

Fully Automated Approach for High Throughput Microinjection

info@csem.ch

www.csem.ch

S F Graf¹, H F Knapp¹, R Li²

¹Centre Suisse d'Electronique et de Microtechnique, Alpnach Center, Switzerland

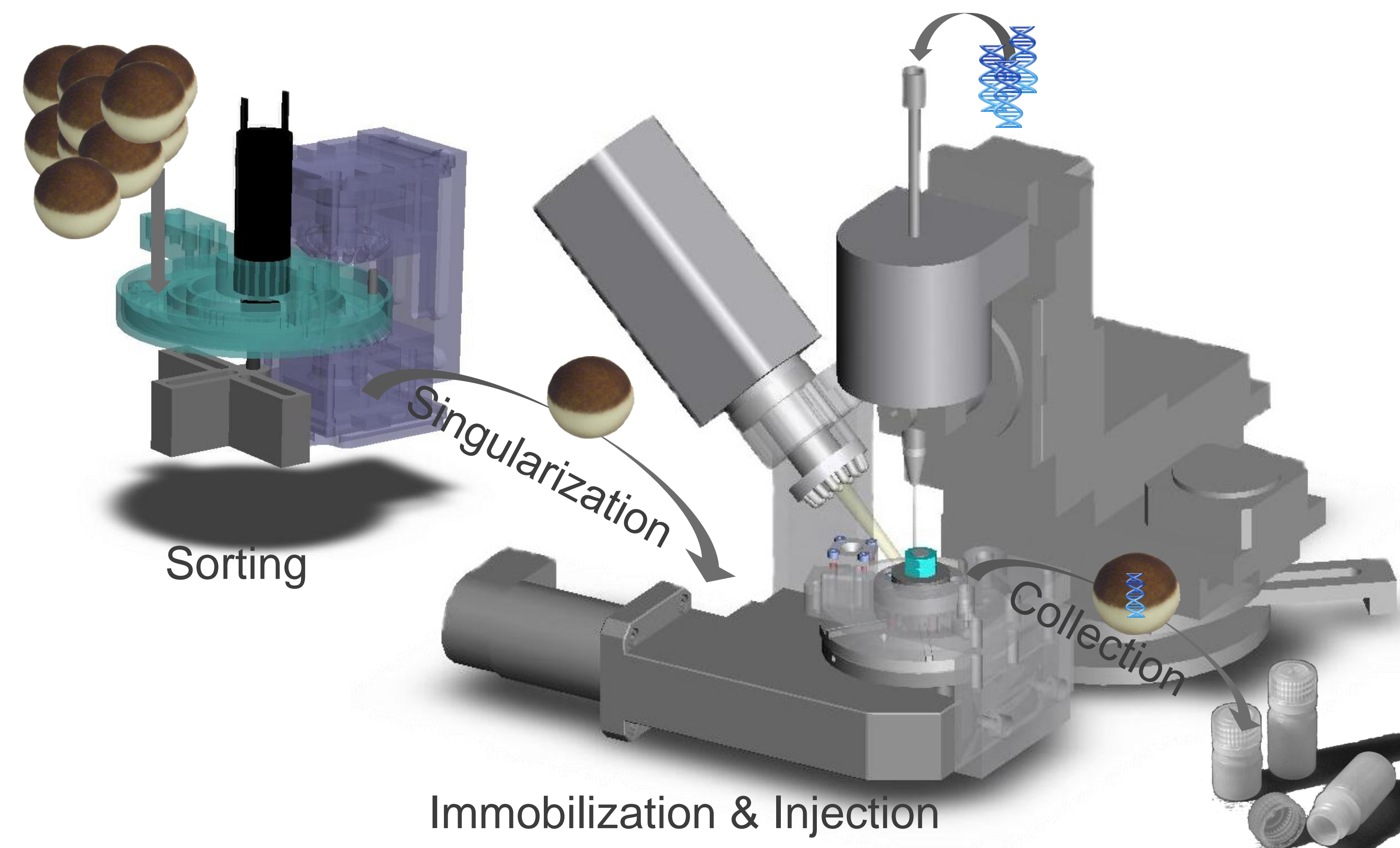
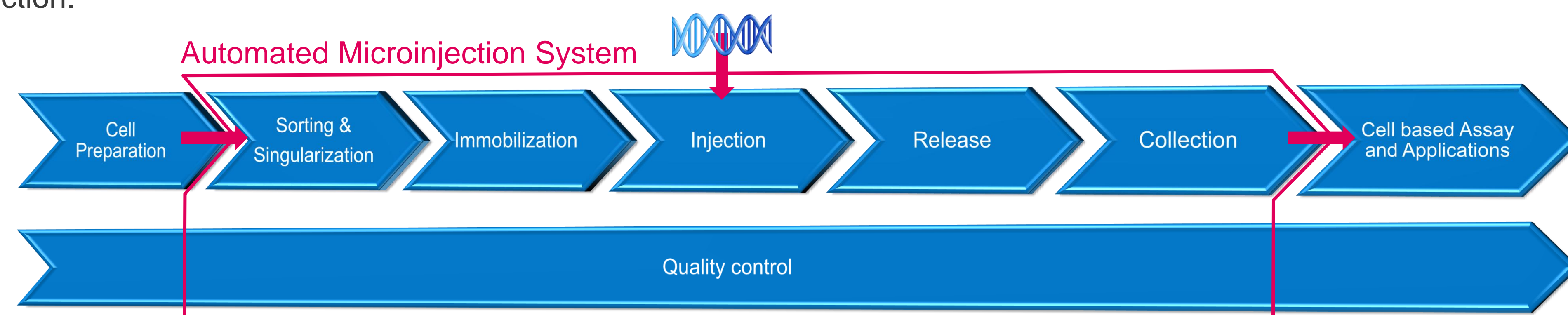
²Bioprédic International, Rennes, France

