Virtual Screening: We hold these truths to be self-evident.

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When in the Course of biomolecular binding events, it becomes necessary for one species to displace the molecules of solvent which have occupied the site of another, and to assume a low-energy bound conformation in this site, a decent respect to the Laws of Chemistry and Physics requires enumeration of the Forces which impel them to associate. We hold these truths to be self-evident, that all biomolecular binding is concerted, that Binding Free Energy is endowed by the Creator with certain unalienable Properties, that among these are Hydrogen Bonds, Coulombic Forces, London Forces and the pursuit of Entropy. --That to calculate these properties, Scoring Functions have been created, deriving their usefulness from correlations with experiment, --That whenever any Form of Scoring Function becomes inaccurate to these ends, it is the Right of the User to alter or to dismiss it, and to institute a new Scoring Function, laying its foundation on such principles of and organizing its algorithms in such form, as to him seem most likely to effect his Predictions and Job Security. Prudence, indeed will dictate that Scoring Functions long established should not be changed for light and transient causes; and accordingly all experience hath shewn, that Users are more disposed to suffer, while inaccuracies are sufferable, than to right the predictions by abolishing the functional forms to which they are accustomed. But when a long train of false positives and false negatives, pursuing invariably the same Lead Compounds evinces a design to reduce the productive hits in Assays, it is their right, it is their duty, to throw off such Scoring Functions, and to obtain new Computational Tools for their future security. The results from conventional Virtual Screening are results of repeated missed opportunities and failures, all having in direct object the establishment of an unsupported paradigm for Drug Discovery. To prove this, let Facts be submitted to a candid world.

Virtual Screening does not, in usual cases, include the effects of solvent Molecules within the active Site that are in practice supporting the binding.

Virtual Screening has affected to ignore the Ionization States of Functional Groups from both the Protein and Ligand; if accounted for, these effects may be quite substantial.

Virtual Screening has deemed it reasonable to calculate Hydrophobic Interactions with Algorithms both overly simple and unsubstantiated.

Virtual Screening provides no redress for the phenomenon of Entropy, that which most assuredly is a vital and inalienable component of Binding Free Energy.