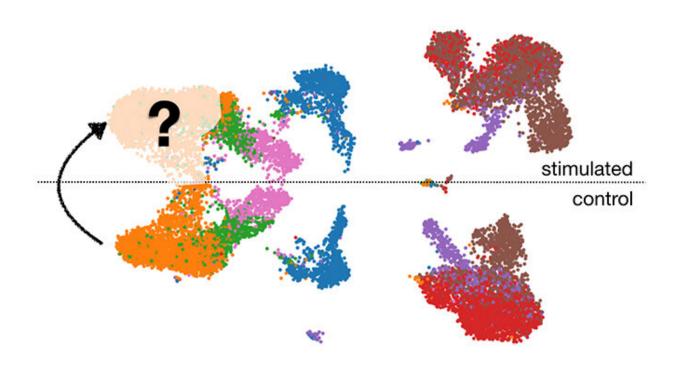


AI-powered tool predicts cell behaviors during disease and treatment

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Predicting cellular behavior in silico: Trained on data that capture stimulation effects for a set of cell types, scGen can be used to model cellular responses in a new cell type. Credit: Helmholtz Zentrum München



Large-scale atlases of organs in a healthy state are soon going to be available, in particular, the Human Cell Atlas. This is a significant step in better understanding cells, tissues and organs in healthy state and provides a reference when diagnosing, monitoring and treating disease. However, due to the sheer number of possible combinations of treatment and disease conditions, expanding these data to characterize disease and disease treatment in traditional life science laboratories is labor-intensive and costly, and therefore not scalable.

Accurately modeling cellular response to perturbations (e.g., disease, compounds, genetic interventions) is a central goal of computational biology. Although models based on statistical and mechanistic approaches exist, no machine-learning-based solution viable for unobserved high-dimensional phenomena has yet been available. In addition, scGen is the first tool that predicts cellular response out-of-sample. This means that scGen, if trained on data that capture the effect of perturbations for a given system, is able to make reliable predictions for a different system. "For the first time, we have the opportunity to use data generated in one model system such as mouse and use the data to predict disease or therapy response in human patients," said Mohammad Lotfollahi, Ph.D. student (Helmholtz Zentrum München and Technische Universität München).

scGen is a generative deep learning model that leverages ideas from image, sequence and language processing, and, for the first time, applies these ideas to model the behavior of a cell in silico. The next step for the team concerns the improving scGen to a fully data-driven formulation, increasing its predictive power to enable the study of combinations of perturbations. "We can now start optimizing scGen to answer more and more complex questions about diseases," said Alex Wolf, Team Leader, and Fabian Theis, Director of the Institute of Computational Biology and Chair of Mathematical Modeling of Biological Systems at Technische Universität München.



More information: scGen predicts single-cell perturbation responses, *Nature Methods* (2019). DOI: 10.1038/s41592-019-0494-8

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