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Ligand Legends

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Biomolecular crystallography is based on a solid foundation of rich experimental data combined with an extensive body of prior knowledge. As a prime example for modern experimental science, it relies on evidence-based reasoning assessing the plausibility of its models based on prior knowledge, while at the same time constantly delivering some of the most novel and exciting results originating from new experimental evidence. Because of the solid underlying physical principles and its mathematical rigor - at least up to the point of electron density generation - crystallography as a mature science should be almost fool-proof - were it not for the human element. The human element enters at the stage of electron density interpretation, where sparseness of evidence can become inversely proportional to the increasing liberties taken in divining poorly supported models, often associated with extraordinarily strong claims. The temptation of projecting strong preconceptions into weak electron density must be balanced by an equally strong demand for irrefutable proof positive in form of minimally biased, clear electron density. There is good reason why scientific epistemology requires proof positive and falsifiability to validate a claim or hypothesis: Absolute absence of evidence in form of zero electron density can never be proven - there will invariably be noise in the electron density reconstruction, beckoning to harbor fragments of any desirable model. Safeguards against overinterpretation in statistical and epistemological terms within a Bayesian framework of reasoning will be discussed.

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