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Sean Nee

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Mutualism, parasitism and competition in the evolution of coviruses

Sean Nee

Institute of Cell, Animal and Population Biology, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT, UK (sean.nee@ed.ac.uk)

Coviruses are viruses with the property that their genetic information is divided up among two or more different viral particles. I model the evolution of coviruses using information on both viral virulence and the interactions between viruses and molecules that parasitize them: satellite viruses, satellite RNAs and defective interfering viruses. The model ultimately, and inevitably, contains within it single-species dynamics as well as mutualistic, parasitic, cooperative and competitive relationships. The model shows that coexistence between coviruses and the self-sufficient viruses that spawned them is unlikely, in the sense that the quantitative conditions for coexistence are not easy to satisfy. I also describe an abrupt transition from mutualistic two-species to single-species dynamics, showing a new sense in which questions such as 'Is a lichen one species or two?' can be given a definite answer.

Keywords: coviruses; metapopulation; mutualism; parasitism; competition

1. INTRODUCTION

A number of plant viruses are 'coviruses', which are very strange parasites of plants. In a covirus, no single virus particle contains all the genetic information required for a complete cycle of infection: instead, the genome is split into two or more separately encapsidated, packaged components (Fraenkel-Conrat & Wagner 1977; Van Regenmortel & Fraenkel-Conrat 1986). They are all RNA viruses, but so are most plant viruses. With one interesting exception, discussed below, there are no known animal coviruses.

For example, tobacco rattle virus (TRV), which infects many species in addition to tobacco, consists of two particles, a long and a short one (for a picture see http://helios.bto.ed.ac.uk/icapb/research/evolecol/evolecol.html). The long particle contains the so-called RNA1 that encodes the replicase, while the short particle contains RNA2, encoding the coat protein. The long particle can establish an infection and disease on its own, although the RNA1 is trapped in the plant in the absence of coat protein. A full cycle of infection ultimately requires infection by both particles. In addition to the tobraviruses (e.g. TRV), the comoviruses and nepoviruses also have this biology. On the other hand, other coviruses, such as dianthoviruses, require all components in order to establish infection of the plant (Mayo *et al.* 1999). We will refer repeatedly to the biology of TRV.

Nee & Maynard Smith (1990) suggested that this strange situation arose as a result of trade-offs between self-sufficiency—having a complete genome—and replicative advantages accruing to shorter genomes when their deficiencies are complemented by other virus genomes in the plant. The phenomena of defective interfering (DI) viruses (Graves *et al.* 1996; White & Morris 1999), which are shorter parasites of the viruses from which they are derived, and satellite RNAs and viruses (Garcia-Arenal & Palukaitis 1999; Scholthof *et al.* 1999), which are unrelated to the host viruses they parasitize, provide much evidence for this trade-off (a satellite virus encodes its own coat protein whereas a satellite RNA does not). DI viruses and satellites are effectively viruses of viruses. The molecular biology of the trade-offs can be straightforward—shorter molecules may be replicated faster—but more interesting trade-offs have been found (for a review, see Nee & Maynard Smith 1990).

Figure 1 illustrates the scenario for the evolution of coviruses considered by Nee & Maynard Smith (1990), in which mutually complementing defective molecules outcompete and possibly eliminate a complete virus. The very fuzzy distinction between mutualism and parasitism (Maynard Smith & Szathmáry 1995; Begon *et al.* 1996) is evident here: Are the partners in the covirus mutualists or mutual parasites?

We do not need to commit ourselves to whether the incomplete but complementing viruses arose from different deletions of the same complete virus (the defective interfering virus route) or two different ones (the satellite virus or RNA route). Pea enation mosaic virus (PEMV) is an example of the latter: it is a two-component virus whose components are clearly derived from unrelated viruses and each encodes its own replicase (de Zoeten *et al.* 1995). Movement within and between plants requires both components (Falk *et al.* 1999). One of the components has a luteovirus origin, which is interesting as many members of the luteovirus group are known to be regularly 'helpful' to other viruses in nature, rendering them aphid transmissable when the alien genome is encapsidated in luteovirus coat protein (Falk *et al.* 1999). PEMV also illustrates the ontological conundrum coviruses pose us: it has recently been reclassified by viral taxonomists as being two distinct viruses

