Adaptive dating and fast proposals: revisiting the phylogenetic relaxed clock model

Jordan Douglas[1,2*], Rong Zhang[1,2], Alexei J. Drummond[1,2,3], Remco Bouckaert[1,2]

1 Centre for Computational Evolution, University of Auckland, Auckland, New Zealand
2 School of Computer Science, University of Auckland, Auckland, New Zealand
3 School of Biological Sciences, University of Auckland, Auckland, New Zealand

* jordan.douglas@auckland.ac.nz

S1 Appendix: Tree operators for rate quantiles

Zhang and Drummond 2020 introduced several tree operators for the *real* parameterisation – including Constant Distance, Simple Distance, and Small Pulley [1]. In this appendix, these three operators are extended to the the *quant* parameterisation. Following the notation presented in the main article, let t_i be the time of node i, let $0 < q_i < 1$ be the rate quantile of node i, and let $r_i = F^{-1}(q_i)$ be the real rate of node i where F^{-1} is the inverse cumulative density function (i-CDF).

Constant Distance

Let $\mathcal{X}$ be a uniformly-at-random sampled internal node on tree $\mathcal{T}$. Let $\mathcal{L}$ and $\mathcal{R}$ be the left and right child of $\mathcal{X}$, respectively, and let $\mathcal{P}$ be the parent of $\mathcal{X}$. Under the *quant* parameterisation, the `ConstantDistance` operator works as follows:

Step 1. Propose a new height for $t_\mathcal{X}$:

$$t_\mathcal{X}' \leftarrow t_\mathcal{X} + s\Sigma \tag{1}$$

where Σ is drawn from a proposal transition distribution (Uniform or Bactrian), and s is a tunable step size. Ensure that $\max\{t_\mathcal{L}, t_\mathcal{R}\} < t_\mathcal{X}' < t_\mathcal{P}$, and if the constraint is broken then reject the proposal.

Step 2. Recalculate $q_\mathcal{X}$ as:

$$\begin{aligned}
q_\mathcal{X}' \leftarrow & F\Big(r_\mathcal{X}'\Big) \\
\leftarrow & F\Big(\frac{t_\mathcal{P} - t_\mathcal{X}}{t_\mathcal{P} - t_\mathcal{X}'} r_X\Big) \\
\leftarrow & F\Big(\frac{t_\mathcal{P} - t_\mathcal{X}}{t_\mathcal{P} - t_\mathcal{X}'} F^{-1}(q_\mathcal{X})\Big).
\end{aligned} \tag{2}$$

This ensures that the genetic distance between $\mathcal{X}$ and P remains constant after the operation by enforcing the constraint:

$$r_{\mathcal{X}}(t_{\mathcal{P}} - t_{\mathcal{X}}) = r_{\mathcal{X}}'(t_{\mathcal{P}} - t_{\mathcal{X}}'). \tag{3}$$

<u>*Step 3*</u>. Similarly, propose new rate quantiles for the two children $\mathcal{C} \in \{\mathcal{L}, \mathcal{R}\}$:

$$\begin{aligned} q_{\mathcal{C}}' \leftarrow & F\Big(r_{\mathcal{C}}'\Big) \\ \leftarrow & F\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{C}}}{t_{\mathcal{X}}' - t_{\mathcal{C}}} \times r_{\mathcal{C}}\Big) \\ \leftarrow & F\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{C}}}{t_{\mathcal{X}}' - t_{\mathcal{C}}} \times F^{-1}(q_{\mathcal{C}})\Big). \end{aligned} \tag{4}$$

Ensure that $0 < q_i' < 1$ for all proposed nodes $i \in \{\mathcal{X}, L, R\}$, and if the constraint is broken then reject the proposal. This constraint can only be broken from numerical issues.

<u>*Step 4*</u>. Finally, in order to calculate the Metropolis-Hastings-Green ratio, return the determinant of the Jacobian matrix:

