

Perspex Biotech

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# Protein engineering with roPROTix: an AI-powered platform for drug discovery

Perspex Biotech's roPROTix platform combines artificial intelligence, robotics, and wet biology in a closed-loop feedback system for the discovery of next-generation multi-targeting biological therapeutics.

The challenge of treating complex, multifactorial diseases like cancer and chronic inflammatory conditions with mono-specific therapies, including monoclonal antibodies (mAbs), has raised interest in multi-specific biological therapies that combine the functional activities of two or more mAbs into a single biological entity. Yet to date, the development of multi-targeting biological therapies has been expensive and time consuming—with candidates showing a high rate of attrition.

Perspex, a new biotech headquartered in Frankfurt, Germany, aims to turn this around. The company is developing the roPROTix platform for the rapid design and synthesis of next-generation multi-targeting agents with a higher likelihood of advancing through the pipeline to clinical trials.

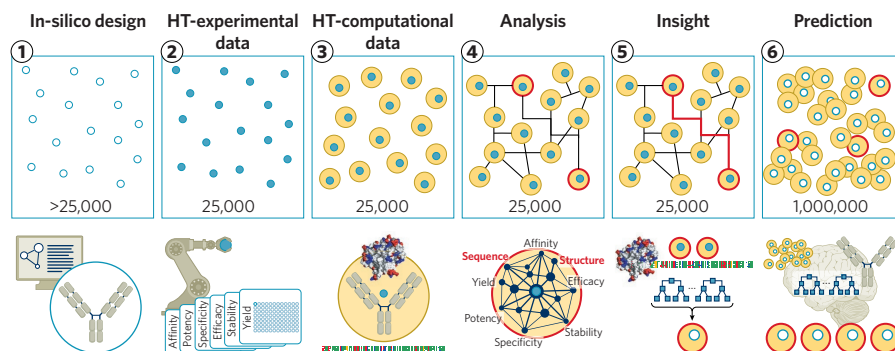
roPROTix utilizes validated technologies for end-to-end automation of protein-engineering processes pioneered by Perspex's co-founder and CSO, Joerg Birkenfeld<sup>1</sup>, and outputs data on the biophysical and functional characteristics of tens of thousands of synthesized multi-targeting agents simultaneously. The physical production and analysis stages of roPROTix are in turn connected in a closed loop to artificial intelligence (AI) that uses these data to uncover design principles for creating multi-specific biologics with higher efficacy and improved developability thanks to superior biophysical properties.

A key challenge to using AI for developing multi-specific agents is a lack of appropriate data to train systems. Although the biophysical and functional properties of multi-specific agents are interrelated and influence each other in multiple dimensions, standard approaches to optimizing them tend to do so serially, one at a time—creating one-dimensional datasets, long development times, and frequent 'optimization dead-ends'.

## The roPROTix advantage

roPROTix, by contrast, analyzes multiple properties simultaneously, producing unique multi-dimensional datasets that fill the current data gaps for training AI systems to identify principles for designing multi-specific drugs with high efficacy, good biophysical features, and a higher likelihood of success. "With its unprecedented data-generation capabilities, I am convinced that Perspex will be at the forefront of AI-based innovation in the area of next-generation multi-specific antibody therapeutics design and development", said Hartmut Michel, Nobel laureate and Perspex scientific advisor.

roPROTix begins with the format- or modality-agnostic in-silico design of multi-specific biological drug entities, which can create not only



**Fig. 1 | The roPROTix process.** Multi-targeting molecules are designed in a format-agnostic manner (1), and then produced in mammalian hosts and analyzed in multiple dimensions (2), providing data on molecules that are further enriched with in-silico data (3). Deep analytics identifies variants with favorable developability properties (4), and their structural and sequence features build AI models that can predict the developability of in-silico-designed molecules (5), as well as screening large in-silico-design spaces or being used to design molecules with favorable drug-like properties de novo (6). HT, high throughput.

multi-specific antibodies but also any other kind of multi-specific protein therapeutic. In roPROTix, the output of the in-silico 'digital design' stage is connected to the physical wet-lab stages of cloning, expression, and analysis in an automated end-to-end process, with all multidimensional experimental and metadata captured in a gapless fashion. As such, roPROTix sits at the intersection of three big trends: the move towards multi-specific drugs, flexible biotechnology platforms, and AI/machine learning (ML)-powered biological drug design.

With roPROTix, up to 25,000 individual molecules of any kind—mono-, bi-, tri-, tetra- or penta-specific—can be produced in a parallelized process. Each molecule is expressed in its soluble drug-product format in an isolated mini-bioreactor-like compartment, which allows for the unbiased determination of multiple functional and biophysical properties—such as yield, potency, stability, and specificity—for each molecular design. And unlike other approaches such as display-based optimization, which enrich only positive variants, roPROTix preserves data on all variants, including those that perform poorly, providing information on what works and what doesn't (Fig. 1).

## Translating the data

The huge sets of contextualized, multidimensional experimental data produced on both positive and negative variants are collated in machine-readable form and fed back to AI models to improve in-silico design. Crucially, the flexibility of roPROTix means that experimental designs can be adapted to generate the specific data required to improve AI models.

The experimental data are augmented by a wealth of in-silico data that, when combined, are used to identify sequence-structure-activity (SSA) relationships—which are the design principles of the multi-specific biological drug-entity of interest. These SSA/design principles can then be used in the short term to train AI for enhanced in-silico screening, and in the longer term to create a solid basis for the de-novo design of multi-specific agents. And as the roPROTix process emulates the final industrial drug-production process, identified candidates are de-risked for progression into large-scale production and through development to commercial manufacturing.

Perspex is currently focused on multi-specific antibodies and aims to develop a portfolio of internal and partnered oncology programs based upon novel combinations of targets with strong clinical evidence. Looking ahead, Perspex's vision is to decipher the design principles of next-generation multi-targeting biological drugs to reduce attrition and development costs and make them more affordable. The company welcomes discussions with investors or partners about the game-changing potential of roPROTix.

1. Furtmann, N. et al. *mAbs* **13**, 1955433 (2021).

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