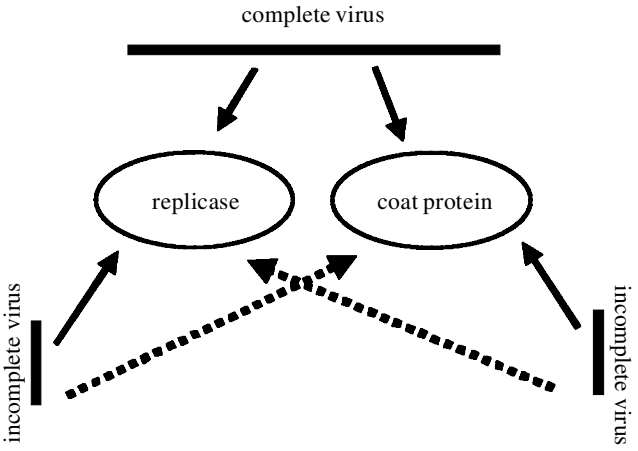

Figure 1. A simple system consisting of a complete viral genome that encodes a replicase and a coat protein and two deletion mutants that encode one or the other. A solid arrow indicates that the molecule both encodes and uses the indicated protein. A broken arrow indicates that the molecule just uses the protein. The deletion mutants can have their deficiencies complemented by either the complete molecule or each other and have a fitness advantage over the complete molecule when complemented.

that are mutually dependent (M. Mayo, personal communication).

DI animal viruses are ubiquitous, at least in the laboratory. An example of the DI route to covirus evolution is provided by simian virus 40 (SV40). Mutually complementing DI viruses of SV40 were observed to eliminate completely the wild-type virus in one study (O'Neill *et al.* 1982), i.e. the evolution of a covirus by this route has actually been observed in an *in vitro* study of an animal virus.

However, DI viruses are not as widely observed in plant as in animal viruses. And possibly the only study to look for them in nature (tomato and aubergine plants in Spanish greenhouses) failed to find any, although the virus in question, tomato bushy stunt virus (TBSV), generates them readily in the laboratory (Celix *et al.* 1997). On the other hand, the handful of studies looking for satellite RNAs of plant viruses in nature have all found them (Celix *et al.* 1997; Grieco *et al.* 1997; Aranda *et al.* 1997). Finally, the accumulating natural history from studies of large satellite RNAs reveals a spectrum of relationships from obvious parasitism to obvious mutualism (Mayo *et al.* 1999). For all these reasons, I am inclined to think that coviruses evolved via the satellite rather than the DI route: however, the actual modelling is simplified, with no great violence done to the conclusions, by assuming a DI route, i.e. one complete progenitor virus.

The quantitative model of the evolution of coviruses discussed in Nee & Maynard Smith (1990) is peculiar and seems to have in mind some sort of well-mixed cell culture as the environment in which evolution is occurring. In particular, it is completely lacking any epidemiology, which is a curious feature for a model of virus evolution.

I will remedy this omission in this paper with a new model of covirus evolution. I will begin with a description of the modelling framework—metapopulation theory—in the simple context of the population dynamics of a single species. I will then introduce a model of two mutualists studied elsewhere (Nee *et al.* 1997) which will be modified to make it more meaningful for coviruses. Then, the qualitative behaviour of these two models as a varying parameter will be used to address the question: As a mutualistic association becomes more intimate, is there a clear transition from a two-species system to a single-species system? The answer is yes. This analysis will provide us with some useful results, as well as useful special cases, to facilitate understanding of the full covirus evolution model. The principal question I will pose the model is this: Can coviruses readily coexist with the complete progenitor viruses from which they are derived? The answer is no, which is consistent with the fact that such coexistence has not been observed in nature.

2. METAPOPULATION MODELLING FRAMEWORK

Our modelling framework is that of Levins' metapopulation model (Hanski & Gilpin 1997; Hanski 1999). The Levins model is a useful abstraction that allows many systems that are biologically very disparate to be described in a common framework. The model is as follows, where we use inverted commas to emphasize that the interpretation of the words can be very broad. We imagine 'patches' of suitable habitat for a species distributed in a 'landscape': empty patches may be 'colonized' by a species and 'local populations' on occupied patches may 'go extinct', leaving an empty patch or, in some interpretations, the patch itself may disappear causing local extinction, with new, empty patches being created over time.

