Modelling epidemiological scenarios

One of the most important potential applications of the genomic transmission graph is to assist in using genetic data to understand epidemiological changes over time. For example, if there is a sudden rise in the local prevalence of infection, we would like to know whether this is due to a local increase in transmission intensity, or to an influx of infections due to migration, or to other factors. In previous sections, we have glossed over the issue of temporal variation by assuming that the transmission parameters are constant over time.

In this section we incorporate temporal variation in N_h, Q, χ and N_m into our Markov chain simulations of the genomic transmission graph. In order to assess changes in the genetic state of the population over time, we need to sample the population at different points of time - we call these *observation times*. For each observation time we must launch a separate Markov chain simulation of the coalescent process going backwards in time.

The `coalestr` module. To accompany this paper, a Python package called `coalestr` has been developed for running coalescent simulations and computing genetic variation based on the genomic transmission graph. This allows the user to specify a hierarchical population structure and for the transmission parameters to vary over time. It returns time series data for multiple observation times. Jupyter notebooks containing worked examples and help on how to install and use `coalestr` are available at `d-kwiat.github.io/gtg`.

Effects of a step change in transmission parameters of a local subpopulation within the global metapopulation. In these examples we examine a small local subpopulation with $N_h = 10$, $Q = 5$ and $\chi = 0$ with an ongoing level of migration ($N_m = 1$) from a global metapopulation with $N_h = 14660$, $Q = 3$ and $\chi = 0.2$ as illustrated in figure **??**. In each case we examine the effects of a step change in the transmission parameters at 100 to 50 generations before the present. We are looking at the nucleotide diversity of the subpopulation π_S, mean within-host nucleotide diversity π_W, haplotype homozygosity of the subpopulation at a 2cM locus γ_S, mean within-host haplotype homozygosity at a 2cM locus γ_W, the fixation index F_{ST} and the inbreeding index F_{WS}.

χ	N_h	N_m	π_S	π_W	γ_S	γ_W	F_{ST}	F_{WS}
↑	–	–	↑	↑↑	↓	↓↓	↓	↓↓
–	↑	–	(↓)	↓	(↑)	↑	↑	↑
–	–	↑	↑	↑	↓	↓	↓	↓

Table 1: **Effects of a step change in transmission parameters.** We examine three scenarios in a local subpopulation that is embedded within the global metapopulation: (i) a sharp transient increase in χ as in fig. 1; (ii) a sharp transient increase in N_h as in fig. 2; (iii) a sharp transient increase in N_m as in fig. 3. This table summarises the effect of these step changes on nucleotide diversity (π_S and π_W), haplotype homozygosity at a 2cM locus (γ_S and γ_W), F_{ST} and F_{WS}. View code

We consider three scenarios (table 1). In the first scenario, the level of χ in the subpopulation transiently increases from 0 to 1 during the period 100 to 50 generations before the present (figure 1). The result is a sharp rise in π_W and a sharp fall in γ_W, F_{ST} and F_{WS}. There is also a modest rise in π_S and a modest fall in γ_S.

In the second scenario, the rate of migration N_m from the metapopulation into the subpopulation transiently increases from 1 to 5 during the period 100 to 50 generations before the present (figure 2). This causes a sharp rise in π_W, a more modest rise in π_S and a sharp fall in γ_W, γ_S, F_{ST} and F_{WS}. Thus the effects of an increase in N_m are rather similar to those of an increase in χ.

In the third scenario, the level of N_h in the subpopulation transiently increases from 10 to 30 during the period 100 to 50 generations before the present (figure 3). The result is a sharp rise in F_{WS}, a modest rise in F_{ST} and γ_W, a modest fall in π_W, and small reduction in π_S. These results

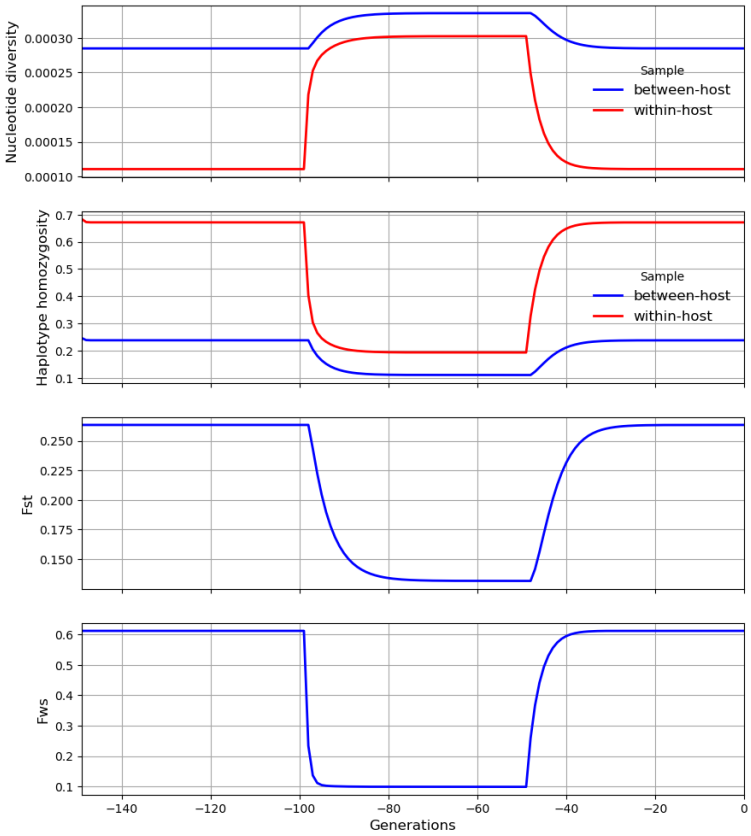

Figure 1: **Increase in the crossing rate of transmission chains.** In our first scenario χ transiently increases from 0 to 1 at 100 to 50 generations before the present. Nucleotide diversity rises, haplotype homozygosity falls View code

