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► **To cite this version:**

Elsa Rousseau, Frédéric Fabre, Jérôme Coville, Ludovic Mailleret, Alain Palloix, et al.. Joint estimation of the strength of genetic drift and selection from next generation sequencing time-sampled data: a case study on the adaptation of virus populations to host plant resistance. SMBE Satellite meeting SMBEBA 2015 "Investigating biological adaptation with NGS: data and models", May 2015, St Martin de Londres, France. , 2015. hal-02797375

HAL Id: hal-02797375

<https://hal.inrae.fr/hal-02797375>

Submitted on 5 Jun 2020

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Joint estimation of the strength of genetic drift and selection from Next Generation Sequencing time-sampled data : a case study on the adaptation of virus populations to host plant resistance

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Several methods have been proposed to estimate the intensity of genetic drift assuming neutrality of genetic markers. When no neutral markers are available, distinguishing the effects of selection from drift remains puzzling (Foll *et al.* 2014). Here, we aim at disentangling the role of genetic drift and selection taking advantage of Next Generation Sequencing (NGS) time-sampled data representing temporal changes in allele frequencies. We focused our work on an agricultural issue : the emergence of resistance-breaking (RB) pathogens after the deployment of virus-resistant crops, suppressing the yield benefit provided by the resistance (Fabre *et al.* 2012a). However, it has been proved for several pathosystems that the genetic background of plants can increase the durability of the resistance (Palloix *et al.* 2009, Quenouille *et al.* 2013). Two mechanisms can explain this result : either (i) a decrease of the selection advantage of the RB mutant, or (ii) an increase of genetic drift acting on the virus population.

We carried out an experiment that consisted in following the within-host demo-genetic dynamics of several *Potato virus Y* (PVY) variants in different pepper plant genotypes, carrying a resistance gene and contrasted genetic backgrounds. PVY variants carried distinct mutations, each mutation conferring weak to strong adaptation to the resistance. We estimated the within-host variants frequencies at different time points by NGS. Raw NGS data showed highly contrasted patterns of virus populations dynamics between host genotypes, suggesting contrasted effects of the host genetic background on genetic drift and selection acting on virus populations. The respective effects of those two evolutionary forces were evaluated by fitting mechanistic-statistical models to these data, relying on Lotka-Volterra population dynamics equations and Dirichlet-multinomial distributions (Fabre *et al.* 2012b). We estimated the fitness of the virus variants through the dynamics of the mean variants frequencies, and the strength of genetic drift through the between-host variances of these frequencies at all time points. The approach was first validated using simulation experiments with data-sets generated with a Wright-Fisher model (Zanini & Neher 2012). The models were then fitted to our experimental data-sets. Results notably indicated that the effective population size (N_e), a proxy of drift intensity, was substantially varying, from 40 to 500, depending on host genotype. Whether such plant genetic factors, increasing genetic drift acting on virus populations, can be used to slow down virus adaptation at larger scales (field, landscape) still remains to be investigated. More generally, the proposed methodology is of wide interest to co-estimate the strength of genetic drift and selection during species evolution.

References : Foll *et al.* 2014, PLoS Genet, 10(2), e1004185 ; Fabre *et al.* 2012a, New Phytol., 193, 1064-1075 ; Palloix *et al.* 2009, New Phytol., 183, 190-199 ; Quenouille *et al.* 2013, Mol. Plant Pathol., 14, 109-118 ; Fabre *et al.* 2012b, PLoS Path., 8(4), e1002654 ; Zanini & Neher 2012, Bioinformatics, 28(24), 3332-3333.