Tracking aging and environmental adaptation of single-cells with microfluidics, timelapse microscopy and deep-learning

T. Aspert[1,2,3*], G. Charvin[1,2,3]

[1]Institut de Génétique et de Biologie Moléculaire et Cellulaire
[2]Institut de Génétique Moléculaire Génomique et Microbiologie
[3]Université de Strasbourg
*theo.aspert@gmail.com

Microorganisms such as budding yeast are a powerful model to study cellular division, aging, or environmental adaptation. However, the intrinsic heterogeneous and dynamic nature of these phenomena requires their analyses at the single-cell level.
To address this technical challenge, we have developed two microfluidic-based platforms to follow single cells for several days in different contexts:

i) Replicative aging, where a mother cell divides and ages while its progeny is rejuvenated. Here, microfluidics is used to isolate and follow mother cells in a high throughput manner throughout their lifespan while automatically dissecting the daughter cells that would otherwise overwhelm the device due to their exponential growth [1].

ii) Adaptation to autonomous environmental degradation, where a growing culture progressively exhausts nutrients from its media. Cells have evolved to adapt to the different phases of this exhaustion, but studying the biological programs behind this adaption requires population-scale growth experiments to allow cell proliferation to have a collective impact on the environment, while tracking the same individuals for days. To this purpose, we developed an integrated microfluidic device based on continuous separation of the cells from the media (~5.10^5 cells/µL) and subsequent perfusion of the filtrated media into an observation chamber containing isolated single-cells [2].

Yet, these microfluidic tools coupled with video-microscopy offer such a quantity of data that it is not possible to analyze by conventional means, thus leaving their full potential unexploited. Therefore, we also developed a deep-learning approach to automate the detection of cell divisions, death, size, fluorescence, or temporal events, from week-long time-lapses [1]. It was proven to work equally well with data from different microfluidic devices, allowing widespread use of this tool among the community.

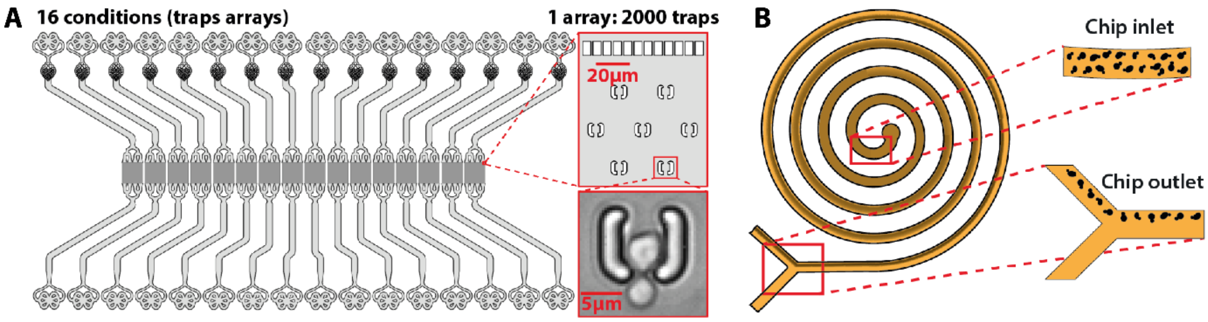

Figure 1: (A) Device to trap single yeast cells and track them throughout their replicative lifespan. (B) Device to separate yeast cells from the media in a continuous manner.

References

[1] T. Aspert, D. Hentsch, G. Charvin, DetecDiv, a generalist deep-learning platform for automated cell division tracking and survival analysis, Elife. 11 (2022) e79519.

[2] B. Jacquel, T. Aspert, D. Laporte, I. Sagot, G. Charvin, Monitoring single-cell dynamics of entry into quiescence during an unperturbed life cycle, Elife. 10 (2021) e73186.