appear paradoxical because we might expect an increase in N_h to cause π_S to rise whereas it falls slightly. The paradox can be explained by recalling that $N_m = mN_h$. Although N_m is constant, the rise in N_h causes m to decline, and this reduction in the proportion of hosts that have migrated from the metapopulation counterbalances the local increase in effective number of hosts, causing π_S to remain almost unchanged.

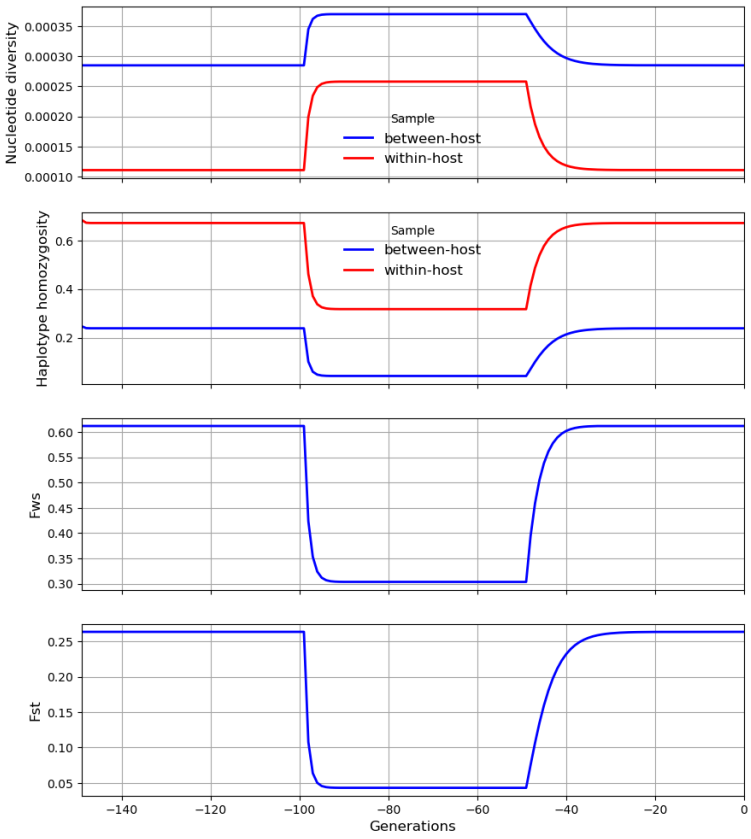

Figure 2: **Increase in the rate of migration from the global metapopulation.** In this scenario N_m transiently increases from 1 to 5 at 100 to 50 generations before the present. Nucleotide diversity rises, haplotype homozygosity falls View code

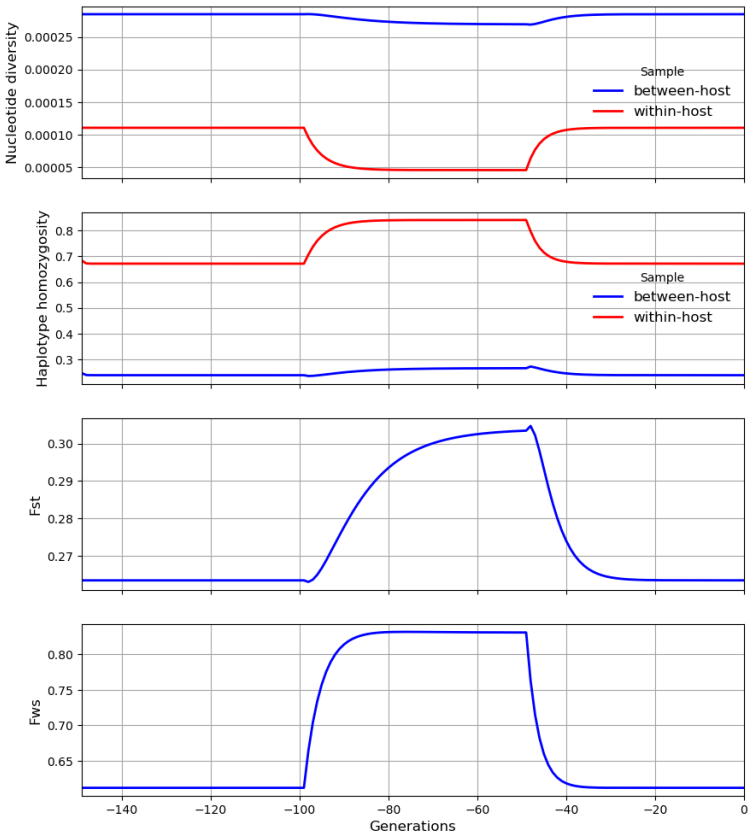

Figure 3: **Increase in the effective number of hosts.** In this scenario N_h transiently increases from 10 to 30 at 100 to 50 generations before the present. Paradoxically, nucleotide diversity falls, haplotype homozygosity rises. View code