ScuDo

Scuola di Dottorato ~ Doctoral School

WHAT YOU ARE,TAKES YOU FAR

XXXII Cycle

Characterization of Gated Nanochannels Membrane for Active Control of Charged Molecules

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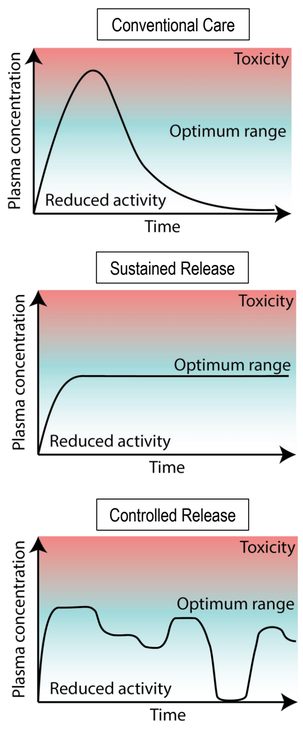
Research context and motivation

Chronic diseases constitute a major public health problem. Only the 50% of individuals with chronic diseases adhere to treatment regimens, posing significant risks of complication and even mortality. [1]

Current strategies for therapeutics administration are ***systemic***. Upon bolus administration, drug concentration in the body rapidly increases reaching potentially toxic levels and exponentially clears resulting in a small therapeutic window.

On the other hands, ***sustained release*** platforms use zero-order drug release kinetics, however once implanted there is no option for controlling dosage. Dosing and timing are key factors for effective treatment of chronic diseases. ***Chronotherapy*** and ***personalized medicine*** focus a ***controlled release***, allowing the administration of therapeutics to follow the specific ***circadian rhythm*** of the diseases under treatment.

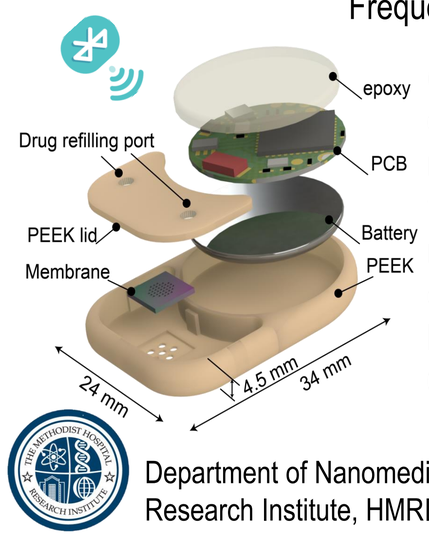


[1] Centers for the Medicare&Medicaid Services, Chronic Conditions Prevalence State/Country Table: All Free-for-Service Beneficiaries, 2015. NCOA: National Concil of Aging, www.ncoa.org

Addressed research questions/problems

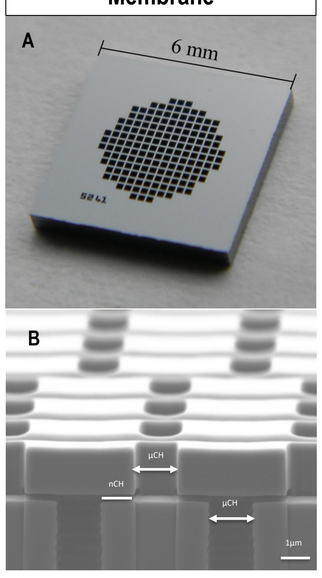
Implantable Capsule Remotely Controlled For Drug Release

The Implantable Delivery Systems has been implementated utilizing the Radio Frequency approach.



(A) Coated membrane with SiC or SiO_2; (B) Magnification of the membrane architecture showing the support structure, the nanochannel and macro-channels layers. Final structure holds 121 macro-channels and 680000 nanochannels.

Gated Nanochannels Membrane



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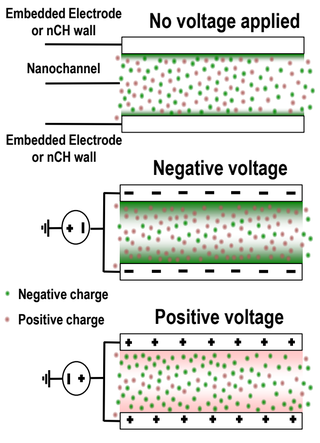
Novel contributions

Nanochannels membrane offers the possibilty to compare the size of molecules and nanochannels, generating an electrostatic interaction between the liquid and the ***electrical double layer EDL***. EDL is the surface-charge distribution at the liquid-solid interface caused by fixed surface charge and compensating counter-ions near the surface. The ***transport rate*** of the charged molecules can be modulated by altering the EDL. Many drug molecules are charged in solution and thus their diffusion through a nanochannels membrane can be controlled.