Let x be the fraction of empty patches and y the fraction of occupied patches. With colonization and extinction rates denoted by c and e, respectively, the basic Levins metapopulation model, modified to allow variation in the total number of patches, is

$$\frac{dx}{dt} = -cxy + ey,$$
$$\frac{dy}{dt} = cxy - ey, \qquad (1)$$
$$x + y = h,$$

where h is the fraction of habitat that is suitable for occupation, with $h = 1$ in the 'pristine' world. (There is an important truth contained in Jeremy Jackson's (unpublished) definition of 'pristine' as 'what the world looked like when you were growing up'.) We can model the effects of 'habitat destruction' (one topical interpretation) by decreasing h.

At a balance between colonization and extinction, equilibrium patch occupancy, y^*, is given by

$$y^* = h - \frac{e}{c}. \qquad (2)$$

With declining h, the equilibrium frequency of occupied patches declines continuously to zero. Extinction occurs at a threshold level of destruction, $h = e/c$: hence, it is not necessary to destroy all suitable habitat in order to eradicate a species. In two influential papers, Lande (1987, 1988) seems to have been the first to note this threshold behaviour in the conservation context. In his

models, a 'patch' was a territory for a 'local population' of a single breeding female who would eventually die, or 'go extinct', leaving the territory open for 'colonization' by another female.

The threshold result has long been known in epidemiology, which is simply another biological specification of metapopulation theory: habitat patches are host individuals, colonization is infection, extinction is host recovery or death, and vaccination programmes are wanton acts of habitat destruction, from the point of view of the infectious disease organism (Nee *et al.* 1997). The threshold result in epidemiology is the fact that you do not need 100% vaccination coverage to eradicate a disease (Anderson & May 1991). Model (1) is a very simple epidemiological model in which, for example, the disease is fatal but the population is regulated by other factors, so that births exactly balance deaths. Our subsequent models are generalizations of it. (I note in passing that the threshold behaviour of model (1) is found in a much broader ecological context than that discussed here; see Nee 1994.)

3. MUTUALISM MODEL

Nee *et al.* (1997) presented a simple metapopulation model of mutualism. They envisaged a situation in which the first partner can survive in a patch on its own but needs the second for dispersal to new patches, whereas the second depends on the first for both survival and reproduction. They had in mind the relationship between a plant species and its specialized seed disperser or pollinator. They also suggested that the model may provide a description of TRV dynamics as well. I will first present this mutualism model and then extend it to correct one of its obvious inadequacies as a description of TRV.

Patches may be either empty, occupied by the plant only, or occupied by both plant and disperser. As in equations (1), x refers to the proportion of empty patches, y is now the proportion of plant-only patches and z is the proportion of plant plus disperser patches. The original model allowed for plant propagules and disperser propagules to have different colonization parameters and for y and z patches to have different local extinction rates. We do not need this extra complexity here, and so assume single colonization and extinction rates. Incorporating the assumptions of the previous paragraph, the natural extension of equations (1) is

$$\begin{aligned} \frac{\mathrm{d}x}{\mathrm{d}t} &= ey + ez - czx, \\ \frac{\mathrm{d}y}{\mathrm{d}t} &= czx - ey - czy, \\ \frac{\mathrm{d}z}{\mathrm{d}t} &= czy - ez, \\ x + y + z &= h, \end{aligned} \tag{3}$$

which has the solution

$$\begin{aligned} x^* &= h - y^* - z^*, \\ y^* &= \frac{e}{c}, \\ z^* &= \frac{1}{2}\left(h - \frac{2e}{c} \pm \sqrt{h^2 - \frac{4eh}{c}}\right). \end{aligned} \tag{4}$$

