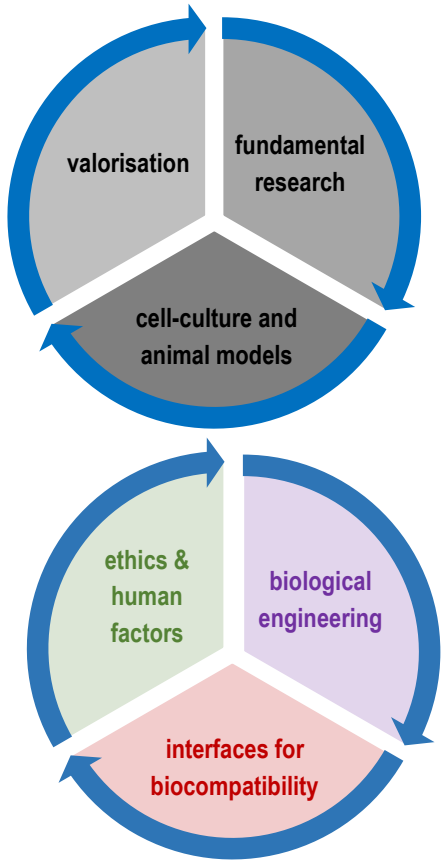
- ✓ an integrated multidisciplinary project to develop novel medical devices to solve clinical needs and to improve healthcare
  - ➢ novel medical devices = smart[1], hybrid[2] and symbiotic[3] medical devices,
  - ➢ need for advanced structural electronics[4] on flexible substrates for conformable sensing and actuating devices
- ✓ SymDis will base the development of novel medical devices on:
  - ➢ fundamental research – utilising interdisciplinary skills for multidisciplinary project goals *(including biology, biochemistry, biophysics, bioengineering, human factors, ethics, etc …)*
  - ➢ applied research – cell-culture and animal models for testing, ethical considerations and human factors
  - ➢ valorisation – publications **+** commercialisation of patents (licence, startup) for clinical use
- ✓ development of novel medical devices requires SymDis to have:
  - ➢ capabilities of biological engineering,
  - ➢ capabilities for advanced body-device interfaces to ensure biocompatible systems,
  - ➢ capabilities for ethical considerations and human factors to be integrated from the start of the design and prototyping