Applying a ***potential*** to the wall of the nanochannels, it is possible to expand or reduce the EDL, attracting counter-ions and to repelling co-ions.



Submitted and published works

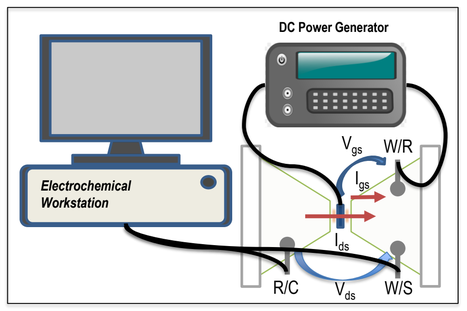
- Shin, S.R., Zhang, Y.S., Kim, D.J., Manbohi, A., Avci, H., Silvestri, A., Aleman, J., Hu, N., Kilic, T., Keung, W., Righi, M., Assawes, P., Alhadrami, H.A., Li, R.A., Dokmeci, M.R., Khademhosseini, A., "*Aptamer-based microfluidic electrochemical biosensor for monitoring cell-secreted trace cardiac biomarkers*", American Chemical Society, 2016, 88.20: 10019-10027.
- Shin, S.R., Kilic, T., Zhang, Y.S., Avci, H., Hu, N., Kim, D., Branco, C., Aleman, J., Massa, S., Kang,J., Desalvo, A., Hussaini, M.A., Chae, S.K., Polini, A., Bhise, N., Hussain, M.A.,Lee, H.Y., Dokmeci, M.R., Khademhosseini, A., "*Label-Free and Regenerative Electrochemical Microfluidic Biosensors for Continual Monitoring of Cell Secretomes*", Advanced Science, 2017.
- Zhang, Y.S., Aleman, J., Shin, S.R., Kilic, T., Kim, D., Shaegh, S.A.M., Massa, S., Riahi, R., Shae,S.,Hu, N., Avci, H., Zhang, W., Silvestri, A., Nezhad, A.S., Manbohi, A., De Ferrari, F., Polini, A., Calzone, G., Shaikh, N., Alerasool, P., Budina, E., Kang, J., Bhise, N., Ribas, J., Pourmand,, A., Skardak, A., Shupe, T., Bishop, C.E., Dokmeci, M.R., Atala, A., Khademhosseini, A., "*Multisensor-integrated organs-on-chips platform for automated and continual in situ monitoring of organoid behaviors*", Proceedings of the National Academy of Sciences, 2017, 201612906.
- Demarchi, D., Silvestri, A., Aiassa, S., "IRDS International Roadmap for devices and systems", IEEE, 2017 Edition.
- Di Trani, N., Silvestri, A., Bruno, G., Geninatti, T., Chua, C.Y.X., Gilbert, A., Rizzo, G., Filgueira, C.S., Demarchi, D., Grattoni, A., "*Remotely controlled nanofluidic implantable platform for tunable drug delivery*", Lab on a Chip, 2019

Adopted methodologies

Electrochemical Characterization of the membrane

Electrochemical Impedance Spectroscopy EIS: Measurements of the EDL capacitance C_{dl} and Resistance of Charge Transfer R_{ct}. (A) Nanochannel wall immersed in electrolyte; (B) Equivalent Circuit of the nanochannel's system; (C) Nyquist plot of the measured impedance.

Electrochemical System Setup

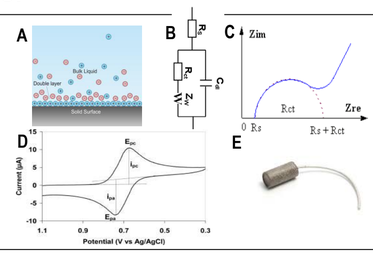


Cyclic Voltammetry Measurements: Measurements at different scan rate Transmembrane current I_{ds} at different gate voltage V_{gs}. (D) Anodic Peak of current I_{pa} corresponds to Oxidation and Cathodic Peak of current I_{pc} corresponds to Reduction.

Current-Voltage Measurements I-V: Measurements of Transmembrane current I_{ds} at different V_{gs} for different transmembrane potential V_{ds}. Characterization of Conductance of the nanochannels.

