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The human intellect is the source of its own problems: Ligands of fancy

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Fundamental scientific epistemology requires that a strong claim is supported by strong and convincing proof. As an example, the proposition of a ligand bound to a target protein in a precise conformation and pose presents a very strong claim, and confirming (positive omit difference) electron density will provide the correspondingly strong experimental evidence. A survey of ligand structure models has revealed that in an unexpectedly large number of ligand structures, the required electron density is not present or does not sufficiently support the proposed ligand pose. Upon detailed analysis, it emerged that the origin of such fanciful models lies in the simple neglect of the most basic fundamentals of scientific epistemology, which appears not to be formally taught in some science curricula. A brief introduction into the importance of evidence and its balance with prior expectations in a Bayesian system of empirical reasoning on hand of protein-ligand complex structure examples is therefore provided for young and aspiring scientists. It particular affects early career researchers when fictitious models intended to support bio-medically relevant hypotheses delay the progress of science by unsupported claims: grants cannot be funded when they contradict models believed to be true, and valuable taxpayer money can be squandered trying to pursue science based on false premises. Poor and at minimum self-deceptive work threatens to become systemic and accepted over the course of time unless young researches take full ownership and responsibility for their exciting and important work and resist any postmodern relativism threatening to erode the credibility of their profession.

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