

Ecole doctorale SMAER  
Sciences **M**écaniques, **A**coustique, **E**lectronique, **R**obotique

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**Thesis subject 2018**

Laboratory : ISIR

University: Sorbonne University

Title of the thesis: **Closed loop trajectory control for cell sorting in microfluidics**

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This subject can be published on the doctoral school's web site:

The ambition of the thesis is to develop innovative methodologies for the trajectory control of micrometer size biological objects inside fluidic chips. These methodologies will be directly applied to create a new generation of chips dedicated to automated cell sorting, the smart cell sorters, where each cell is tested to determine its biological affinities and is individually tracked until the final sorting stage. The individual handling of a large number of cells to define their biological criteria guarantees selectivity higher than the current methods. It paves the way to adoptive cell therapy for anticancer treatments. This innovative and highly personalized technique is based on the cloning of naturally occurring tumor-reactive lymphocytes or on the ability to genetically engineer lymphocytes to express conventional T lymphocyte receptors or chimeric antigen receptors. However it must face a major challenge, the identification of rare natural lymphocytes having a concentration lower than 0.1%, which is beyond the detection level of current techniques.

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**Ecole doctorale SMAER**  
**Sciences Mécaniques, Acoustique, Electronique, Robotique**

**Subject**

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Since the inertia of micrometer size objects is drastically reduced compared to macrometer size ones their acceleration can be important which necessitates adapted position sensors. Current pattern tracking methods are designed to work on images, or frames, acquired at a fixed rate. Image acquisition is usually limited to the order of tens of milliseconds in real-time applications. This drastically restricts the ability to track correctly high-velocity objects. Increasing the frame rate is often not a solution as the increasing amount of acquired data sets a limit to real-time computation.

A recent and evolving branch of artificial vision exploits the unique characteristics of a novel family of asynchronous frame-free vision sensors whose principles of operation are based on abstractions of the functioning of biological retinas (Lichtsteiner, Posch, & Delbruck., 2008), (Lenero-Bardallo, Serrano-Gotarredona, & Linares-Barranco, 2011). The vision sensor output consists of asynchronous address events that signal scene reflectance changes at the times they occur. Effective visual data compression rate directly depends on the dynamic contents of the scene. Each pixel detects changes in log intensity larger than a threshold since the last emitted event (typically 15% contrast) to increase the dynamic range. When the change in log intensity exceeds a set threshold, an ON (+1) or OFF (-1) event is generated by the pixel depending on whether the log intensity has increased or decreased. The redundancy free encoding of the visual information from a dynamic scene, delivered by this camera, is naturally suited for real-time processing in high-speed vision tasks like object recognition and tracking.

These sensors open up the potential to introduce a shift in the methodology of acquiring and processing visual information in various demanding machine vision applications (Benosman, Ieng, Clercq, Bartolozzi, & Srinivasan, 2012), (Serrano-Gotarredona, et al., 2009). There has been a lot of research on visual pattern-based tracking. The algorithms differ in three main aspects: the

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## Ecole doctorale SMAER

### Sciences Mécaniques, Acoustique, Electronique, Robotique

appropriate representation for the patterns of interest, the transformation model used to transform the source model to match with the target pattern, and the tracking criterion used to estimate the optimal transformation parameters given a pattern representation and a transformation model. The ISIR Institute from CNRS has been very active on that area of research (**Erreur ! Nous n'avons pas trouvé la source du renvoi.**) (Ni Z. , 2013). It has proposed a novel methodology to perform pattern-based tracking in real time. The event-based computation presented in (Ni, Ieng, Posch, Régnier, & Benosman, 2015) allows shape tracking at an equivalent frame rate of 200 kHz. The process is data driven and iterative and it provides a natural robustness to occlusions at the lowest computational cost.

The phd student will be in charge of controlling the trajectory of the cells during their journey in the microfluidic chip. Most of the time, they will be conveyed using the fluidic flow. While arriving on the fluidic chamber or the sorting areas The phd student will implement closed loop control laws to guarantee that their trajectory is precisely controlled. Three modes are foreseen depending on the required precision of the trajectory:

The **conveying** of the microobjects before they reach the detection chamber will be achieved without any sensor feedback. These long range displacements will be performed by controlling the pressure inside the fluidic channels based on a commercially available microfluidic pressure controller

**Coarse open loop trajectory control** based on dielectrophoretic actuation is foreseen to move the microobjects toward the appropriate channel when they reach an intersection.

**Fine closed loop trajectory control and positioning** It will be based on the control laws for an asynchronous event based sensor and impedance spectroscopy measurements

The control laws developed by the phd students will be adapted to the specificities of the control of the cells, and in particular to high accelerations due to the low inertia of the objects and the highly non-linear force fields. He will address two main issues: maximizing the velocity of the microrobjects and tackling the non-linearity of the behavior