Unrealistic phylogenetic trees may improve phylogenetic footprinting

| Título                        | Unrealistic phylogenetic trees may improve phylogenetic footprinting |
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**Motivation** The computational investigation of DNA binding motifs from binding sites is one of the classic tasks in bioinformatics and a prerequisite for understanding gene regulation as a whole. Due to the development of sequencing technologies and the increasing number of available genomes, approaches based on phylogenetic footprinting become increasingly attractive. Phylogenetic footprinting requires phylogenetic trees with attached substitution probabilities for quantifying the evolution of binding sites, but these trees and substitution probabilities are typically not known and cannot be estimated easily.

**Results** Here, we investigate the influence of phylogenetic trees with different substitution probabilities on the classification performance of phylogenetic footprinting using synthetic and real data. For synthetic data we find that the classification performance is highest when the substitution probability used for phylogenetic footprinting is similar to that used for data generation. For real data, however, we typically find that the classification performance of phylogenetic footprinting surprisingly increases with increasing substitution probabilities and is often highest for unrealistically high substitution probabilities close to one. This finding suggests that choosing realistic model assumptions might not always yield optimal predictions in general and that choosing unrealistically high substitution probabilities close to one might actually improve the classification performance of phylogenetic footprinting.

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