Nine and 60 ways of particle tracking

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A contest for the best technique of intracellular particle tracking (simultaneous tracking of the motions of hundreds and thousands of intracellular organelles, virions and even individual molecules), that is an important issue in cellular biology and has applications in search for appropriate medicines against certain diseases (including Parkinson's and Alzheimer's diseases), has found no undeniable winner. Techniques proposed by all the participants, including the Lomonosov Moscow State University professor Yannis Kalaidzidis, find their own ways for solving the problem.

The article published in Nature Methods describes not a scientific invention or discovery but the results of a contest of scientific techniques. The task was to find an original solution for a certain scientific problem, and as many as 14 groups from all over the world have taken part. Participants are co-authors of this article, while its leading authors are the organizers. Paper preparation took more than a year; it was accepted in December 2013. The problem was formulated in May 2012 in Barcelona during the IEEE International Symposium on Biomedical Imaging (ISBI'12).

"In live cell imaging, there is an incompletely solved problem of simultaneous tracking of hundreds to thousands of intra-cellular organelles, vesicles, virions and individual fluorescent molecules," explains contestant Yannis Kalaidzidis, professor of the Faculty of Bioengineering and Bioinformatics, MSU and research scientist at Max Planck Institute of Molecular Cell Biology and Genetics, Dresden.

Inside the cells, there are numerous vesicles (small intracellular formations, sort of membrane-protected containers inside which nutrients and signaling molecules are stored and transported; viruses and mycobacteria also hijack them to penetrate the cell) responsible for intracellular transport, and disorders of this vesicular transport may cause a vast variety of diseases. Apart from metabolic failures, these include neurodegenerative diseases such as Alzheimer's and Parkinson's diseases and many senile genetic disorders.

In order to trace this transport, vesicles are marked and imaged by time-lapse microscopy. Previously, tracking was performed by manual connection of vesicles on sequential frames, but today, since hundreds and thousands rather than tens of objects are tracked, manual tracking becomes problematic. Such an extensive study requires computer-based analysis. There are number of numerical algorithms developed for tracking and practically every research group uses its own. To compare the efficiencies of different methods, organizers used an artificially generated time series of images for which the participants had to track all the particles. Reconstructed particle trajectories were then compared to the real trajectories used during the simulations.

The contest actually ended with no single winner. The problem was equally well resolved by different techniques, meaning that, as in Kipling's verse, "There are nine and sixty ways of constructing tribal lays, And every single one of them is right!" To be more precise, in this particular case, every single one is equally right.

According to Kalaidzidis, who featured the contest during his program "MotionTracking," the negative result of the competition was predetermined by the the inadequately posed problem and its complexity. The drawback of the problem formulation, which should be corrected in future contests, was the over-simplification of the test images, making the problem solvable for algorithms that may actually

fail when confronted with real data. At the same time, organizers note that the inability to track particles without errors even in such simplified image series means the problem remains unsolved and requires more profound analysis.

"This simplified approach," says Kalaidzidis, "underestimates the influence of some problems present in applied quantitative microscopy, and may thus be biased toward algorithms designed specifically for the contest."

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