NUMERICAL SIMULATIONS OF THE FORMATION PROCESS OF NANOPARTICLES

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Introduction

Nanoparticles (NPs) are increasingly used as delivery system to carry and release drugs to a specific target; since they prove to be able to protect the payload from degradation, to improve drug solubility and bioavailability and to modify drug pharmacokinetic [1]. Microfluidic production technique is widely used for the NPs manufacture since, through this approach, the NPs size and homogeneity can be easily controlled [2]. Furthermore, the Microfluidic process allows to increase the formulation reproducibility thanks to a deepen control of the fluid dynamic parameters involved in the mixing process [3]. In the proposed work two different techniques are exploited for the production of NPs, passive mixing with herringbone and droplet generation by hydrodynamic flow focusing. Computational Fluid Dynamic (CFD) approach can be exploited to understand which fluidic condition can be adopted and used as boundary conditions to produce NPs. Hence, the present work aims at showing the efficiency of a computational approach to optimize the production of nanoparticles.

Methods

The geometries of different microfluidic chips are recreated through Autodesk Inventor 2020 and the computational grid is created using Ansys Workbench 2021R2. To mimic the interaction between different fluids (e.g., water-immiscible or miscible) two different multiphase models (i.e., Volume of Fluid and Mixture models) can be exploited.
In order to study the changes in the droplets formation or the mixing processes due to changes in the boundary conditions, data referring the volume fractions of the different phases can be exploited.

Results

The mixture model was able to capture the macroscopic effect of geometrical and fluid dynamic variations onto the fluids mixing process and consequent NPs production (Fig.1 A). Moreover, in order to preliminary validate the numerical model, experimental results were also collected, and several significant effects were highlighted (Fig.1 B, C) [4].
The VOF in-silico model proved to be able to capture with detail the principal phases of the droplet formation (i.e., separation and elongation) (Fig.1D). and analyze the morphological properties (e.g., bubble length) (Table 1).

Discussion and conclusions

Although one of the limitations of proposed CFD analysis is the impossibility to capture small scale effect (e.g., molecular dynamics) they are able to highlights the effects of geometry and fluid-dynamic parameters over the NPs mixing zones and droplets morphology.
In conclusion, the present approach can be used to identify the fluid-dynamic parameters able to maximize the mixing efficiency and optimize the production parameters.

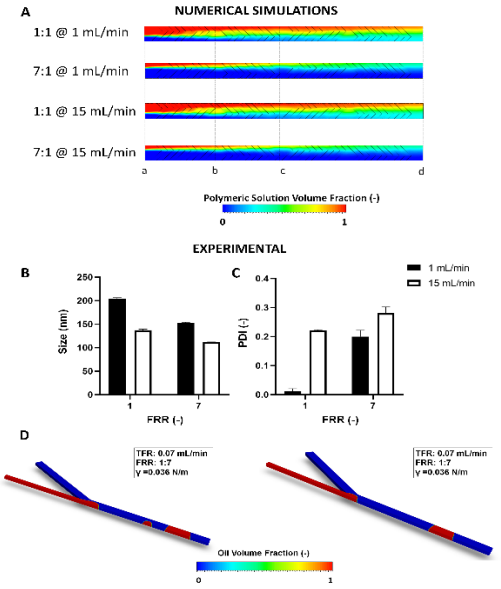

Figure 1: Contour plots of the mixing process with different boundary conditions (A). Distribution of NPs size (B) and polydispersity index (PDI) (C) obtained with a herringbone microfluidic chip with the same numerical boundary conditions. Droplets formation with different boundary condition (D).

FRR	Droplet Volume (mm^3)	Droplet Length (mm)	Time of Rupture (s)
1:3	4.26e-3	26.4e-2	2.98e-2
1:7	4.95e-3	31.2e-2	2.13e-2

Table 1: Morphological data and rupture event timing at different flow rate ratio (FRR) condition.

References

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