Dear PLoS Computational Biology Editorial Board,

Please find attached the manuscript “Component response rate variation drives stability in large complex systems”, which I hope you will consider for publication as a Research Article.

Complex systems theory has widespread applications across the biological sciences. Discovering universal principles that underpin stability in complex systems is therefore of broad interest and importance. In 1972, Robert May first showed that the probability of a system being stable decreases as its complexity increases, and May identified a threshold value of complexity above which the probability of stability is negligible. In the attached manuscript, I investigate a yet unconsidered, but likely ubiquitous, property of all complex biological systems. I show that when individual components of a complex system respond to system perturbation at different rates, the potential for stability is increased well above May's threshold. This result is surprising because variation in component response rate necessarily increases variation in the strength of interactions among system components, which by itself is destabilising. Additionally, using a genetic algorithm, I show that the probability of system stability can be increased up to four orders of magnitude for highly complex systems given a targetted manipulation of component response rates. This result shows that stability of complex systems can potentially be facilitated solely by manipulating the response rates of individual system components.

Consistent with the scope of PLoS Computational Biology, my manuscript applies computational methods to a key question in theoretical biology, and the insights of my manuscript are significant for understanding complex biological systems across all scales (e.g., gene-regulatory, biochemical, neurological, ecological, and social-ecological networks). This manuscript drives future research forward by predicting how variation in the dynamics of individual system components affects stability at the broader scale of a complex biological system. It will inspire future theoretical and empirical studies to consider such variation when investigating complex biological systems.

This manuscript includes an abstract of 124 words and main text of 2682 words (excluding figure legends, acknowledgements, and references). It also includes 4 figures, 0 tables, and 23 references. Supporting results are included in Supplementary Information. I certify that this manuscript is original work and not under review at any other journal or book; a pre-print version of this manuscript is available on arXiv (http://arxiv.org/abs/1806.01029).

Sincerely,

A. Bradley Duthie
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