

Numerical Optimization of Plasmid DNA Delivery Combined with Hyaluronidase Injection for Electroporation Protocol

Daniele Peri⁽¹⁾, Manon Deville⁽²⁾, Clair Poignard⁽²⁾, Emanuela Signori⁽³⁾, Roberto Natalini⁽¹⁾

⁽¹⁾:CNR-IAC – National Research Council, Istituto per le Applicazioni del Calcolo "Mauro Picone" Via dei Taurini 19, 00185 Rome, Italy

⁽²⁾:Team MONC, INRIA Bordeaux-Sud-Ouest, Institut de Mathématiques de Bordeaux, CNRS UMR 5251 & Université de Bordeaux, 351 cours de la Libération, 33405 Talence Cedex, France

⁽³⁾:CNR-IFT – National Research Council - Istituto di Farmacologia Traslazionale, Via Fosso del Cavaliere 100, 00133 Rome, Italy

d.peri@iac.cnr.it and emanuela.signori@ift.cnr.it

Abstract

The definition of an innovative therapeutic protocol requires the fine tuning of all the involved operations in order to maximize the efficiency. In some cases, the price of the experiments, or their duration, represents a great obstacle and the full potential of the protocol risks to be reduced or even hidden by a non-optimal application.

The implementation of a numerical model of the protocol may represent the solution, allowing a systematic exploration of all the different alternatives, shedding the light on the most promising combination and also identifying the key elements/parameters.

In this paper, the injection of a plasmid, preceded by a hyaluronidase injection, is simulated through a mathematical model. Some key elements of the administration protocol are identified by means of a mathematical optimization procedure, maximizing the efficacy of the therapy. As a side effect of the extensive investigation, robust solutions able to reduce the effects of human errors during the administration are also obtained.

References

- [1] Whatcott, Clifford J and Han, Haiyong and Posner, Richard G and Hostetter, Galen and Von Hoff, Daniel D, Targeting the tumor microenvironment in cancer: why hyaluronidase deserves a second look, *Cancer discovery*, Vol. 1, N. 4, pp. 291–296, 2011
- [2] Deville, Manon and Natalini, Roberto and Poignard, Clair, A Continuum Mechanics Model of Enzyme-Based Tissue Degradation in Cancer Therapies, *Bulletin of Mathematical Biology*, Vol. 80, N. 12, pp. 3184–3226, 2018.
- [3] Signori, Emanuela and Wells KE and Fazio VM and Wells DJ, Optimisation of electrotransfer of plasmid into skeletal muscle by pretreatment with hyaluronidase - increased expression with reduced muscle damage, *Gene Therapy*, Vol. 8, pp. 1264–1270, 2001
- [4] Self-learning metamodels for optimization, Daniele Peri, *Ship Technology Research*, Vol 56, N. 3, pp. 95–109, 2009.