Joint estimation of effective population sizes and selection coefficients from time-sampled data: a case study on virus populations submitted to plant resistance

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Recent results indicate that quantitative trait loci (QTL) of the host genetic background modulate the durability of major resistance genes to plant viruses (Quenouille *et al.* 2013, 2014). This is particularly interesting for plant breeders. Two biological mechanisms can explain such observations: (i) QTLs increase the genetic drift acting on virus population and (ii) QTLs decrease the selective advantage of the most adapted virus variants. Up to date, several methods have been proposed to estimate the intensity of drift when neutral genetic markers are available. However few methods allow to jointly estimate effective population sizes (N_e), which determine the intensity of genetic drift, and selection coefficients (s) when no neutral markers are available (Foll *et al.*, 2014).

Here, taking advantage of time-sampled data representing the frequency changes of within-host competing pathogens strains, we propose a modeling approach to jointly estimate the N_e of a viral population and the selection coefficients associated to several loci involved in pathogenicity properties. Experiments were set up to follow the within-host dynamics of 5 *Potato virus Y* (PVY) variants in 15 pepper plant genotypes carrying the major resistance gene *pvr2³* and several QTL combinations. The PVY variants carried distinct mutations, each conferring weak to strong adaptation to *pvr2³*. We determined the frequency of virus variants within the host plants at 6 time points, from 6 to 34 days after inoculation, using high-throughput sequencing. Estimates of N_e and of the selection coefficients s of each variant were inferred for each pepper genotype by fitting mechanistic-statistical models relying on Lotka-Volterra equations and Dirichlet-multinomial distributions (Fabre *et al.,* 2012).

Results showed that the ranking of the selection coefficients among the 5 virus variants was identical in all plant genotypes but the selection differential between variants varied greatly from one plant genotype to another. Importantly, the fittest virus variants were the same in all plant genotypes and we did not identify any plant genotype that could counter select these variants. Results also indicated that N_e was varying from 35 to 1200 depending on pepper genotypes and revealed contrasted patterns of genetic drift in the inoculated leaf and in systemically infected leaves. Whether plant genetic factors increasing the drift acting on virus populations could be used to slow down virus adaptation at larger scales (field, landscape) still remains to be investigated. More generally, the proposed methodology here is of wide

interest to disentangle the relative roles of drift and selection without neutral loci using high-throughput sequencing and a time-sampling scheme of independent hosts.

References: Fabre *et al.* 2012, PloS Path., 8(4), e1002654 ; Foll *et al.*, 2014, PloS Genet., 10(2), e1004185 ; Quenouille *et al.* 2013, Mol. Plant Pathol, 14, 109-118 ; Quenouille *et al.* 2014, Heredity, 112, 579-587.

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