Title	Intelligent DEsign of Microfluidic devices (IDEM)

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# months (min.3)	6

Project description (2 page max):

Introduction - The development of new computational strategies based on statistical learning tools enables a novel and original approach to the design and optimization of Microfluidic Devices (MFDs) for chemical synthesis. In the literature, a significant trend is emerging towards the use of statistical learning for partial optimization of device parameters and components [1], designing biomimetic and spectroscopic micro-devices [2], and fully designing MFDs [3,4].

Project goals - The 'intelligent design' of MFDs operating as microreactors for organic Multicomponent Reactions (MCR) is of particular interest. MCRs are convergent reactions in which three or more starting compounds react to form a product, with all or most of the atoms contributing to the newly formed product. In an MCR, a product forms according to a cascade of elementary chemical transformations. Thus, there is a series of reactions, usually bimolecular, which all finally flow into an irreversible step yielding the product. The challenge is to conduct a MCR in such a way that the network of pre-equilibrated reactions channels into the main product without yielding parasite side products. The result is clearly dependent on the reaction conditions: solvent, temperature, catalyst, concentration, the kind of starting materials, and functional groups. Such considerations are of particular importance in connection with the design and discovery of novel MCRs. For this purpose, we intend to combine standard MD/continuum fluid dynamics approaches to flow properties in the MFDs with the search for the best performing arrangement conducted employing metaheuristic optimization approaches. In particular, we intend in this Doctoral project to develop a novel approach to the a priori design of microfluidic architectures in two and three dimensions, to obtain the best suited MFDs for specific reactions of increasing complexity, using a combination of hybrid molecular dynamics/hydrodynamic characterization of a single MFD and optimization of MFDs' geometry (inlets and outlets, mixing chambers, channels), and reaction parameters via statistical learning methods.

Methods - During the three-year PhD period, at first the student will develop robust techniques for the full in-silico characterization of given MFDs for MCRs both in homogenous and controlled heterogeneous phases (slurries) to avoid channels clogging; to this purpose both molecular dynamics methods (MD) and hydrodynamic continuous descriptions (HD) will be employed. Next the student shall optimize the design of MFDs based on different statistical methods, including but not limited to:

- swarm-particle + support vector machines (SWP+SVM), based on linear classifiers sampling the parameters space, for simple 2D geometries;
- genetic algorithms (GA), exploring the parameters space via stochastic global optimization methods inspired by the biological mechanisms of evolution and heredity, for complex 2D geometries;
- deep neural networks (DNN) for complex reaction networks and 3D geometries.

After the computational design phase, the next step will involve fabrication. This process necessitates cutting-edge manufacturing techniques, advanced materials, and precision to construct the intricate network of channels, chambers, and mixing areas within the microreactor. While this project focusses mainly on the computational design of new MFDs, a first exploration of fabrication techniques will be pursued in the final phase of doctorate period. In pursuit of this, we intend to utilize 3D printing for fabricating the microreactors, as this technology provides a comprehensive solution that addresses complex design requirements, customization needs, and essential performance optimization goals for translating computational designs into functional microreactor prototypes. Advanced 3D printing techniques support a wide range of materials, including polymers, metals, ceramics, and composites, enabling the selection of materials tailored to the desired microreactor functionality, such as chemical compatibility, thermal conductivity, or optical transparency. The PhD student will use a 3D printer available at DiSC and, for advanced applications, a 3D printing external service. In tandem with fabrication, rigorous testing will be conducted to assess the functionality and performance of the fabricated microreactors in selected MCRs. During this period the project will include also a 6 months secondment at ETH Zurich, in the group of Prof. Andrew deMello, well-renown in the area of microfluidics and nanoscale science.

Work-plan (36 months)

Phase I	–	Bibliographic research and planning (2 months)
Phase II	–	In-silico characterization of single MFDs via MD/HD (4 months)
	–	Optimization of MFDs via SP + SVM methods (6 months)
	–	Optimization of MFDs via GA methods definition (6 months)
	–	Optimization of MFDs via DNN methods definition (6 months)
Phase III	–	Implementation and testing of fabrication procedures for designed MFDs (8 months)
	–	Thesis writing (4 months)

References

[1] Talebjedi B. et al., *Frontiers in Bioengineering and Biotechnology*, 10, 878398 (**2022**); Hassani et al, *Physics of Fluids*, 36, 033606 (**2024**)

[2] Raj M.K. et al., *Biomicrofluidics*, 17, 051503 (**2023**); Shahab M. et al., 10, 100141 (**2024**)

[3] Maionchi D.D.O. et al., *International Journal of Heat and Mass Transfer*, 194,123110 (**2022**)

[4] Volk A.A. et al., *Nature Communications*, 14, 1403 (2023); Zheng J. et al., *Biosensors et Bioelectronics*, 194, 113666 (**2021**)