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DOI: 10.1016/j.cub.2008.03.017

Optimal Foraging: A Bird in the Hand Released

Optimal foraging theory aims to elucidate strategies that maximize resource intake. Although traditionally used to understand animal foraging behavior, recent evolutionary experiments with viruses offer a new twist on an old idea.

Joshua Nahum and Benjamin Kerr

Resources ‘at hand’ have intrinsic value over uncertain future resources. Given that resources differ in quality, however, sometimes it may be advantageous to relinquish an inferior item in pursuit of something better. This is the forager’s choice between taking the “bird in the hand” and pursuing “birds in the bush”. The forager’s optimal decision is likely based on quality and distribution of different resources. Optimal foraging theory addresses how this decision depends on the characteristics of resources [1–4].

To appreciate some of the predictions of the theory, imagine a treesnake feeding on bird eggs. Our snake must make (at least) two decisions: whether to forage within a given tree (patch acceptance); and how long to remain in a tree foraging (patch residence time). As our snake forages within a tree, imagine that cumulative egg acquisition increases with diminishing returns (for example, reaching an asymptote). Further, imagine there are two types of tree: a ‘good’ tree species with many nests, and a ‘poor’ tree species with few nests. Optimal foraging theory predicts that, as the abundance of good trees increases, or as the disparity in nest-number between the tree species increases, the snake should be more likely to avoid foraging in a poor tree [2–4]. Suppose our snake specializes on one tree species. As the travel time between individual trees decreases, the snake is predicted to spend less time foraging per tree [1,4]. Thus, our snake faces a (half-literal) “bird in the hand” dilemma — specifically, whether to reject available trees or remaining eggs within a tree.

In the same way that the treesnake must decide whether and how long to forage in different trees, a virus must ‘decide’ what host cell to enter and how long to co-opt the resources of that cell. Lytic phage — viruses that infect bacteria — are particularly conducive to testing predictions from optimal foraging theory [5–8] (see Figure 1 for the life cycle). A phage particle may adsorb (attach) to its bacterial host upon encounter (the transition from stage 2 to stage 3 in Figure 1). But a phage particle may also fail to adsorb to a host after encounter, bringing it back to a dispersal stage (from stage 2 to stage 1). This phage particle may then encounter a new host (from stage 1 to stage 2) and potentially adsorb. Adsorbed phage injects its genome into its host, produces progeny inside and, at a very specific time, lyses the host releasing the progeny. The length of infection is termed the latent period (from stage 3 to stage 5). For some phage species, experimentally delaying lysis past its normal time increases the number of progeny released [7,9]. In such cases, the phage has not exhausted the resources of its host at the time of lysis. Like our treesnake, the phage faces the “bird in the hand” dilemma: whether to reject encountered hosts and whether to destroy a host that can be used to make more phage.

Indeed, the phage particle can be likened to a forager moving between resource patches (bacterial cells). In this analogy, the dispersal period is the inter-patch travel time, adsorption is a choice to enter a patch, latent period is the residence time within a patch, and the rate of progeny accumulation gives patch quality. While some of these elements are outside phage control (for example, host density will influence dispersal time and host physiology will influence progeny accumulation [5,7,8]), other elements are influenced by the phage directly. For instance, phage tail proteins affect patch choice (adsorption) and phage holins affect residence time (latent period) [6,7,9–11]. These components are thought to be modular [7], suggesting that the evolution of one phage property may be unconstrained by pleiotropic effects. Further, given the short generation time and large population size of phage, real-time experimental evolution can be executed in which predictions from optimal foraging theory can be put to the test [10–12].

Two ingenious recent studies [10,11] used phage T7 for just such a test. In the first of these, Heineman *et al.* [11] allowed T7 to evolve in the presence of two host strains differing in their phage-attachment surface moieties. In a preliminary experiment, one host was permissive (allowing progeny production), but another was genetically engineered to abort phage progeny during infection. While the ancestral phage adsorbed to both hosts, the authors discovered that the virus evolved to adsorb preferentially to the permissive host, a change mediated by a single mutation in a tail fiber gene. Thus, the viral forager evolved to become a ‘picky eater.’