Frequency: 0.1Hz - 10KHz
AC: 50mV
V_{gs} :-3V - 3V; V_{ds}:-3V - 3V
Scan Rate: 0.01V/sec - 0.005 V/sec

Electrolytes: Phosphate Buffer Saline (PBS), Potassium Chloride (KCl)

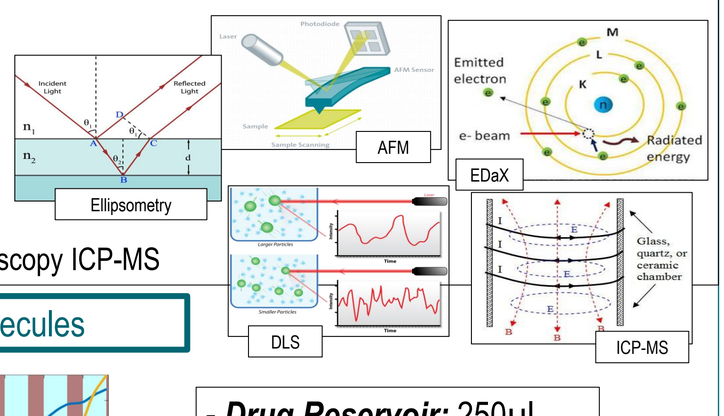


Corrosion Tests on Nanochannels Membrane

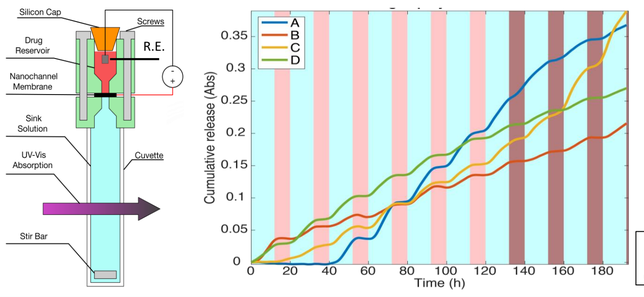
Stability Test of Nanochannel Membrane in Sodium Fuoride and Bovine Serum Albumine.

Surface Analysis:
- Scanning Electron Microscope SEM
- Energy Dispersive X-ray EDaX
- Atomic Force Microscopy AFM
- Ellipsometry

Solution Analysis:
- Dynamic Light Scattering DLS
- Inductively Coupled Plasma Mass Spectroscopy ICP-MS



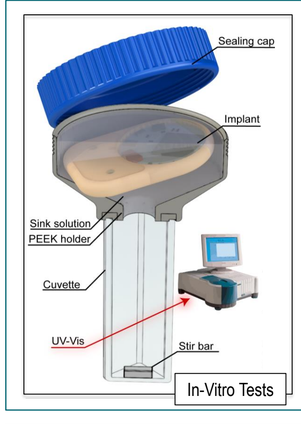
In-vitro Release of Charged Molecules



- ***Drug Reservoir:*** 250μl
- ***Sink:*** 4.25ml
- ***Wavelenght:*** 256 nm
- ***Phases:*** Active / Passive

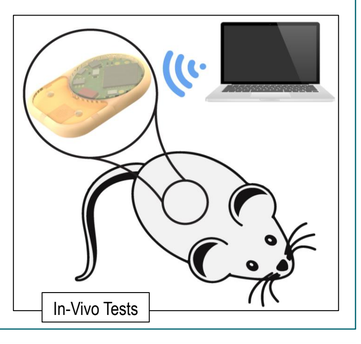
Molecule: Poly(sodium 4-styrenesulfonate)

Future work



- Development of a printed circuit board (PCB) for the application of potential to the gate control of the nanochannel membrane.

- In-vitro and in-vivo experimental tests for validation of the remote control modulation of the release of therapeutic drugs in small and large animals.



List of attended classes

- 02LWHRV – Communication (16/02/2017, 1 cfu)
- 01RISVR – Public speaking (16/02/2017, 1 cfu)
- 01QORRV – Writing Scientific Papers in English (23/03/2017, 3 cfu)
- 01QRNRV – Electromagnetic dosimetry in MRI: computational and experimental methods (27/07/2017, 4 cfu)
- 01PJMRV – Etica informatica (05/05/2017, 4)
- 01LCPIU – Experimental modeling: costruzione di modelli da dati sperimentali (03/07/2017, 6 cfu)
- 01QZTRR – Progettazione di dispositivi medici per la chirurgia (20/07/2017, 4 cfu)
- 01QAAAA – BIO/CMOS interfaces and co-design (18/10/2017, 3)
- 01RGGRV – Telemedicine and Distributed Healthcare (20/11/2017, 4)
- 01SIHRV – Bio-Nano Electronics and BioMolecular Computing (07/09/2018, 4)

POLITECNICO DI TORINO

PhD program in
Electrical, Electronics and Communications Engineering