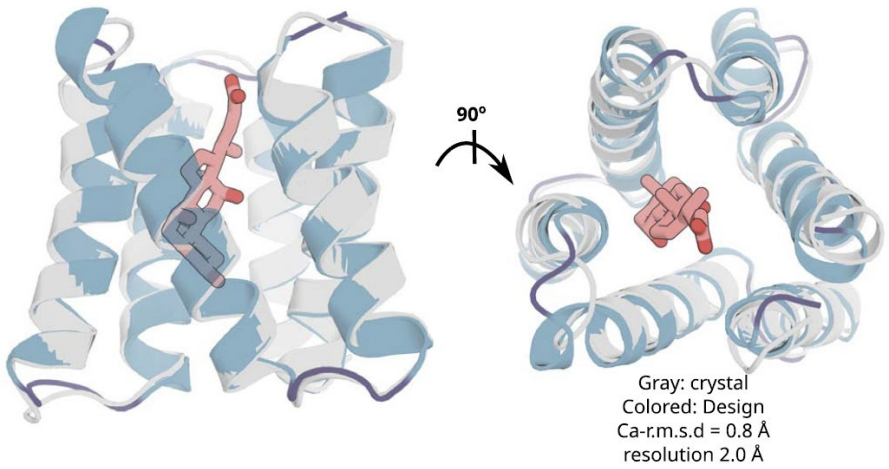
Small-Molecule Binding and Sensing through AI-Driven Protein Design

17-ID-1
AMX



X-ray crystallography demonstrates accuracy of design approach: The crystal structures of the experimental protein (gray) closely match their design models (colored).

An L, Said M, Tran L, Majumder S, Goreshnik I, Lee GR, Juergens D, Dauparas J, Anishchenko I, Coventry B, Bera AK, Kang A, Levine PM, Alvarez V, Pillai A, Norn C, Feldman D, Zorine D, Hicks DR, Li X, Sanchez MG, Vafeados DK, Salveson PJ, Vorobieva AA, Baker D. Binding and sensing diverse small molecules using shape-complementary pseudocycles. *Science*. 2024 Jul 19;385(6706):276-282.

Work was performed in part at NSLS-II

Scientific Achievement

Researchers used deep-learning tools to design proteins capable of binding and sensing diverse small molecules with high precision.

Significance and Impact

This breakthrough enables the creation of novel diagnostic tools and demonstrates the potential of AI-driven approaches to expand the boundaries of protein design.

Research Details

- Deep learning AI software tools were used to design complementary models of uniquely structured proteins.
- Target molecules included challenging compounds like methotrexate, thyroxine, and a de novo cyclic tetrapeptide.
- Designs were validated using X-ray crystallography at the NSLS-II AMX beamline.