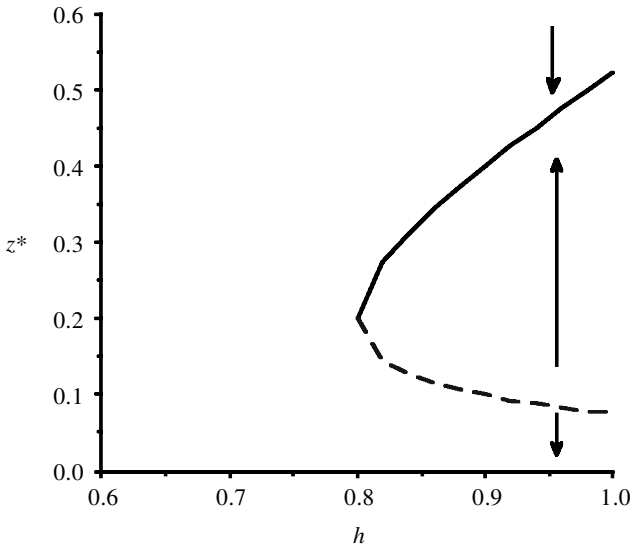

Figure 2. For any h above the extinction threshold there are two equilibria. The upper one is stable and the lower one is unstable: the arrows show the direction of motion of z in the vicinity of z^*. As h declines, these equilibria approach each other and their collision results in mutual annihilation—a mathematical catastrophe. The only equilibrium for h below the threshold is 0. This figure was constructed with $c/e = 5$.

Like equations (1), this also exhibits threshold behaviour, with extinction occurring at $h = 4e/c$. However, the behaviour of the model in the vicinity of this threshold is very different and is illustrated in figure 2. For h slightly larger than $4e/c$, there may be a substantial level of patch occupancy, with equilibrium patch occupancy plunging catastrophically to zero with a tiny increase in habitat destruction. As Nee *et al.* (1997, p. 136) put it, 'a perfectly viable association of mutualists living in great abundance across a large region can be completely destroyed by the construction of just one more shopping mall'.

Model (3) can be viewed as a model of TRV dynamics if we consider y to refer to plants infected by RNA1 and z to refer to plants infected by both RNA1 and RNA2. A possible major inadequacy of model (3), if we want it as a strategic description of TRV, is that it supposes (in terms relevant to TRV infection of plants) that plants are always initially infected by only the long particle, with possible subsequent infection by the short particle as well, whereas we have no reason to think that a fully productive simultaneous infection does not also occur. In fact, perhaps simultaneous infection is the rule—it would certainly facilitate the evolution of the covirus in the first place.

So, does the nematode vector of TRV typically transmit *both* particles, or is it a common occurrence that plants are successfully infected with only the long particle and, perhaps, subsequently infected with the short particle as well? We do not know the answer to this basic natural history question, which simply reflects the fact that research into TRV is concerned entirely with its molecular biology and not its natural history.

In the field, we do know that potatoes exhibiting symptoms of TRV infection are commonly infected only by RNA1. This suggests that infection by single particles does indeed occur in nature, but it could also be the case

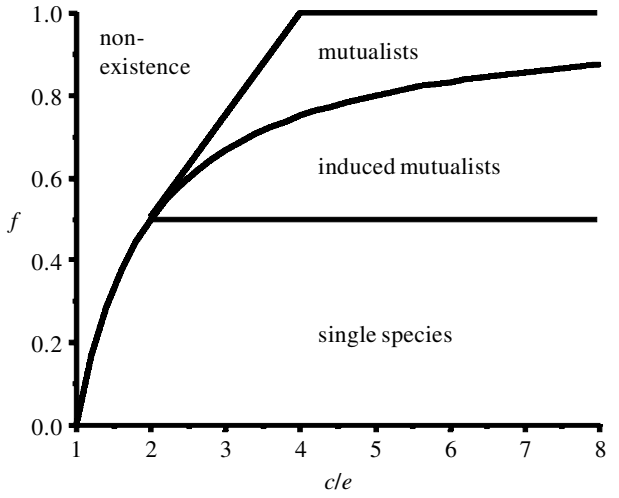

Figure 3. Illustrating the qualitative behaviour of the solutions of model (3). See § 3 for discussion.

that some potatoes are resistant to RNA2: we simply do not know (S. Macfarlane, personal communication). In other crops, like *Narcissus* (Amaryllidaceae), only infections by both partners have been reported.

In any case, we will now generalize model (3) to include the possibility of transmission of both particles. Of the new infections occurring in a time interval, a fraction f consist only of the long particle:

$$\begin{aligned}\frac{dx}{dt} &= ey + ez - czx,\\ \frac{dy}{dt} &= fczx - ey - czy,\\ \frac{dz}{dt} &= (1-f)czx + czy - ez,\\ x + y + z &= h.\end{aligned} \tag{5}$$

For $f = 1$, we recover the previous model of two mutualists. For $f = 0$, so the partners are always transmitted together, we recover the single-species metapopulation model (1): from the point of view of population dynamics, we are effectively dealing with a single entity. The question we will pose of this model has an obvious inspiration (Maynard Smith & Szathmáry 1995): Is there a clear boundary between these two situations and, if so, what is it? To put it another way, is there an identifiable minor transition in population dynamics?

