Supplementary information for: Simultaneously estimating evolutionary history and repeated traits phylogenetic signal: applications to viral and host phenotypic evolution.

Bram Vrancken¹, Philippe Lemey¹, Andrew Rambaut^{2,3}, Trevor Bedford⁴, Ben Longdon⁵, Huldrych Gunthard⁶, and Marc A. Suchard^{7,8}

¹Department of Microbiology and Immunology, KU Leuven, Leuven, Belgium.

²Institute of Evolutionary Biology, University of Edinburgh, Edinburgh, UK. ³Fogarty International Center, National Institutes of Health, Bethesda, MD, USA.

⁴Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.

⁵Department of Genetics, University of Cambridge, Cambridge, UK.

 ⁶Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Zürich, University of Zürich, Zürich, Switzerland.
 ⁷Departments of Biomathematics and Human Genetics, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA 90095-1766, USA

⁸Department of Biostatistics, UCLA Fielding School of Public Health, University of California, Los Angeles, CA 90095-1766, USA

September 3, 2014

Additional Figure



Figure 1: Marginal prior and posterior densities of $\lambda_{\rm B}$ for the MSM strict data set. The black lines indicate the prior (solid) and posterior (dashed) densities under a $\beta(2,2)$ prior, whereas the grey lines indicate the prior (solid) and posterior (dashed) density under a $\beta(1,1)$ prior.

Additional simulations

We complement the performance assessment of $\lambda_{\rm B}$ based on the approach proposed by Alizon et al. (2010) with an additional simulation study based on the approach taken by Shirreff et al. (2013). In the Methods section of the main manuscript, we describe how this approach differs from the previous simulation procedure. The simulations are performed along the maximum clade credibility tree inferred from the MSM strict analysis. The additional analyses essentially replicate the findings reported in the main manuscript: the $\lambda_{\rm B}$ estimator shows less bias and has lower variance than the $\lambda_{\rm ML}$ and Blomberg's K estimators of phylogenetic signal (Table 1). Again, the markedly larger variance of $\lambda_{\rm ML}$ is particularly noticeable at intermediate heritability values (Figure 2). Similarly, when comparing the effect of several prior settings on $\lambda_{\rm B}$ in reducing the sigmoidal pattern of phylogenetic signal estimates (Figure 3), we find the $\beta(2,2)$ prior again shows higher coverage and lower variance than all other tested priors. However, the bias is slightly higher (~2%) than under the $\beta(1,1)$ prior.

Table 1: Comparison of bias, mean squared error (MSE) and coverage for different phylogenetic signal estimators across a range of heritability values.

Estimator	bias			MSE	coverage
	total	$h^2 < 0.5$	$h^2 > 0.5$		
Blomberg's K	-0.400	-0.454	-0.346	0.190	NA
Pagel's $\lambda_{\rm ML}$, MLE	0.050	-0.147	0.310	0.042	0.919
$\lambda_{\scriptscriptstyle m B}$, $eta(1.0, 1.0)$	0.000	-0.009	-0.004	0.020	0.869
$\lambda_{\scriptscriptstyle\rm B}$, $\beta(2.0,2.0)$	0.020	-0.068	0.018	0.017	0.954



Figure 2: Estimator performance of Blombergs K, Pagels λ_{ML} and λ_B on simulated data. The evolution of an infection trait with known heritability ($h^2 = 0.05$ to 0.95, stepsize 0.05) was modeled through 100 simulations of the trait on a fixed tree following the method of Shirreff *et al.* (2013). The box plots show the median values, the three quartiles and the outliers for Blombergs K (yellow), Pagels λ_{ML} (blue) and λ_B (green) estimates of phylogenetic signal. The dashed line in the plot for Blomberg's K indicates estimated phylogenetic signal equal to 1.



Figure 3: Performance of the Bayesian phylogenetic signal estimation under various priors on $\lambda_{\mathbf{B}}$. Various $\beta(\alpha,\beta)$ priors are explored for $\alpha = \beta$. We plot bias (filled black circles) and MSE (crosses) according to the primary axis and coverage (open squares) according to the secondary axis. The dotted horizontal line represents zero bias and MSE.

References

- Alizon, S., von Wyl, V., Stadler, T., Kouyos, R.D., Yerly, S., Hirschel, B., Böni, J., Shah, C., Klimkait, T., Furrer, H., Rauch, A., Vernazza, P.L., Bernasconi, E., Battegay, M., Bürgisser, P., Telenti, A., Günthard, H.F., Bonhoeffer, S. & Swiss HIV Cohort Study (2010) Phylogenetic approach reveals that virus genotype largely determines hiv set-point viral load. *PLoS Pathogens*, 6, e1001123.
- Shirreff, G., Alizon, S., Cori, A., Günthard, H.F., Laeyendecker, O., van Sighem, A., Bezemer, D. & Fraser, C. (2013) How effectively can hiv phylogenies be used to measure heritability? *Evolution, Medicine and Public Health*, **2013**, 209–24.