$$\begin{aligned} J = & \begin{bmatrix} \frac{\partial t_{\mathcal{X}}'}{\partial t_{\mathcal{X}}} & \frac{\partial t_{\mathcal{X}}'}{\partial q_{\mathcal{X}}} & \frac{\partial t_{\mathcal{X}}'}{\partial q_{\mathcal{L}}} & \frac{\partial t_{\mathcal{X}}'}{\partial q_{\mathcal{R}}} \\ \frac{\partial q_{\mathcal{X}}'}{\partial t_{\mathcal{X}}} & \frac{\partial q_{\mathcal{X}}'}{\partial q_{\mathcal{X}}} & \frac{\partial q_{\mathcal{X}}'}{\partial q_{\mathcal{L}}} & \frac{\partial q_{\mathcal{X}}'}{\partial q_{\mathcal{R}}} \\ \frac{\partial q_{\mathcal{L}}'}{\partial t_{\mathcal{X}}} & \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{X}}} & \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} & \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{R}}} \\ \frac{\partial q_{\mathcal{R}}'}{\partial t_{\mathcal{X}}} & \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{X}}} & \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{L}}} & \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}} \end{bmatrix} \\ = & \begin{bmatrix} \frac{\partial t_{\mathcal{X}}'}{\partial t_{\mathcal{X}}} & 0 & 0 & 0 \\ \frac{\partial q_{\mathcal{X}}'}{\partial t_{\mathcal{X}}} & \frac{\partial q_{\mathcal{X}}'}{\partial q_{\mathcal{X}}} & 0 & 0 \\ \frac{\partial q_{\mathcal{L}}'}{\partial t_{\mathcal{X}}} & 0 & \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} & 0 \\ \frac{\partial q_{\mathcal{R}}'}{\partial t_{\mathcal{X}}} & 0 & 0 & \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}} \end{bmatrix}. \end{aligned} \tag{5}$$

As J is triangular, its determinant $|J|$ is equal to the product of diagonal elements:

$$\begin{aligned} \ln|J| = & \ln\{\frac{\partial t_{\mathcal{X}}'}{\partial t_{\mathcal{X}}} \times \frac{\partial q_{\mathcal{X}}'}{\partial q_{\mathcal{X}}} \times \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} \times \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}}\} \\ = & \ln 1 + \ln\ DF\Big(\frac{t_{\mathcal{P}} - t_{\mathcal{X}}}{t_{\mathcal{P}} - t_{\mathcal{X}}'} \times F^{-1}(q_{\mathcal{X}})\Big) + \ln \frac{\partial}{\partial q_{\mathcal{X}}} \frac{t_{\mathcal{P}} - t_{\mathcal{X}}}{t_{\mathcal{P}} - t_{\mathcal{X}}'} F^{-1}\Big(q_{\mathcal{X}}\Big) \\ & + \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}} \times F^{-1}(q_{\mathcal{L}})\Big) + \ln \frac{\partial}{\partial q_{\mathcal{L}}} \frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}} F^{-1}\Big(q_{\mathcal{L}}\Big) \\ & + \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}} \times F^{-1}(q_{\mathcal{R}})\Big) + \ln \frac{\partial}{\partial q_{\mathcal{R}}} \frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}} F^{-1}\Big(q_{\mathcal{R}}\Big) \\ = & \ln\ DF\Big(\frac{t_{\mathcal{P}} - t_{\mathcal{X}}}{t_{\mathcal{P}} - t_{\mathcal{X}}'} \times F^{-1}(q_{\mathcal{X}})\Big) + \ln\ DF^{-1}\Big(q_{\mathcal{X}}\Big) + \ln \frac{t_{\mathcal{P}} - t_{\mathcal{X}}}{t_{\mathcal{P}} - t_{\mathcal{X}}'} \\ & + \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}} \times F^{-1}(q_{\mathcal{L}})\Big) + \ln\ DF^{-1}\Big(q_{\mathcal{L}}\Big) + \ln \frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}} \\ & + \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}} \times F^{-1}(q_{\mathcal{R}})\Big) + \ln\ DF^{-1}\Big(q_{\mathcal{R}}\Big) + \ln \frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}}. \end{aligned} \tag{6}$$

The derivatives DF and DF^{-1} can be computed using numerical approximations. As its final step, the operator returns $\ln |J|$.

Simple Distance

While `ConstantDistance` proposes internal node heights, `SimpleDistance` operates on the root. Let $\mathcal{X}$ be the root node and let $\mathcal{L}$ and $\mathcal{R}$ be its two children.

Step 1. Propose a new height for $t_\mathcal{X}$:

$$t_\mathcal{X}' \leftarrow t_\mathcal{X} + s\Sigma \tag{7}$$

Ensure that $\max\{t_\mathcal{L}, t_\mathcal{R}\} < t_\mathcal{X}'$, and if the constraint is broken then reject the proposal.

