

Comments on the Feeney-Zaba HIV model

I agree with the idea of a model of "intermediate" complexity, although having infective age and sexually active/inactive folks puts your model much closer to the complex ones than to the simple ones ! I'm just surprised this sort of stuff hasn't already been done, and I hope you won't be accused of re-inventing the wheel with an umpteenth HIV model. But I am sure you know the literature better than I do, and I will trust you that there is a need for such a model. My interest and contribution are primarily on the mathematics.

I had a quick look at the full age-structured model, which is similar in spirit to the one I presented in Copenhagen: a classical Leslie-type model with an infection rate that is a function of the *structure* of the populations. (Let's call it a *structure-dependent* function). There seems to be two versions of the "Model Design" document on Griffith's site. I printed one that was 10 pages long (in which $\lambda_S(a,t)$ was not yet specified) and then I realized there was an updated 14-page long document elsewhere, with $\lambda_S(a,t)$ appearing as a homogeneous function of the population vector (i.e. a function that is unchanged if all components of the population vector are multiplied by a common constant c - this would be the mathematical definition of what I called a *structure-dependent* function).

I had a very similar specification for the infection rate, in which I was attempting to model, in a more complicated fashion, the choice of partners in such a macro-fashion. It is gratifying to see these ideas make their way into the work of "mainstream" AIDS researchers like you. And I have no quarrel with the simplifications involved. I'll let others comment on these epidemiologic aspects. (It will be interesting to see how the idea of the "Bulletin Board" works out in that respect. I'm not using it because my comments are long, detailed, and involve mathematical notations that would not go down well on such a bulletin board).

Anyway, the model looks right to me. In a model that strives for simplicity I just wonder how vital the distinction is between the sexually active and inactive uninfected, and whether a separate state is really needed. You say yourself that it's difficult to decide on transition rates between these two states, and I wonder if you won't have problems with data. Why not have both together and simply reflect different levels of sexual activity in the age-specific infection rates $\lambda_S(a,t)$?? (lower levels or zero levels for the very young, etc). I think the model would gain in simplicity and lose little in realism. That is really the crucial issue here: what are the most important components of the transmission dynamics that must be in the model - and what can be left aside.

I fully agree with your central premise that one wants to try to extract the essence of what determines the spread - and leave aside what are details in the big picture. You chose to have the "infective age" in addition to the chronological age, which is of course a valid choice but complicates things considerably. I had chosen not to have the infective age, precisely to make a big gain in simplicity. You see, simplification is in the eye of the beholder: I tried a macro modeling of the choice of partner but left out the infective age structure - you chose to do the opposite. One approach here of course is to compare results with different models.

You may get some criticism for the notations - like I did in the past. It's incredibly hard to keep track of who's who with X,Y, Z notations. For example why not $U_{I_S}(a,t)$ for "Uninfected Inactive" of sex S instead of $X_S(a,t)$. And $U_{A_S}(a,t)$ for the active; $I_S(a,d,t)$ instead of $Z_S(a,d,t)$, etc. Two-letter variables are not particularly elegant, but it's very important when reading the text to not have to constantly make the mental effort of having to remember who's who. (You could also have double subscripts: $U_{I,S}(a,t)$ for the uninfected (inactive, sex S) etc.- a bit cumbersome, but that's the price to pay for "ease of reading").

The mathematics and the dynamics of the full age-structured model should be quite complex and interesting - as I have found out. I will leave you to it, as it is a big job still in progress.

I have spent some time studying the "bare bones" model and it's quite interesting. I think you can expect some criticism for the obvious extreme simplifications made, but I personally find it a useful and helpful exercise. One tries to extract the essence of the ideas that have a more complete expression in the age-structured model.

My humble contribution will involve the stability analysis of this simple discrete two-dimensional dynamical system. I was at first a bit puzzled by the "equilibrium equations" (4) and (5) that you have in the "Numerical approximations" section. Here is how I look at them, your perspective may or may not have been different.

At first I couldn't see where these two equations come from. They are certainly not the *exact* equilibrium equations one could write as solutions of the system (1)-(2). I was also intrigued by the term $i = \iota + \kappa p$ (eq. (4)) that you call the incidence. With $\theta(t)$ equal to 0 for large t (as is specified in p. 3), and $\iota(t) = \iota =$ a constant, this term $\iota + \kappa p$ looked more to me like the long-run, asymptotic value of $\lambda(t)$ of eq. (3). (Since $Z(t)/P(t)$ converges to p , the equilibrium prevalence, when $t \rightarrow \infty$). I sort of understand eq. (5): the stable growth rate r is the net growth rate $\beta - \mu$ minus the extra HIV-induced mortality which is applied only to the fraction p that is infected. Fair enough, but it's still not clear to me how these equations are derived from (1), (2).