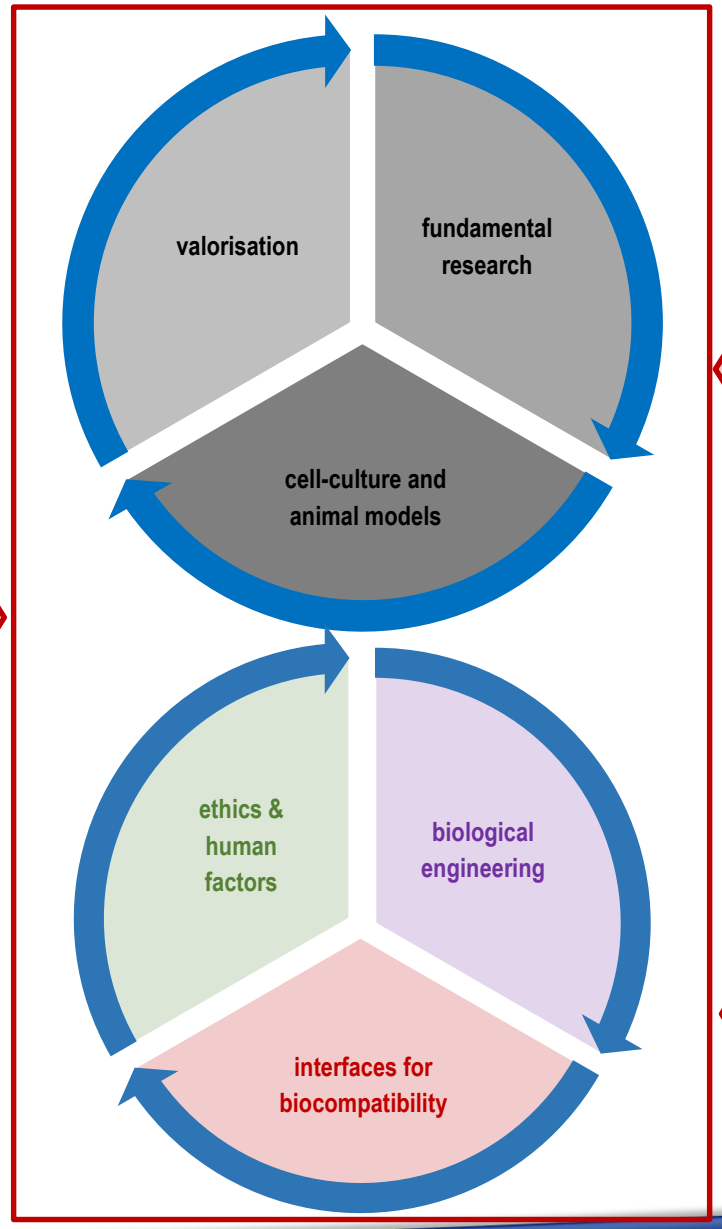
Core "motors" for SymDis



[1] **smart:** an auto-responsive medical device that can adapt its function autonomously in response to a biological stimulus. That is, the feedback control system is not simply programmed
[2] **hybrid:** a dynamic system that includes active and passive components, combined with a biological component, to condition an input or output signal
[3] **symbiotic:** a dynamic system that supports the duplex communication of biological molecules and energy to and from living tissues
[4] **structural electronics:** flexible/stretchable/hybrid electronic components at the core and surface of objects that are designed to be smart medical devices

EXISTING TECHNOLOGICAL PLATFORMS

- ADDITIVE MANUFACTURING *(CEA - Liten/DTNM)*
- FLEXIBLE and PRINTED ELECTRONICS *(CEA - Liten/DTNM)*
- µ-ELECTRONICS *(CEA - Leti/DPFT-DCOS)*
- INTEGRATED MICROFLUIDICS *(CEA - Leti/DTBS)*
- CELL and TISSUE IMAGING PLATFORM *(UGA - TIMC)*
- ECCAMI (Excellence Center for Computer Assisted Medical Interventions) *(UGA - TIMC)*
- ANIMAL FACILITIES *(UGA, CEA, CHUGA)*



MEDICAL DEVICE DESIGNERS

Proof-Of-Concept → Preindustrialisation → Products (TRL/CML)