The answer is yes, as we will now see. The behaviour of the single-species model in the face of habitat destruction is qualitatively different from the behaviour of the mutualist system. In the former case, for increasing levels of habitat destruction we have a continuous decline in equilibrium population size to zero. In the latter case, we have a discontinuity: at the critical level of destruction, equilibrium population size jumps to zero from a possibly large distance. We wish to identify a critical level of f, f_{crit}, that has the following properties: for $f < f_{\mathrm{crit}}$, the model behaves qualitatively like the single-species model and, for $f > f_{\mathrm{crit}}$, the model behaves like the mutualist model. (If $f_{\mathrm{crit}} = 1$, the behaviour of the mutualist model (3) is structurally unstable.)

Model (5) has two possible non-trivial equilibria in z, given by the formulae

$$z^* = \frac{1}{2}\left(h - \frac{2e}{c} \pm \sqrt{h^2 - \frac{4feh}{c}}\right). \tag{6}$$

We will confine our attention to the larger, stable solution. As before, if the smaller solution is feasible, it is unstable. We will no longer consider y^*, as the fate of this class of patches depends entirely on z^*.

To locate the transition in the qualitative dynamical behaviour of the model, we first note that, as intuition would suggest, z^* is a monotonically increasing function of h or, equivalently, z^* declines with declining h. For the model to exhibit mutualist dynamical behaviour, it must be the case that, as h declines, there is an h, $0 < h < 1$, for which (i) $h - 2e/c$ is positive; and (ii) the square-root term in z^* goes from real to complex (which happens when the two equilibria collide). Together, these two conditions yield

$$\frac{2e}{c} < h < \frac{4fe}{c}. \tag{7}$$

This gives us $f = 1/2$ as the line dividing mutualistic behaviour from single-species behaviour.

The story is not complete. In what region of parameter space can the virus exist ('existence' meaning $z^* > 0$ when $h = 1$)? It can readily be seen from equation (6) that the region is given by

$$\begin{aligned} f &< 1 - \frac{e}{c}, \qquad & \frac{c}{e} &< 2,\\ f &< \frac{c}{4e}, \qquad & \frac{c}{e} &> 2. \end{aligned} \tag{8}$$

Finally, we also wish to note the region of parameter space in which, in a world with $h = 1$, the virus can increase when very rare. This requires that the lower, unstable equilibrium is unfeasible, i.e. it is negative. This region is defined by

$$f < 1 - \frac{e}{c}. \tag{9}$$

Figure 3 presents a summary of this analysis.

As we can see, for $f < 1/2$, the qualitative behaviour of the system is entirely like that of the single-species model, regardless of the colonization rate: there is a single, stable equilibrium population abundance that declines smoothly to zero with increasing habitat destruction.

For $f > 1/2$, the situation is more complicated. In this region, for $f > 1 - e/c$ we have unambiguous mutualists whose qualitative behaviour is the same as in our original mutualism model. For $f < 1 - e/c$, habitat destruction creates mutualistic dynamics out of single-species dynamics. In this region, when $h = 1$, the model is qualitatively a single-species model, with a single, stable equilibrium abundance. But as h declines, a new, lower, unstable equilibrium appears and, with decreasing h, rises until it annihilates the stable equilibrium, resulting in a mathematical and real catastrophe for the population.

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As c/e gets larger, the mutualist region is squeezed out by this 'induced' mutualist region. Perhaps a better way of thinking about it is that for larger c/e, mutualistic dynamics are masked, i.e. the lower, unstable equilibrium is swamped out of existence by a high colonization rate in the pristine environment.

In any case, the fact that the qualitative behaviour of the model depends on both f and c/e is not surprising. What is surprising is that the behaviour is independent of c/e for $f < 1/2$.

4. EVOLUTION OF COVIRUSES

We will model the population dynamics of a virus–covirus system in a metapopulation of plants by generalizing model (5), where the word 'virus' is reserved for the complete, autonomous virus. We are interested in the circumstances under which the covirus completely ousts the virus from the population. As far as I am aware, there is no example of virus–covirus coexistence: for the theoretical framework presented here to be plausible it must, at the very least, be consistent with this fact.