An innovative system to meet the need of drug researchers is being developed in this project. The solution combines novel concepts from microrobotics and microfluidics to achieve a higher throughput, which will replace time consuming and costly manual operations used today. The system is capable of automatically handling a cell suspension sample from sorting/singularization over immobilization, microinjection, release, and collection of cells, including quality control. To achieve a this, dedicated microfluidics systems for preparation and handling of cell suspensions are combined with microrobotic systems specialized to address, handle and observe individual cells in solution. The first fully automated system focuses on large cells like *Xenopus* oocytes. A specially designed flow cytometer for large opaque cells is combined with a carousel based microinjection system. The viability of cells is quality-controlled by a vision-algorithm within the flow cytometer. Viable cells are then transferred on demand to the microinjection system where individual cells are reversibly immobilized and injected, guided by a vision-feedback system. The fully automated system allows reducing the microinjection cycle from 300 seconds (manual approach) down to 6 seconds or less (automated approach) per cell. Further development steps are the integration of a force-feedback system for the microinjection to further enhance the success rate and the adaptation for injecting, many times smaller, hard-to-transfect-cells.

Introduction

Microinjection into large cells like *Xenopus laevis* oocyte is a common transfection method in the field of drug discovery. The drawback of this method is its low throughput, costly manual operation, and operator dependent success rate.

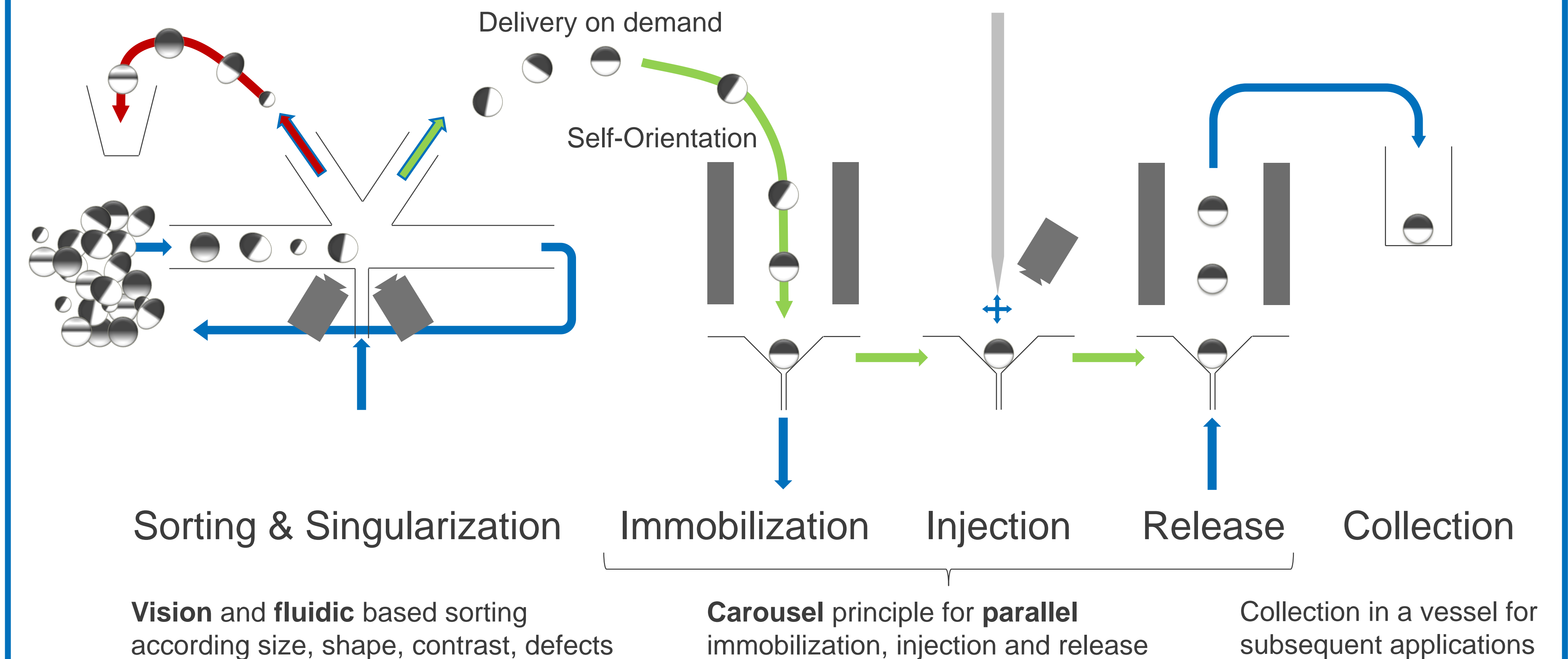
Our solution is a fully automated microinjection system, which is being developed within the EU-project HYDROMEL. The system provides the complete cell handling cycle including sorting/singularization, immobilization, injection, release, and collection.



