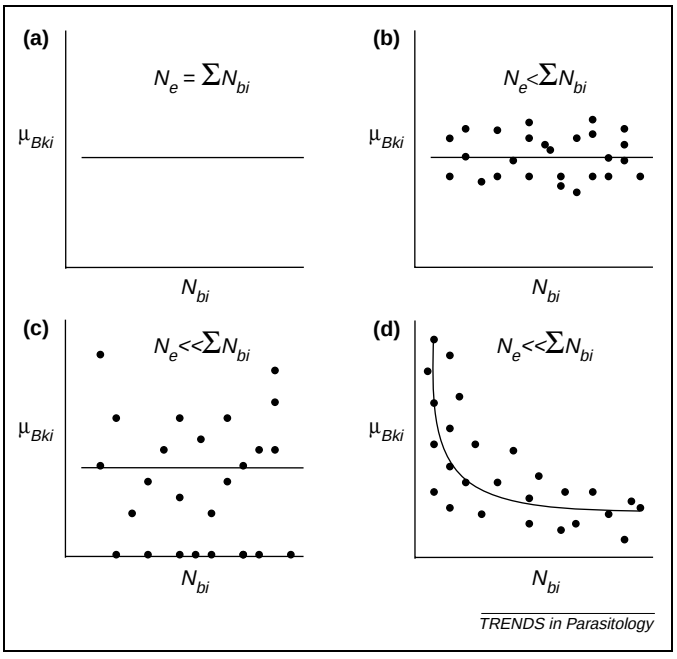

Figure 1. How relationships between the mean numbers of offspring per effective breeder within host *i* (μ_{Bki}) and the effective number of breeders within host *i* (N_{bi}) might affect N_e. **(a)** All μ_{Bki} values are equal, therefore N_e equals the sum of the individual N_{bi} values (this is implausible in nature). **(b)** No correlation between μ_{Bki} and N_{bi}, but random variation in productivity among infrapopulations still reduces N_e below ΣN_{bi}. **(c)** An extension of b; however, the correlation between survival and transmission, including the extinction of several infrapopulations (i.e. $\mu_{Bki}=0$), increases the variance among infrapopulations. Therefore, N_e is greatly reduced below ΣN_{bi}. **(d)** A hypothetical, density-dependent relationship between μ_{Bki} and N_{bi}. N_e is greatly reduced below ΣN_{bi} because a small number of breeders are responsible for a disproportionately large fraction of the total offspring.

empirical support. In this hypothetical case (Figure 1d), N_e will be greatly reduced below ΣN_{bi} because a small number of breeders (those in uncrowded infrapopulations) are responsible for a disproportionately large fraction of the total offspring contributed to the next generation.

Non-independent survival and non-random mixing of progeny from infrapopulations also make X_i disproportional to N_{bi} (see Figure Ib in Box 1). Progeny of some infrapopulations might die (i.e. $X_i=0$) as a group because of either the release of progeny into an unsuitable habitat or host death. Complete, random mixing of the progeny in the external environment is unlikely for many macroparasite species (except conceivably in some aquatic systems). For example, we know from ecological studies that infective larval stages might be aggregated [27] and that definitive hosts might acquire infective stages from certain foci of infection in a given habitat [28]. Indeed, such aggregated transmission is one common explanation for the highly skewed abundance distributions that are typical among hosts (Box 2). Aggregated transmission might increase the reproductive success of some infrapopulations relative to others. Therefore, correlation between survival and transmission is likely to increase the variance of μ_{Bki} values and greatly reduce N_e below σN_{bi} (Figure 1c). In an analogous situation, Crow and Morton [29] show that non-independent survival of family units in a non-subdivided population greatly reduces N_e [30]. There is an adjustment for family unit survival, which, in the subdivided-breeders model, is applied at the level of infrapopulations [29]. However, in practice, we envision no easy means of estimating the realized contribution of each infrapopulation to the next generation.

Future directions

We have described several links between ecological concepts in parasitology and demographic determinants of N_e. The subdivided-breeders model illustrates how several features of the life cycles of macroparasites are likely to function in concert to reduce the N_e of a component population below that expected in a single free-living population of equivalent census size. First, subdivision of breeders into infrapopulations exacerbates the effect of deviations from a 1:1 sex ratio. Second, factors that inflate VRS among individuals in the population as a whole are intensified by the subdivision of breeders into different hosts. In particular, aggregated distribution results in the exposure of parasites to different crowding conditions. Furthermore, chance and differences in the condition of the host might make the proportional contributions of infrapopulations to the next generation variable, even for infrapopulations of the same census size.

Our framework also points to several new areas of research that are crucial to the understanding of the factors that control N_e in parasites. For example, experimental infections are needed to understand the response of σ^2_{ki}/μ_{ki} to crowding. Often we are interested in controlling disease-causing parasites, so it is also important to see how VRS within infrapopulations responds to changes in host immunity, host nutrition and drugs. In addition, epidemiological studies might benefit from simulation modeling of the transmission process to examine the effects of correlated survival and transmission on N_e.

In practice, we are limited to estimating a N_e/N ratio from a sample of definitive hosts. Therefore, we must use data on the mean abundance of parasites and census size of the host to obtain a value for total census size of the parasite population. This value is then multiplied by the N_e/N ratio obtained from our sample to get a value for N_e of the entire component population. For some parasites, it is not feasible to obtain demographic estimates of N_e. However, several genetic methods can estimate N_e in natural populations [31–34]. For example, disequilibrium and temporal methods [31,33] can estimate N_e of entire component populations, and the heterozygote-excess method [34] estimates individual N_{bi} values. It is puzzling that these methods have not been applied to macroparasites. Estimating N_e genetically, by comparing either parasite species or populations that display different ecological attributes (e.g. degree of aggregation), could test which demographic variables are most important for determining the N_e of parasites.

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