"Predictions and experiments in structure determination".

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Accurate protein structure prediction from sequence has been a game-changer and not just in the structural biology community: researchers in every branch of the life sciences are consulting such models1. The current success of artificial intelligence on a long-standing quest, showcases a power for harnessing prior knowledge that will go deeper in the next years as we learn how to steer it into particular questions.

While AlphaFold predictions are useful hypotheses about protein structures, experimental information remains essential for creating an accurate model2. Predictions have been effectively incorporated in our structural determination methods3. The new balance demands a redefinition of how we integrate prior knowledge in experiment interpretation4 and verification of the information gained beyond the starting model.

Conversely, conditioning predictions with experimental knowledge opens new opportunities to gain a dynamic view by using experimental structures to establish the background of a prediction or impose boundary conditions.

The broad scale search for structural and genomic information preceding a prediction simultaneously retrieves knowledge on all possible contacts and states a sequence may fulfill in time or under different conditions. Our method systematically deconvolves the signal from multiple states. VAIRO informs AF predictions with experimental structures, setting boundary conditions to target particular states within a dynamic or recover weak interactions.

References
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