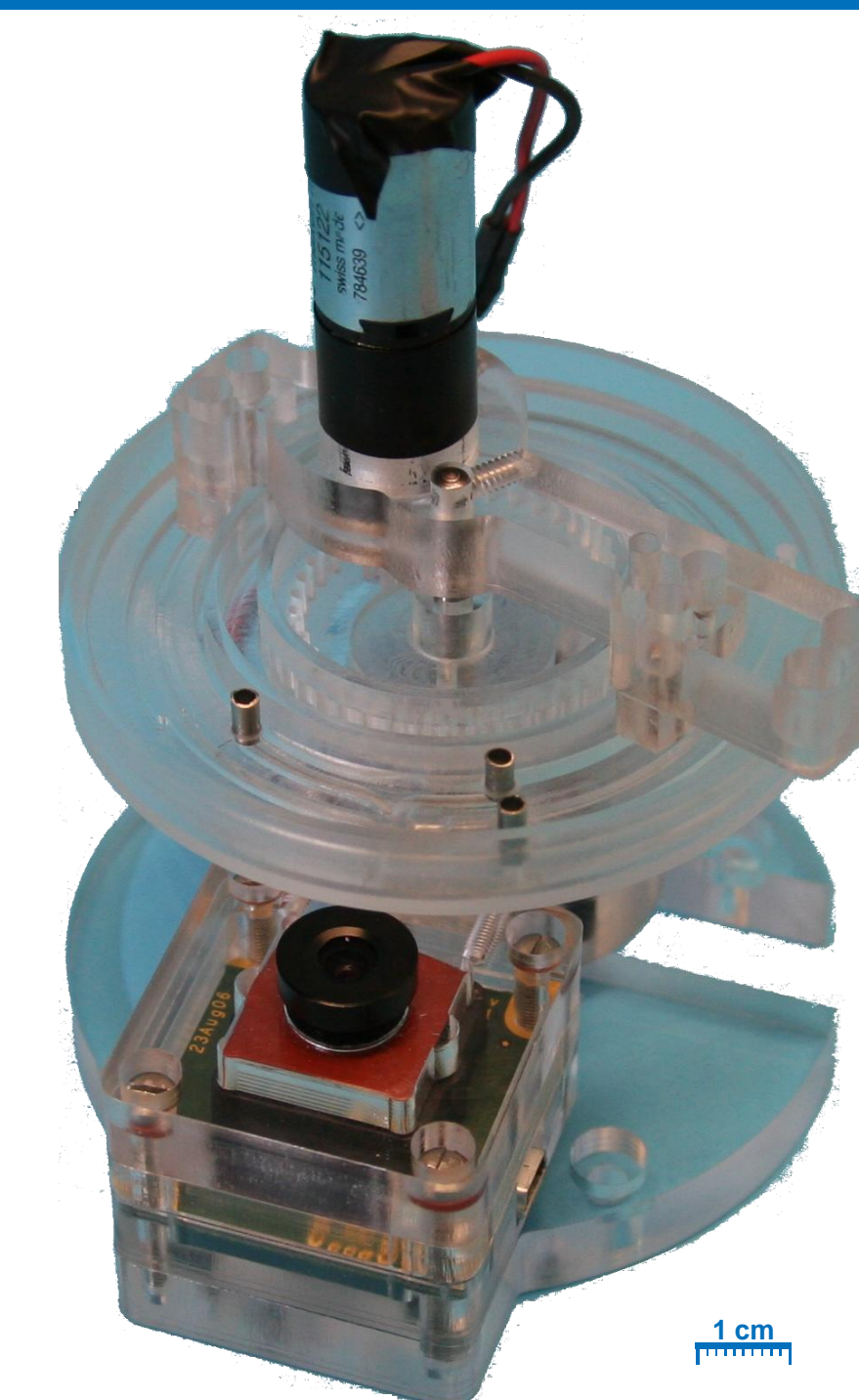
Challenges for automation:

