

Clear sight in the data fog with PAGA

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PAGA based embedding of the developmental trajectories in the Zebrafish embryo, colored by timepoint. Credit: Original data from Wagner et al., Science (2018)

Experimental molecular assays with single-cell resolution generate big and complex data. Researchers at Helmholtz Zentrum München and the Technical University of Munich are now presenting their computer

algorithm PAGA. They create data-driven, easily interpretable maps that reveal cellular processes and fates in complex contexts. Their paper has been published in *Genome Biology*.

The fate of individual [cells](#) in the body is relevant in many ways. Researchers want to study developmental processes and understand how diseases progress. "Experiments generate [large data sets](#), which is to say [big data](#)," explains Professor Fabian Theis, Director of the Institute of Computational Biology (ICB) at Helmholtz Zentrum München and professor of Mathematical Modelling of Biological Systems at the Technical University of Munich (TUM). Researchers gather information not only about cells per se, but also about their interactions with other cells and other tissue types. "Previously, however, it was not possible to model complex processes at the [cellular level](#) in a clear and comprehensible manner."

PAGA interprets big data

So far, researchers have taken two approaches to data analysis. Either they searched for cells with similar properties and grouped them (clustering), or they described the timing of cells along their developmental pathways (trajectory inference). "If you look at the data through these very different lenses, divergent and unclear interpretations inevitably arise," adds Alex Wolf, who until recently headed a machine learning team at the ICB. "PAGA does everything that clustering and trajectory inference can do in a single analysis, with a single method and with a single consistent modeling approach." Depending on the desired resolution, the tool groups cells by type (such as skin cells) and biological state (such as cells in undergoing mitosis) and reveals transitions between cell types and states.

Use in research

In recent months, several articles have been published that show the possibilities PAGA opens up. Mireya Plass of the Max Delbrück Center of Molecular Medicine within the Helmholtz Association together with Wolf and colleagues reconstructed the first cellular lineage tree of an adult animal – an achievement the journal *Science* hailed as one of the foremost scientific breakthroughs of 2018. Recently, a team headed by Blanca Pijuan-Sala of Cambridge University used PAGA to reconstruct the developmental processes of a mouse embryo. Other papers show that PAGA delivers important results in a clinical context. Using PAGA to determine the lineages of intestinal cells, researchers at the Broad Institute of MIT and Harvard gained an understanding of the different cellular contributions to chronic inflammatory bowel disease. This also sees great future potential in the tool: "Basically, any biological phenomenon that can be attributed to a cellular process can be analyzed with PAGA as soon as the data are available."

More information: PAGA: graph abstraction reconciles clustering with trajectory inference through a topology preserving map of single cells, *Genome Biology*. [DOI: 10.1186/s13059-019-1663-x](https://doi.org/10.1186/s13059-019-1663-x)

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