Step 2. Propose new rate quantiles for the two children $\mathcal{C} \in \{\mathcal{L}, \mathcal{R}\}$:

$$\begin{aligned} q_\mathcal{C}' \leftarrow & F\Big(r_\mathcal{C}'\Big) \\ \leftarrow & F\Big(\frac{t_\mathcal{X} - t_\mathcal{C}}{t_\mathcal{X}' - t_\mathcal{C}} \times r_\mathcal{C}\Big) \\ \leftarrow & F\Big(\frac{t_\mathcal{X} - t_\mathcal{C}}{t_\mathcal{X}' - t_\mathcal{C}} \times F^{-1}(q_\mathcal{C})\Big). \end{aligned} \tag{8}$$

These proposals ensure that the genetic distance between $\mathcal{X}$ and its children $\mathcal{C}$ remain constant after the operation by enforcing the constraint:

$$r_\mathcal{C}(t_\mathcal{X} - t_\mathcal{C}) = r_\mathcal{C}'(t_\mathcal{X}' - t_\mathcal{C}). \tag{9}$$

Ensure that $0 < q_C' < 1$, and if the constraint is broken then reject the proposal.

Step 3. Finally, in order to calculate the Metropolis-Hastings-Green ratio, return the determinant of the Jacobian matrix:

$$\begin{aligned} J = & \begin{bmatrix} \frac{\partial t_\mathcal{X}'}{\partial t_\mathcal{X}} & \frac{\partial t_\mathcal{X}'}{\partial q_\mathcal{L}} & \frac{\partial t_\mathcal{X}'}{\partial q_\mathcal{R}} \\ \frac{\partial q_\mathcal{L}'}{\partial t_\mathcal{X}} & \frac{\partial q_\mathcal{L}'}{\partial q_\mathcal{L}} & \frac{\partial q_\mathcal{L}'}{\partial q_\mathcal{R}} \\ \frac{\partial q_\mathcal{R}'}{\partial t_\mathcal{X}} & \frac{\partial q_\mathcal{R}'}{\partial q_\mathcal{L}} & \frac{\partial q_\mathcal{R}'}{\partial q_\mathcal{R}} \end{bmatrix} \\ = & \begin{bmatrix} \frac{\partial t_\mathcal{X}'}{\partial t_\mathcal{X}} & 0 & 0 \\ \frac{\partial q_\mathcal{L}'}{\partial t_\mathcal{X}} & \frac{\partial q_\mathcal{L}'}{\partial q_\mathcal{L}} & 0 \\ \frac{\partial q_\mathcal{R}'}{\partial t_\mathcal{X}} & 0 & \frac{\partial q_\mathcal{R}'}{\partial q_\mathcal{R}} \end{bmatrix}. \end{aligned} \tag{10}$$

As J is triangular, its determinant $|J|$ is equal to the product of diagonal elements:

$$
\begin{aligned}
\ln|J| &= \ln\{\frac{\partial t_{\mathcal{X}}'}{\partial t_{\mathcal{X}}} \times \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} \times \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}}\} \\
&= \ln\frac{\partial t_{\mathcal{X}}'}{\partial t_{\mathcal{X}}} + \ln\frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} + \ln\frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}} \\
&= \ln 1 \\
&\quad + \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}} \times F^{-1}(q_{\mathcal{L}})\Big) + \ln\frac{\partial}{\partial q_{\mathcal{L}}}\frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}}F^{-1}\Big(q_{\mathcal{L}}\Big) \\
&\quad + \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}} \times F^{-1}(q_{\mathcal{R}})\Big) + \ln\frac{\partial}{\partial q_{\mathcal{R}}}\frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}}F^{-1}\Big(q_{\mathcal{R}}\Big) \\
&= \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}} \times F^{-1}(q_{\mathcal{L}})\Big) + \ln\ DF^{-1}\Big(q_{\mathcal{L}}\Big) + \ln\frac{t_{\mathcal{X}} - t_{\mathcal{L}}}{t_{\mathcal{X}}' - t_{\mathcal{L}}} \\
&\quad + \ln\ DF\Big(\frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}} \times F^{-1}(q_{\mathcal{R}})\Big) + \ln\ DF^{-1}\Big(q_{\mathcal{R}}\Big) + \ln\frac{t_{\mathcal{X}} - t_{\mathcal{R}}}{t_{\mathcal{X}}' - t_{\mathcal{R}}}. \qquad (11)
\end{aligned}
$$

As its final step, the operator returns $\ln|J|$.

Small Pulley

Just like the previous operator, `SmallPulley` operates on the root. Let $\mathcal{X}$ be the root node and let $\mathcal{L}$ and $\mathcal{R}$ be its two children. However, unlike `SimpleDistance`, this operator alters the two genetic distances $d_{\mathcal{L}} = r_{\mathcal{L}}(t_{\mathcal{X}} - t_{\mathcal{L}}) = F^{-1}(q_{\mathcal{L}})(t_{\mathcal{X}} - t_{\mathcal{L}})$ and $d_{\mathcal{R}} = r_{\mathcal{R}}(t_{\mathcal{X}} - t_{\mathcal{R}}) = F^{-1}(q_{\mathcal{R}})(t_{\mathcal{X}} - t_{\mathcal{R}})$, while conserving their sum $d_{\mathcal{L}} + d_{\mathcal{R}}$.