- Sorting and singularization of cells out of suspension
- Correct orientation of oocytes (for later injection into the nucleus)
- Reliable, reversible immobilisation
- Undefined cell adhesion
- Quality control

Approach



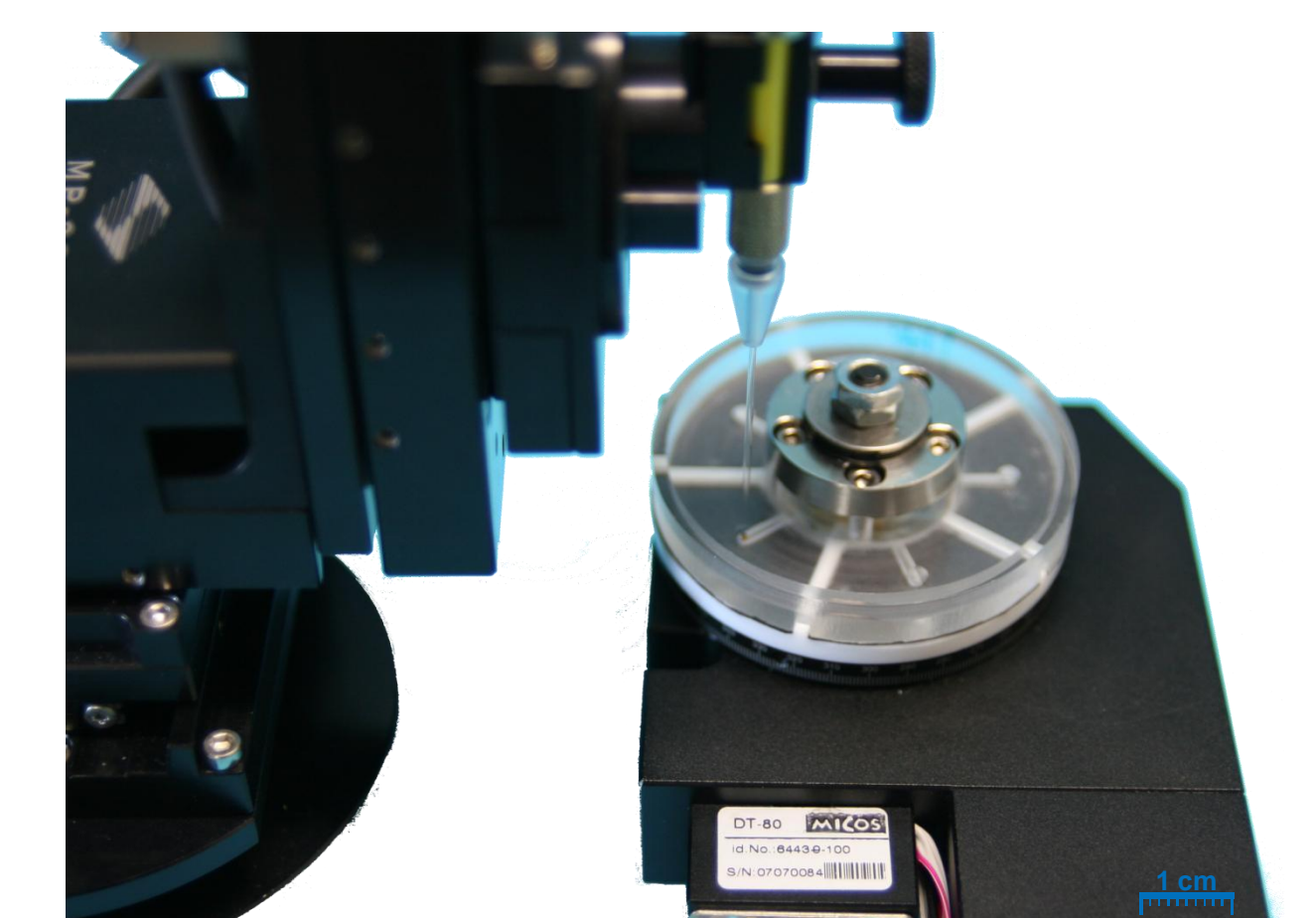
Current System



Flow cytometer for large opaque cells which stores, sorts and delivers viable oocytes on demand of the injection system.



Automated immobilization carousel with self-orientation into a cone in parallel with injection and release



Vision guided injection and quality control of correct oocyte orientation and successful injection