- DIGITAL MEDICAL DEVICES
- LOCAL LABOS MEDICAL DEVICES
- EXTERNAL LABOS MEDICAL DEVICES

↔ Hub4AIM Alliance *(CEA, UGA, CHUGA, JBT Hub Up)* ↔ MEDICAL DEVICE industrials

END-USERS

MEDICAL NEEDS, ETHICS, CO-DESIGN, HUMAN FACTORS

PATIENTS, INDUSTRIALS, HOSPITALS, PRECLINICAL AND CLINICAL TRIALS

SymDis: Symbiotic Medical Devices ⇨ ecosystem

EXISTING TECHNOLOGICAL PLATFORMS

- ADDITIVE MANUFACTURING *(CEA - Liten/DTNM)*
- FLEXIBLE and PRINTED ELECTRONICS *(CEA - Liten/DTNM)*
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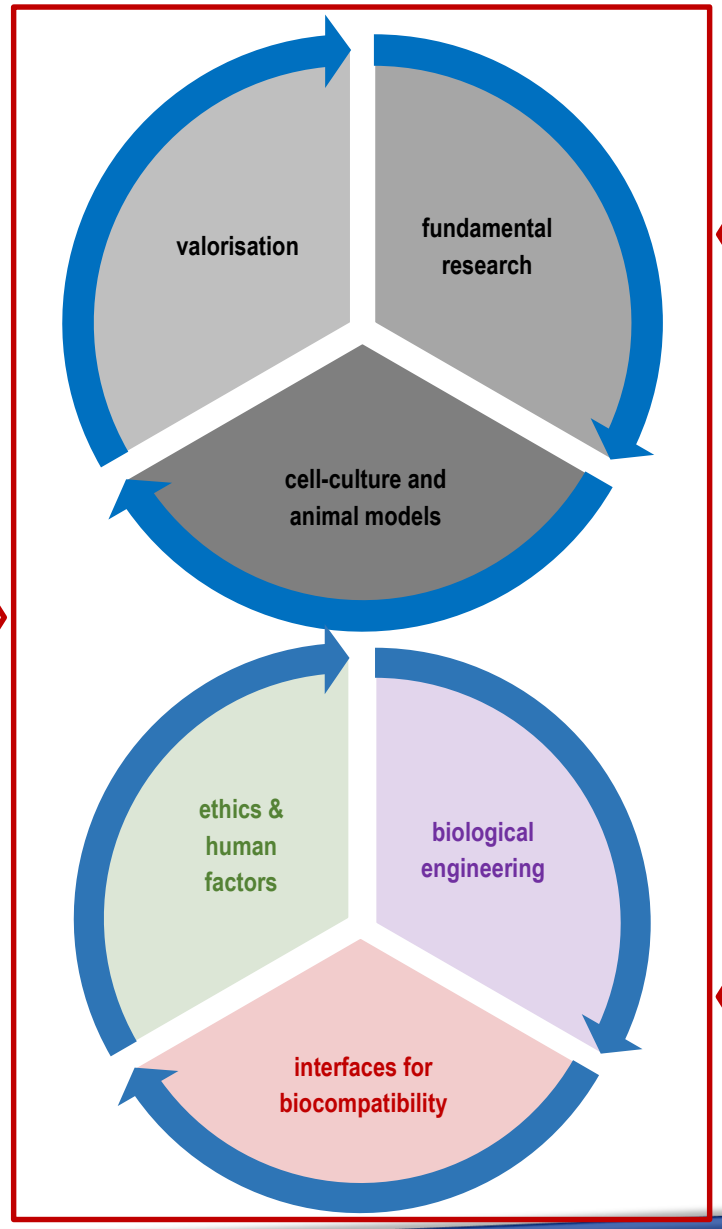
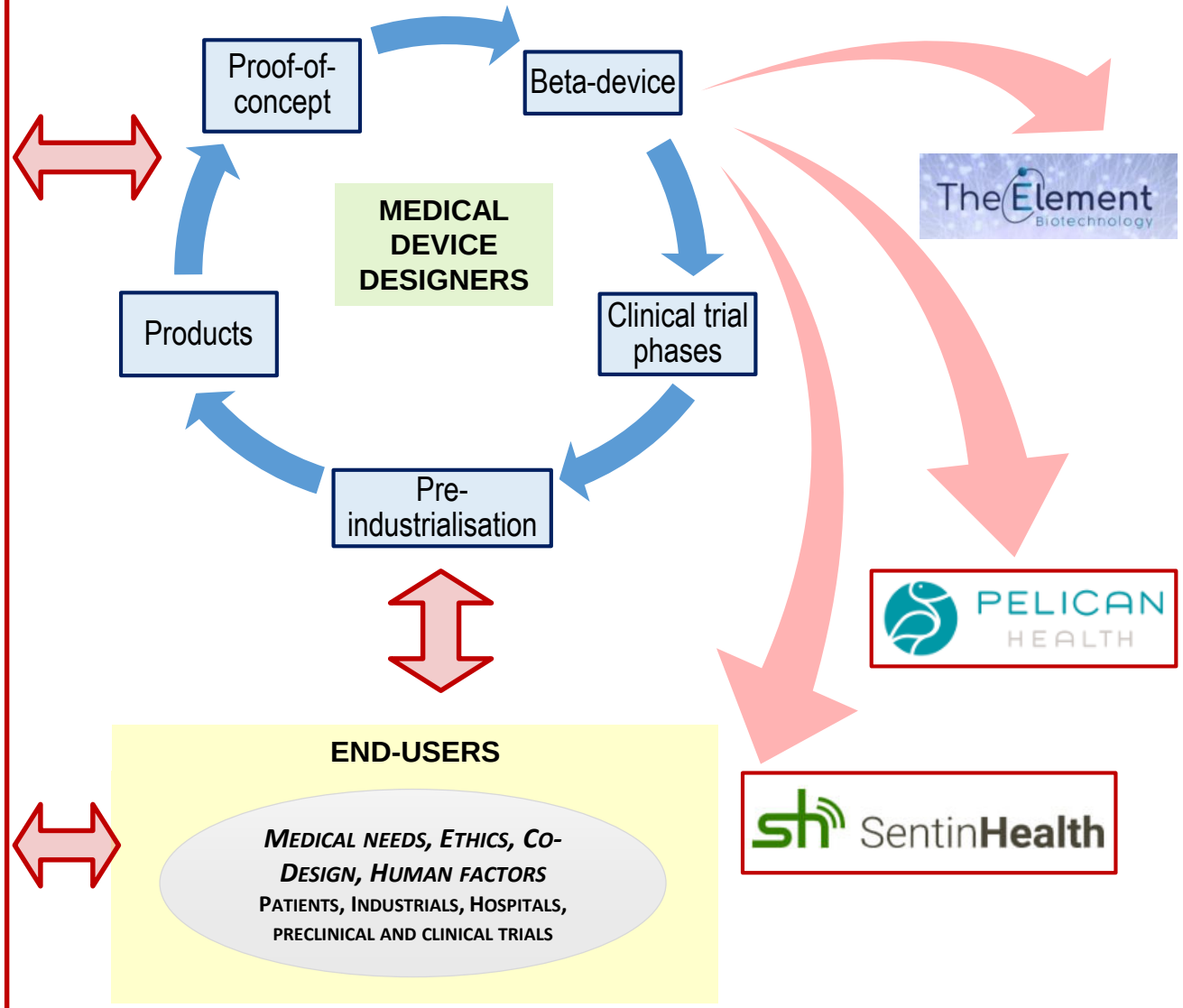




