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Estimating Ribozyme Kinetics from Analysis of *in Vitro* Selection

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Ribozymes and other biological reagents generated through in vitro selection have become important tools in medicine and the life sciences; but as selection methodology advances, our understanding of the evolutionary dynamics involved lags far behind. Selections often fail, require additional rounds to converge on a candidate sequence, or simply behave erratically. Existing theory does little to predict such difficulties or offer solutions, relying on distribution parameters and assumptions never tested in a selection environment. By combining selection theory with observations of real-world evolving molecular populations, it should be possible a mathematical description of the actual dynamics involved in a ribozyme selection. Here, we demonstrate several statistical techniques and that show promise in analyzing the ideality, scope of evolution, and fitness landscape present in a selection for a triphosphorylation ribozyme. Using new methodology, we find evidence for novel models of stochastic effects during in vitro selection, as well as of an initial distribution of chemical activity in random molecular space. The magnitude of such distributions is consistent with existing difficulties in selection design, suggesting that stochastic effects play a significant role in complicating selections, and suggesting selection parameters for optimizing future similar selection. Our results also show some correlation between estimated fitness and measured ribozyme activity, suggesting a viable alternative to the heuristic methods typically used to interpret high-throughput selection data, with further significance to many types of in vivo selection.