Nature Reviews Materials | Published online 27 Feb 2018; doi:10.1038/natrevmats.2018.11

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OPTOFLUIDICS

You never hop alone

The kinetic motion of dielectric objects can be changed by applying light, making it possible to use optical potential energy landscapes to arrange, guide, deflect or trap particles and cells in distinct potential energy wells. How light causes single particles to hop from well to well along the energy landscape is relatively well understood, but how multiple particles behave and how particle–particle interactions change the hopping dynamics remain elusive.

Writing in *Nature Communications*, Aiqun Liu, Chengwei Qiu and colleagues now report the mechanisms of multi-particle hopping within microfluidic channels and demonstrate how such interactions can be used for the determination of the binding efficiency of antibodies to single bacterial cells.

The researchers have developed an optofluidic chip, which enables them to control both the optical and hydrodynamic forces that drive particle hopping between potential energy wells. The optical forces in the fluid create a discrete optical interference pattern, featuring an array of hotspots in which particles and cells can be trapped. "By delicately balancing optical and hydrodynamic forces, a 2D closed-loop particle hopping trajectory can be created, which generates a platform to manipulate the kinetics and thus, the hopping of multiple microparticles in the microfluidic system," explain Qiu and Liu. "Using this setup, we identified three distinct hopping mechanisms, that is, particle bypassing, collision and aggregation, just like in the game snooker."

These particle–particle interactions substantially impact the residence time of the particles in specific wells and determine if particles hop together to the next well. This hopping behaviour can be mathematically modelled and thereby exploited for the quantitative measurement of the interaction between cells and antibodies.

When a fluid that contains bacteria is injected into the microfluidic device, individual bacterial cells can be trapped in the hotspots of the microfluidic channel through the control of the light intensity and the fluid flow. Biotin-labelled antibodies that specifically recognize and bind to the bacteria can then be detected by the binding of streptavidin-coated silica microparticles owing to the strong biotin–streptavidin interaction. Once bound together, the cell, the antibody and the particle hop to the next hotspot; however, when the antibody does not recognize the bacterium and, therefore, does not bind, the particle moves on and the bacterial cell remains trapped. This behaviour can then be quantified by applying the mathematical model of multi-particle hopping, and thus, the specific binding efficiency between the antibody and one individual cell can be calculated.

"This method enables us to screen biological binding agents and to evaluate the binding affinity and specificity at a single-cell level," say Qiu and Liu. "Thereby, we can greatly reduce the sample volume and time required for diagnostic applications, as is usually required for standard methods, such as ELISA (enzyme-linked immunosorbent assay) or FACS (fluorescence-activated cell sorting), which measure bulk interactions rather than single cell behaviour."

However, assessing the binding efficiency in the microfluidic chip still relies on the manual counting of trapped bacteria and microparticle–bacterium complexes. Thus, the researchers are currently developing an image processing module for the automatic tracking and counting of bacteria to improve the efficiency and reproducibility of their method. They are further testing the optofluidic chip for the detection, screening and measurement of viruses, as well as for the compatibility with clinical samples.

Christine-Maria Horejs

> "This method enables us to screen biological binding agents and to evaluate the binding affinity and specificity at a single-cell level"

ORIGINAL ARTICLE Shi, Y. Z. et al. Sculpting nanoparticle dynamics for single-bacteria-level screening and direct-binding efficiency measurement. *Nat. Commun.* https://doi.org/10.1038/s41467-018-03156-5 (2018)