The authors then tested some predictions of optimal foraging theory by competing the evolved ‘choosy’ T7 against its non-choosy ancestor under a set of different conditions. For these competitions, the formerly non-permissive host now supported phage production (red cell in Figure 1), but progeny accumulation

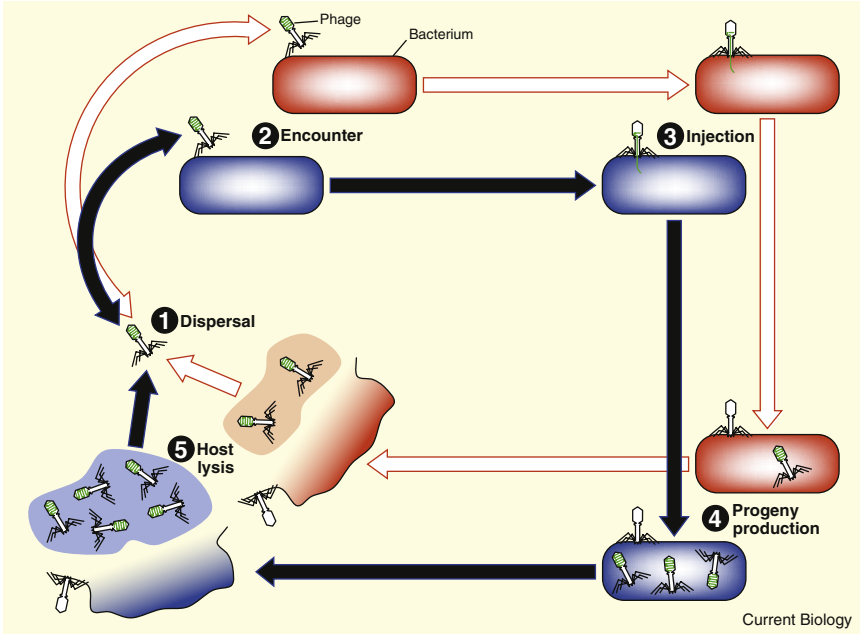

Figure 1. The lytic phage life cycle.

The lytic phage life cycle consists of: (1) dispersal of a free phage particle through the environment; (2) encounter with a host bacterium; (3) attachment to the host (adsorption) and injection of the phage genome; (4) use of host resources by the phage to make progeny particles; and (5) phage-controlled lysis of the host to release progeny to the environment. Encounter with a host may not lead to adsorption, in which case the phage re-enters the dispersal stage. Phage strains may differ with regard to their rate of adsorption to different bacterial hosts. Hosts may differ with regard to their density (which affects the length of stage 1) and the rate of phage progeny accumulation (here the red host is of poorer quality).

was slower than in the permissive host (blue cell in Figure 1). The authors were able to manipulate the rate of progeny accumulation in the less productive host (that is, red host quality). Consistent with optimal foraging theory, they found that the choosy T7 outcompeted its non-choosy ancestor when the quality of the poor (red) host was low and when the density of the good (blue) host was high. In such cases, there is selection for the phage to release the (red) "bird in the hand" in pursuit of (blue) "birds in the bush".

In the second study, Heineman and Bull [10] tracked evolutionary changes in the T7 latent period in response to altered host density. An increase in host density translates to a smaller inter-patch dispersal time, which is predicted to favor a shorter patch residence time. Consistent with this prediction, under high host density, T7 evolved a shorter latent period. Again, the viral forager releases the "bird in the hand" (future progeny in the host) in exchange for the abundant "birds in the bush" (new hosts to infect). Here the virus trades a larger number of offspring for a shorter generation time [5,7–10,13].

Not all the results from these studies are consistent with the theoretical predictions. In the first study, contrary to expectation, the success of 'choosy' phage was influenced by the density of the poor (red) host [11]. In the second study, under low host density conditions, the phage did not evolve to match the predicted long latent period [10]. However, these failures have been informative, as they point to inconsistencies between theoretical assumptions and the biology of the system. For instance, in contrast to model assumptions, the authors found a cost of choosiness in the first study and non-linear progeny accumulation in the second study. Thus, not only do these studies provide the first real-time evolutionary tests of optimal foraging theory, they also suggest ways to adjust theoretical assumptions.

These findings may also have interesting health implications. Within multicellular hosts, viruses can be 'choosy foragers' (tissue tropism). If a non-permissive cell type displays the surface receptors of a preferred 'food item' (the permissive cell), then the non-permissive cell can work like a trap [14]. For instance, transgenic mice with erythrocytes displaying viral-binding receptors had reduced mortality when exposed to high levels of coxsackievirus [15]. While tremendously promising, the use of viral traps may establish strong selective pressure on the virus to detect subtle differences between cells enabling trap avoidance. In this sense, optimal foraging theory may prove instructive to the development of viral trap therapy.

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DOI: 10.1016/j.cub.2008.02.072