Step 1. Propose new genetic distances for $d_{\mathcal{L}}$ and $d_{\mathcal{R}}$:

$$d_{\mathcal{L}}' \leftarrow d_{\mathcal{L}} + s\Sigma \qquad (12)$$

$$d_{\mathcal{R}}' \leftarrow d_{\mathcal{R}} - s\Sigma \qquad (13)$$

Ensure that $0 < d_{\mathcal{L}}' < d_{\mathcal{L}} + d_{\mathcal{R}}$, and if the constraint is broken then reject the proposal.

Step 2. Propose new rate quantiles for the two children $\mathcal{L}$ and $\mathcal{R}$:

$$
\begin{aligned}
q_{\mathcal{L}}' &\leftarrow F\big(\frac{d_{\mathcal{L}}'}{t_{\mathcal{X}} - t_{\mathcal{L}}}\big) \\
&\leftarrow F\big(\frac{F^{-1}(q_{\mathcal{L}})(t_{\mathcal{X}} - t_{\mathcal{L}}) + \Sigma}{t_{\mathcal{X}} - t_{\mathcal{L}}}\big) \qquad (14) \\
q_{\mathcal{R}}' &\leftarrow F\big(\frac{d_{\mathcal{R}}'}{t_{\mathcal{X}} - t_{\mathcal{R}}}\big) \\
&\leftarrow F\big(\frac{F^{-1}(q_{\mathcal{R}})(t_{\mathcal{X}} - t_{\mathcal{R}}) - \Sigma}{t_{\mathcal{X}} - t_{\mathcal{R}}}\big). \qquad (15)
\end{aligned}
$$

Step 3. Return the determinant of the Jacobian matrix:

$$
\begin{aligned}
J &= \begin{bmatrix} \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}}, & \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{R}}}, \\ \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{L}}} & \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}} \end{bmatrix} \\
&= \begin{bmatrix} \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} & 0 \\ 0 & \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}} \end{bmatrix}
\end{aligned} \tag{16}
$$

As J is triangular/diagonal, its determinant $|J|$ is equal to the product of diagonal elements:

$$
\begin{aligned}
\ln|J| =& \ln\{\frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} \times \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}}\} \\
=& \ln \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} + \ln \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}} \\
=& \ln\ DF\big(\frac{F^{-1}(q_{\mathcal{L}})(t_{\mathcal{X}} - t_{\mathcal{L}}) + \Sigma}{t_{\mathcal{X}} - t_{\mathcal{L}}}\big) + \ln \frac{\partial q_{\mathcal{L}}'}{\partial q_{\mathcal{L}}} \frac{F^{-1}(q_{\mathcal{L}})(t_{\mathcal{X}} - t_{\mathcal{L}}) + \Sigma}{t_{\mathcal{X}} - t_{\mathcal{L}}} \\
&+ \ln\ DF\big(\frac{F^{-1}(q_{\mathcal{R}})(t_{\mathcal{X}} - t_{\mathcal{R}}) - \Sigma}{t_{\mathcal{X}} - t_{\mathcal{R}}}\big) + \ln \frac{\partial q_{\mathcal{R}}'}{\partial q_{\mathcal{R}}} \frac{F^{-1}(q_{\mathcal{R}})(t_{\mathcal{X}} - t_{\mathcal{R}}) - \Sigma}{t_{\mathcal{X}} - t_{\mathcal{R}}} \\
=& \ln\ DF\big(\frac{F^{-1}(q_{\mathcal{L}})(t_{\mathcal{X}} - t_{\mathcal{L}}) + \Sigma}{t_{\mathcal{X}} - t_{\mathcal{L}}}\big) + \ln\ DF^{-1}(q_{\mathcal{L}}) \\
&+ \ln\ DF\big(\frac{F^{-1}(q_{\mathcal{R}})(t_{\mathcal{X}} - t_{\mathcal{R}}) - \Sigma}{t_{\mathcal{X}} - t_{\mathcal{R}}}\big) + \ln\ DF^{-1}(q_{\mathcal{R}}).
\end{aligned} \tag{17}
$$

Thus, as its final step, the operator returns $\ln|J|$.

References

[1] Zhang R, Drummond A. Improving the performance of Bayesian phylogenetic inference under relaxed clock models. BMC Evolutionary Biology. 2020;20:1–28.