So this is how I look at things. First I wonder if there isn't a little confusion in (1), (2) between a purely discrete approach (e.g. $\beta(Y(t)+Z(t))$ is the number of births, with β a pure rate, or percentage) and a discrete approximation of continuous rates. (e.g. $\exp\{-\lambda(t)-\mu\}$). I realize you are discretizing continuous "exit rates" because there are two competing risks: death and transition to infected. There is however a slight inconsistency then, and the simple way of seeing it is by forgetting all about HIV in eq (1). Set $Z(t)=\lambda(t)=0$ and you have $Y(t+1)=Y(t)[\exp(-\mu)+\beta]$. The problem is that $\exp(-\mu)+\beta$ is not equal to 1 when $\mu=\beta$, as it should be when death rates equal birth rates. Of course the expression is *close* to 1 when μ and β are equal and *close* to 0. This remark and subsequent ones hinge on the approximation $\exp(x) \cong 1+x$ for x small. Indeed, the arguments of the exponentials in (1)-(2) are all small, so using this approximation the system becomes

$$Y(t+1) = Y(t)(1-\lambda(t)-\mu) + \beta(Y(t)+Z(t)) \quad (1')$$

$$Z(t+1) = Z(t)(1-\alpha+\mu) + Y(t)\lambda(t) \quad (2')$$

The error you make with this approximation is less than 0.5%, a small price to pay for the benefits that will ensue, particularly given that this is such a crude approximation of what's going on anyway. Here all the rates are purely discrete, and of course less than 1. For example $\lambda(t)$ is an infection rate - and no longer a "force of infection" - which can theoretically be larger than 1. Also $\lambda(t)$ is the incidence, which explains your eq. (4) (see below). The inconsistency described above when $\mu=\beta$ disappears. (The data you use are the CBR and CDR for μ and β , which of course means that you are using purely discrete data).

With the slightly modified system (1') and (2'), everything becomes simple and transparent. At the equilibrium, the infection rate $\lambda(t)$ is equal to some λ which must be equal to $\tau+\kappa p$ where p is the equilibrium prevalence - and this is your eq. (4), given that $\lambda(t)$ and its limit represent the incidence. We thus have

$$\lambda = \tau + \kappa p \quad (3')$$

Two other equations obtained from routine stability analysis are:

$$r = \beta - \mu - \alpha p \quad (4') \quad (\text{same as you eq. (5)})$$

$$r = -(\lambda + \mu) + \beta / (1 - p) \quad (5')$$

where r is the limiting growth rate, i.e. the limit of $Y(t)/Y(t-1)-1$ (or of $Z(t)/Z(t-1)-1$) for t going to infinity.

In short, we have a very simple system of three equations in the three unknowns λ , r , and p that can be found in closed form (no need to agonize over numerical approximations). For example p is the root (between 0 and 1) of the quadratic equation

$$(\alpha - \kappa)p^2 + (\kappa - \alpha - \beta - \tau)p + \tau = 0$$

In your numerical example p. 3 you have $\alpha = \kappa = 0.1$; $\tau = 0.004$; $\beta = 0.004$ (there's a typo for β) so the root is simply

$$p = \tau / (\beta + \tau) = 0.091$$

and $r = 0.021$ [same as $\ln(P(t+1)/P(t))$ in your spreadsheet for large t]. Also $\lambda = 0.0131$ - close to the 0.0139 you find in the spreadsheet for t large. (The small discrepancy obviously due to the fact that one model is an approximation of the other).

Some issues remain. We have an equilibrium point, but we still need to check that it is stable. (starting close to that equilibrium point, does one converge to it?). This may not be of interest to demographers but it is still something that needs to be checked. With a nonlinear model like this one, it is possible for an equilibrium point to exist but to be unstable. It turns out that I came across these issues with my own

similar AIDS model and found that the mathematical tools did not exist to investigate this stability. So I created them, and they will appear soon in an article published in *SIAM Journal of Matrix Analysis*. These results can be used fruitfully for the simple case of the bare bones model, and possibly for the age -structured model too.

Also, I wonder if similar simplifications could be envisaged for the age-structured model, i.e. if one could use $\exp(x) \cong 1+x$ in p. 8 to greatly simplify the expressions. I'm not sure it would be necessary for the full-blown model, though, since there would be no question of finding analytical solutions, like in "Barebones".

These are just some simple and preliminary observations - I hope they are of use. The project is interesting and a lot more could be said.

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