March 2nd, 2017

Department of Ecology and Evolutionary Biology

University of Tennessee

569 Dabney Hall

Knoxville, TN 37996-1610

Dear Dr. Near

Editor-in-Chief, *Systematic Biology*:

We are excited to submit our paper entitled “Population Genetics Based Phylogenetics Under Stabilizing Selection for an Optimal Amino Acid Sequence: A Nested Modeling Approach” for your consideration as a full research article in *Systematic Biology*.

In our manuscript, we present a novel phylogenetic modelling framework that is heavily steeped in principles of population genetics. The new set of models, which we collectively call SelAC models, provides biological realism when modelling the evolution of protein-coding DNA under the assumption of stabilizing selection for a gene specific optimal amino acid sequence. We show that when applied to the several yeast genomes our model not only fit phylogenetic data substantially better than popular models, but, when subjected to tests of model adequacy, also produce data sets that closely resemble the empirical data. On the whole, this work illustrates the strong potential for more accurate inference of phylogenetic trees and branch lengths, as well as the it demonstrating that there remains substantially more information in the coding sequences used for phylogenetic analysis than other methods acknowledge.

David Posada may be the most appropriate Associate Editor for this paper. Laura Kubatko or Mark Holder would also be good choices. We would suggest the following as possible reviewers: Drs. Rori Rohlfs or Scott Roy (San Francisco State), Dr. Rasmus Nielsen (U.C. Berkeley), and Dr. Ziheng Yang (Imperial College).

Thank you very much for your consideration, and we look forward to hearing from you.

Sincerely,

Michael Gilchrist

Jeremy M. Beaulieu

Brian O'Meara