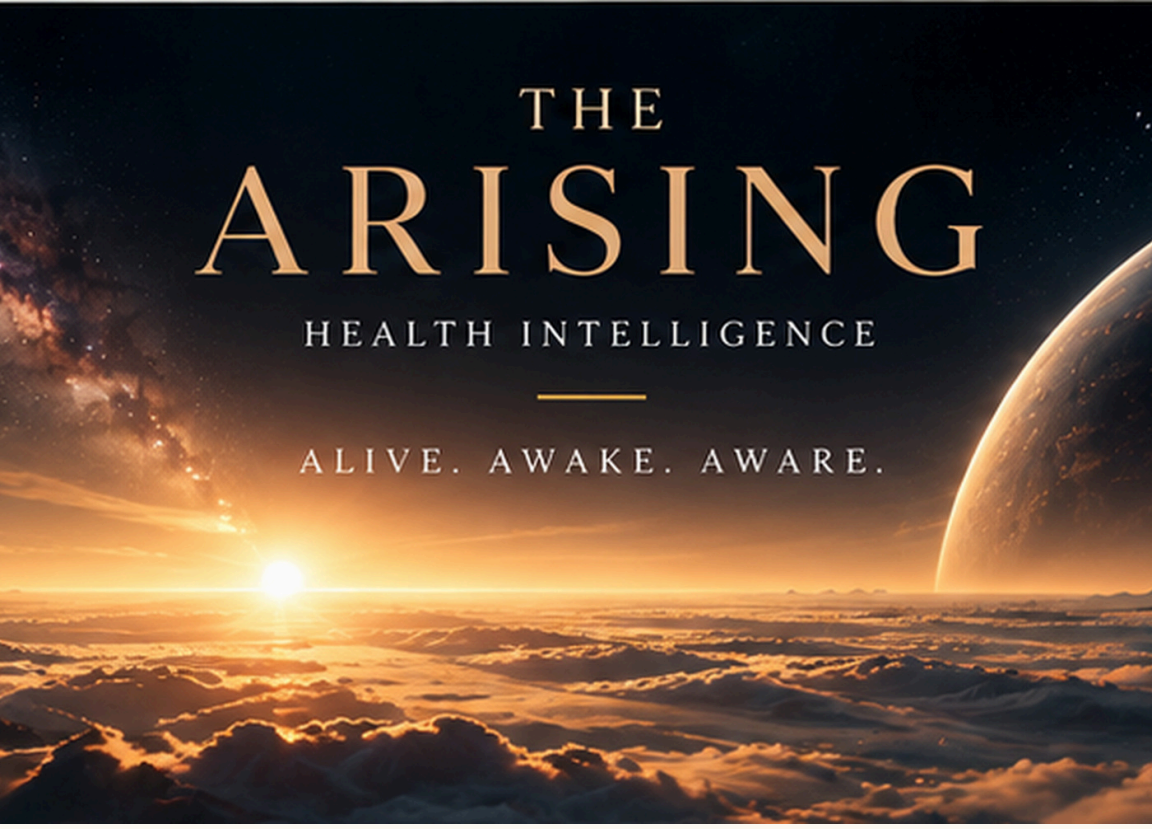


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Molecules We Could Not Previously Make

AI-designed proteins and the experimental work that turns a digital proposal into biology.

JOHN GRIFFIN, MD

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A design is a proposed experiment

A protein is more than a striking folded shape. Its interactions, stability, manufacture, delivery, and behavior in a biological environment determine whether it can do useful work.

AI design tools can widen the set of candidates researchers can consider. The scientific value comes when those candidates are made and tested, and when both successes and failures improve the next round of design.

What RFdiffusion demonstrated

The 2023 RFdiffusion paper described a generative approach to protein backbones and tested a range of designed assemblies, binders, and other structures experimentally. A later study extended related methods to binders for flexible helical peptide targets, including demonstrations relevant to detection and biosensing. [1,2]

These are achievements in protein design and experimental validation. A binder that behaves as intended in an assay has not yet demonstrated therapeutic benefit, acceptable human toxicity, or reliable delivery to a target tissue.

The difficult steps remain visible

A candidate may bind tightly and still be unsuitable as a medicine. It may be unstable, difficult to manufacture, poorly distributed, or provoke an unwanted immune response. Those possibilities are reasons to test, not predictions that a particular design will fail.

The distinction between prediction and design also matters. Predicting a structure from a sequence and proposing a new molecule to meet a specification are related tasks with different success criteria.

The most useful acceleration

A faster design cycle could help researchers spend experiments on more informative candidates. That is a plausible implication, and its practical value should be measured in the relevant workflow.

For a reader following a new claim, useful questions include how many designs were tested, how candidates were selected, what counted as success, and whether comparisons used a fair baseline. Reporting only the best-looking example can conceal the performance of the process.

This frontier is compelling because it expands what can be attempted. Its lasting value will come from molecules that work reproducibly and from a clearer understanding of why they work. The laboratory remains part of the intelligence of the system.

SOURCES & READING SCOPE

Keep the claim beside its evidence

1. Joseph L Watson, David Juergens, Nathaniel R Bennett, et al. De novo design of protein structure and function with RFdiffusion. Nature. 2023 Aug;620(7976):1089-1100. doi:10.1038/s41586-023-06415-8. PMID:37433327. Open source →

2. Susana Vázquez Torres, Philip J Y Leung, Preetham Venkatesh, et al. De novo design of high-affinity binders of bioactive helical peptides. Nature. 2024 Feb;626(7998):435-442. doi:10.1038/s41586-023-06953-1. PMID:38109936. Open source →

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