SymDis: Symbiotic Medical Devices ⇨ ecosystem

-Target 1-

A detailed molecular-level understanding of the nanostructure & function of biomimetic systems

-Target 2-

A fundamental understanding of the biocompatibility of interfacing biomimetic systems with the body *(inter-**ph**ases)*

-Target 3-

Biological engineering with biological proteins and synthetic materials to create hybrid symbiotic implantable medical devices

-Target 4-

An understanding of the ethical issues and human factors for symbiotic medical devices

symbiotic: biological engineering using biological components for medical device systems

Objectives:

(i) to use ***self-assembly*** of biological molecules in ***bioinspired systems*** to biologically engineer ***nanostructured systems***;

(ii) to integrate these ***nanostructured systems*** with synthetic materials for biological engineering of ***hybrid biotechnology systems***;

(iii) to use these ***hybrid biotechnology systems*** to create ***biocompatible biomimetic interfaces*** for integration into the body;

(iv) to utilize this biological engineering to develop implantable ***symbiotic medical devices*** for interaction with nerve and muscles (stimulation, recording), for diagnosis and therapy (bio-detection and sampling), and for long-term generation of power.

-Target 1-

A detailed molecular-level understanding of the nanostructure & function of biomimetic systems

-Target 2-

A fundamental understanding of the biocompatibility of interfacing biomimetic systems with the body *(inter-**ph**ases)*

