New interactive technology makes rare cell types visible

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Researchers from the Leiden University Medical Center (LUMC) and the Delft University of Technology (TU Delft) have presented an interactive technique in the scientific journal *Nature Communications* for the identification of rare cell types in large samples. Professor Frits Koning of LUMC says, "You can find a needle in a haystack."

In order to learn about how certain diseases occur, researchers search for precise information in huge amounts of data. Since 2013, LUMC has used CyTOF, a machine that can characterise millions of cells simultaneously in such samples as intestinal mucous or blood. CyTOF does this by measuring the presence per cell of approximately 40 proteins on the cell wall. Using the new method developed by LUMC and TU Delft, researchers can now study this data in minute detail.

"This kind of sample contains hundreds of different cell types," explains Vincent van Unen, LUMC researcher at the department of Immunohematology and Blood Transfusion (IHB). "There were already methods available to analyse the CyTOF data, but these either gave a global picture of all cells, or a detailed picture of a random group of cells, say about 20 percent. But the most interesting cell types in a tissue sample, cell types that are related to being sick or healthy, are often scarce and you miss them if you only study a group of cells in detail.

Overview

The new analysis technique solves this problem. The system first produces a two-dimensional image in which the cells from the tissue sample are grouped according to their underlying similarities. The cells are not shown individually—doing so would result in an cluttered mass of dots. Instead, they are shown as "landmarks," small areas that represent cells similar to each other. "This overview leaves out the detail, but all available information is used to compute the landmarks," says Nicola Pezzotti, doctoral candidate at TU Delft in Dr. Anna Vilanova's Computer Graphics and Visualization group.

The user can then zoom in on a group of cells of choice until individual cells with the relevant markers are visible. Pezzotti says, "You can compare it to Google Earth, where you begin with the whole Earth and can then zoom right in to your own street." This hierarchical visual methodology, Cytosplore^{+HSNE}, works easily, fast and well. "The landmarks represent known cell groups, such as certain T-cells and B-cells in the immune system," says Thomas Höllt, researcher at LUMC and TU Delft who helped develop the methodology.

"By zooming in, it's possible to find rare cell types which are either missing or indeed present in a particular disease such as the chronic bowel disorder, Crohn's disease. That provides us with leads in the understanding of that disease, its diagnosis and targeted treatment."

The article, "Visual analysis of mass cytometry data by hierarchical stochastic neighbor embedding reveals rare cell types", appeared on 23 November in *Nature Communications*.

More information: Vincent van Unen et al, Visual analysis of mass cytometry data by hierarchical stochastic neighbour embedding reveals rare cell types, *Nature Communications* (2017). DOI: 10.1038/s41467-017-01689-9

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