We will suppose that, in a plant containing both the virus and replicating covirus (either a single component of the covirus, like the RNA1 of TRV, or both), the virus concentration is reduced to such low levels that it is not transmissible. This is a reasonable simplification: DI viruses by definition interfere with the production of virus, and satellite RNAs can be so effective at reducing virus yield that crop plants have been genetically engineered to produce them themselves, e.g. Harrison *et al.* (1987) (although this strategy is not without risk). A closely related, and realistic, assumption is that covirus can infect plants infected with virus, but not vice versa.

We will be interested mainly in the quantitative relationships between the infection rates (parameter c) that determine the dynamical outcome. But what will we assume about the virulence (parameter e) of the virus and covirus?

Remarkably little is understood about virulence in general beyond the generalization that disease symptoms are determined by properties of the host, the virus and the interaction between the two—which is more an admission of ignorance than anything else. There was great hope that viroids would shed light on this area. These plant viruses consist of a few hundred bases of RNA that code for absolutely nothing at all and induce the full spectrum of infections from asymptomatic to lethal (Matthews 1991; Singh *et al.* 1995). Hence, any symptoms are being produced by host proteins. In spite of the simplicity of the system, as well as its substantial economic importance, there has been very little progress in understanding pathogenesis. The reason for this failure seems to be simply the difficulty of identifying which host proteins are responding to the viroid sequence (Matthews 1991). (A satellite of hepatitis B, hepatitis delta virus, is remarkably similar to plant viroids (Taylor 1999).)

Satellite virus and DI virus systems also provide us with no useful generalizations. For example, different strains of the satellite RNA CARNA 5, which parasitizes cucumber mosaic virus (CMV), can attenuate or exacerbate disease symptoms. Furthermore, the same strain of CARNA 5 will attenuate symptoms of CMV infection in tabasco pepper plants while inducing lethal necrosis in tomato (Matthews 1991). Similarly, although the first DI virus found in plants, derived from TBSV, attenuates disease symptoms (Hillman *et al.* 1987), DI turnip crinkle viruses increase symptom severity (Li *et al.* 1989; Simon 1999).

Lacking guidance one way or the other, we will assume that both virus and covirus have the same parameter e. This is, in fact, a satisfactory simplification: inequalities in e change the outcome of the model in an intuitive fashion, so we do not need the extra symbolic clutter.

The variables x, y and z have the same meaning as before. We subscript the colonization parameters to identify them as belonging to the virus, c_v, or covirus, c_c. The variable w refers to the frequency of plants infected by virus. The full model is

$$\begin{aligned}
\frac{dx}{dt} &= ey + ez + ew - c_c zx - c_v wx,\\
\frac{dy}{dt} &= fc_c zx + fc_c zw - ey - c_c zy,\\
\frac{dz}{dt} &= (1-f)c_c zw + (1-f)c_c zw + c_c zy - ez,\\
\frac{dw}{dt} &= c_v wx - c_c zw - ew.
\end{aligned} \tag{10}$$

The full equilibrium solutions of this model will not be discussed here. Instead we will consider two extreme special cases.

(a) $f = 0$

This case describes a situation in which both components of the covirus must simultaneously infect the plant to establish infection. For the covirus to exist, it must be the case that

$$\frac{c_c}{e} > 1, \tag{11}$$

and, if this is satisfied, for the virus to persist it must be the case that

$$\frac{c_v}{e} > \left(\frac{c_c}{e}\right)^2. \tag{12}$$

Notice that c/e corresponds to the R_0 of the epidemiologist: it is the number of new infected plants produced by a single infected plant introduced into a healthy plant population.

If both these conditions are satisfied, then there is an interior stable equilibrium

$$(x^*, y^*, z^*, w^*) = \left(1 - z^* - w^*, 0, 1 - \frac{e}{c_c}, \frac{c_v e - c_c^2}{c_v c_c}\right). \tag{13}$$

This case has at least two interesting features.

(i) It is identical to a model of two competing species that coexist as metapopulations. Coexistence is achieved when the superior competitor—which can exclude the inferior from a patch—has a lower colonization rate. So the inferior competitor survives as a weedy, fugitive species. This model was first studied by Hastings (1980) in the context of the coexistence of coral species and later, independently,

by Nee & May (1992), who were interested in the effects of habitat destruction on the competitors. (They found that habitat destruction works to the advantage of inferior competitors.) The same model reappeared with an epidemiological interpretation in a study of the evolution of virulence (Nowak & May 1994). Here it appears as a model of mutualists competing with a single species.

