Computational Nanomedicine: challenges and opportunities in the rational design of polymeric nanoconstructs *

Paolo Decuzzi

***Abstract* — This work elaborates on challenges and opportunities for computational scientists in the rational design of nanomedicines for drug delivery and imaging.**

Over the past two decades, a variety nano-based systems have been developed for the diagnosis, imaging, and therapy in cancer, cardiovascular and neurodegenerative.[1] These include nanoconstructs; microfluidic chips; nano-sensors; hierarchical scaffolds and so on. The majority of these systems have been developed following rather empirical approaches and only recently the notion of "rationally design" is starting to be realized.[2]

Nanoconstructs for the systemic delivery of therapeutic and imaging agents – nanomedicines – exhibit improved bioavailability and blood longevity; higher accumulation and controlled release at the biological target, as compared to freely administered agents. Despite all this, nanomedicines are yet to be fully integrated into clinical settings. *Computational Nanomedicine* can help in addressing major challenges in the rational design of nanoconstructs.[2]

In this lecture, multi-scale and multi-physics *in silico* approaches for modeling tumor growth, vascular transport and adhesion, and diffusion of nanoconstructs and molecules will be reviewed. This will include continuous finite element models for predicting the progression and response to therapies of tumor masses (Figure.1a); the Isogeometric Analysis for describing and predicting the vascular transport and adhesion of nanoconstructs in complex blood vessel networks (Figure.1b); the Immersed Finite Element Method and Lattice Boltzmann Method for analyzing the vascular and extravascular dynamics of nanoconstructs in microcapillaries (Figure.1c); and Molecular Dynamics simulations for predicting the diffusion of water molecules within porous matrices (Figure.1d). Finally, *in vitro* and *in vivo* data will be presented to describe the experimental tools currently available for validating and refining the predictions of computational models.[3]

More specifically, the author and collaborators have shown that discoidal nanoconstructs with a characteristic size ranging between several hundreds of nanometers and a few microns can efficiently navigate the circulatory system and eventually adhere to the diseased endothelium. This was originally predicted using continuum mechanics models integrated with discrete ligand-receptor interactions and then verified experimentally both in vitro, using microfluidic chips, and in vivo within small-animal tumor models.[3-5]

The geometrical confinement of Gd^{3+}-ions and iron oxide nanoparticles within mesoporous matrices will also be discussed. Using continuum mechanics models and molecular dynamics simulations [6, 7], the author and collaborators have shown that confinement within porous matrices can dramatically enhance the contrast generated in MR imaging.

Using these and other examples, limitations, challenges and opportunities for computational scientists in the field of nanomedicine will be discussed.[2]

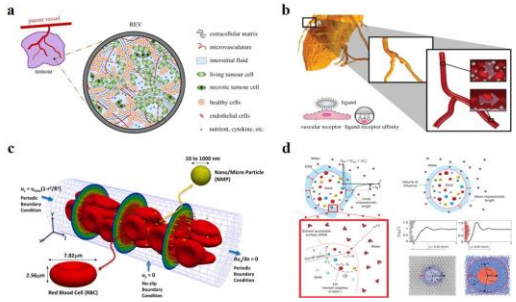

Figure.1: **Multi-scale *in silico* approaches for nanomedicine. a.** Continuous models for predicting the progression and response to therapies of tumors; **b.** Isogeometric Analysis for predicting the vascular transport and adhesion of nanoconstructs; **c.** Immersed Finite Element Methods for analyzing the vascular and extravascular dynamics of nanoconstructs; **d.** Molecular Dynamics simulations for predicting the diffusion of water molecules in porous matrices.

ESSENTIAL REFERENCES

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*Research supported by the European Research Council, under the European Union's Seventh Framework Programme (FP7/2007-2013)/ERC grant agreement no. 616695 and the AIRC (Italian Association for Cancer Research) under the individual investigator grant no. 17664.

Paolo Decuzzi is with the Laboratory of Nanotechnology for Precision Medicine at the Fondazione Istituto Italiano di Tecnologia (IIT) in Genova, Italy (corresponding author to provide phone: +39 010-7178-1941; fax: +39 010- 7178-1228; e-mail: paolo.decuzzi@iit.it).