(ii) It is not going to be easy for the virus to persist after the covirus has arisen. The condition in equation (12) is demanding and requires that the transmission of the covirus is very seriously impaired by its divided nature. The fact that, as far as I am aware, there is no example of virus–covirus coexistence suggests that vector transmission is effective.

(b) $f = 1$

This is a version of the TRV scenario where we assume that co-infection never occurs. The necessary condition for the existence of the covirus, which we have previously found to be $c_c/e > 4$ (figure 3), is more demanding than in the previous case. The reason for this is that newly infected plants are not, themselves, infectious. But, given that the covirus can exist, the conditions for the co-existence of the virus are difficult to satisfy in this case as well.

The relevant equilibrium solution of equations (10) is

$$x^* = \frac{c_c + \sqrt{c_c^2 - 4c_c e}}{2c_v}, \tag{14a}$$

$$y^* = \frac{1}{c_c}, \tag{14b}$$

$$z^* = \frac{c_c + \sqrt{c_c^2 - 4c_c e - 2e}}{2c_c}, \tag{14c}$$

$$w^* = \frac{c_v - \sqrt{c_v^2 - 4c_v^2 e/c_c} - c_c - \sqrt{c_c^2 - 4c_c e}}{2c_v}. \tag{14d}$$

From equation (14*d*), there is a critical value of c_v, $c_{v,crit.}$, below which $w^* = 0$, i.e. the virus cannot persist with the covirus, given by

$$c_{v,crit.} = \frac{1}{2}(c_c^2 + c_c\sqrt{c_c^2 - 4c_c} - 2c_c). \tag{15}$$

In the previous special case, the virus needed a colonization parameter that was the square of that of the covirus in order to persist. That is still the case here, at least approximately for large c_c. For smaller values of c_c, the threshold increases with increasing c_c by ever larger factors, ultimately converging on a factor of c_c: for $c_c = 5$, 6, 7 the threshold is greater than $2\times$, $3\times$ and $4\times c_c$. So, as before, the covirus needs to have a very substantial transmission disadvantage if it is not to supplant the virus entirely. Taken together, these two special cases suggest that it may be true for all f that the virus needs a colonization parameter that is the square of that of the covirus in order for persistence. This is the case, as will be shown when the full behaviour of the model is described elsewhere (S. Nee, unpublished).

5. CONCLUSIONS

Models as simple as equations (10) are often called 'benchmark' or 'strategic' models, the adjective acting as a fig leaf to protect the model's composer from glib accusations of oversimplification. Minimalist it may be as a model of covirus evolution—and I do not have the knowledge to justify rococo elaborations—yet it contains within it, non-trivially, single-species dynamics, mutualism, competition and parasitism—an entire soap opera of ecological relationships. This can be understood in two ways. First, from a biological point of view, it is to be expected in a system of replicating entities that do not have exclusive access to their own gene products (Nee & Maynard Smith 1990), and where population dynamics is occurring at the two distinct levels of within and between plants. Second, from a theoretical point of view, as I hope I have shown, it comes about as a result of a new confidence in using the same models in seemingly quite disparate biological contexts.

The particular emphasis of this paper has been on methodically building up to model (10) from the simplest starting place, the Levins' metapopulation model, equations (1). Giving only a partial treatment of the full model, equations (10), has one somewhat misleading consequence. I have emphasized the coexistence difficulties faced by the progenitor virus(es) when the covirus has arisen, but downplayed the problems faced by the covirus itself—in particular, the threshold density it may first need to attain before it can spread. This was mentioned opaquely by reference to the unstable smaller equilibrium in § 3 and will be discussed fully elsewhere. Still, once the covirus has jumped any initial hurdle, the future is bleak for the progenitor.

As in many areas of biology, most of the recent progress in covirus research has been in working out the fine details of their molecular biology rather than filling in our knowledge of the natural history of these fascinating entities. That one of the clearest overviews of coviruses is now nearly one-quarter of a century old reflects this fact (Fraenkel-Conrat & Wagner 1977). But without the natural history we cannot be confident in our understanding of the origins or maintenance of coviruses. It is to be hoped that the post-genomic world will see balance return.

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