-Target 3-

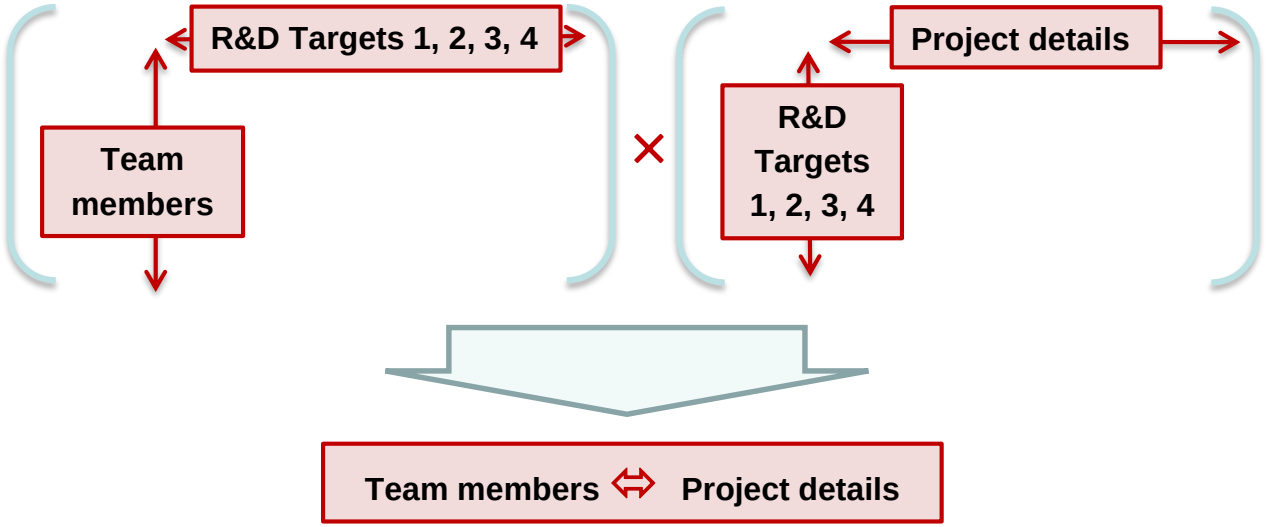
Biological engineering with biological proteins and synthetic materials to create hybrid symbiotic implantable medical devices

-Target 4-

An understanding of the ethical issues and human factors for symbiotic medical devices

Matrix model – can support a large number of multidisciplinary projects with interdisciplinary expertise

(not "linear" nor "hierarchical")



Matrix model – can support a large number of multidisciplinary projects with interdisciplinary expertise *(easily scalable)* **- *example of the team SyNaBi***

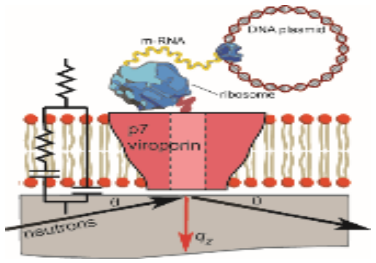
Matrix 1a : Expertise-to-Project *(already funded)*		ANR	European Commission	SATT / Linksium			FINOVI	Région Rhône Alpes		CNRS Maturation	CARNOT LSI
		Azotics	InnovaXN	UROLOC	Symbiont	Endobiocrine	Symbiocare	Enteroprobe	ENZYFLOW	BEPI	BIOEPC
NanoTech	Nano(bio)technology	■	■								
MicroTech	Micro(bio)technology			■		■				■	■
BioMem	Biomimetic membrane		■	■							
Polym	Polymers				■	■	■	■	■	■	■
Chem	Chemistry	■								■	
CMB	Cell & molecular biology		■	■	■		■	■	■	■	
Physiol	Physiology	■			■	■				■	■
MDS	Medical systems design			■	■	■	■	■	■	■	■
EChem	Electrochemistry					■				■	■
EPhys	Electrophysiology		■	■							
Biophys	Biophysics	■	■							■	
microFl	Microfluidics			■							

(Matrix 1a / Matrix 1b) x (Matrix 2) = (People-to-Projects *(% commitments)*)

Matrix 1b : Expertise-to-Project *(submitted)*		Pharion	DIANE	NeuroSysPro	SynapseWatch	SMAPCELLTY
NanoTech	Nano(bio)technology	■		■	■	
MicroTech	Micro(bio)technology			■	■	■
BioMem	Biomimetic membrane	■		■	■	■
Polym	Polymers			■	■	■
Chem	Chemistry					
CMB	Cell & molecular biology	■	■	■		■
Physiol	Physiology	■				■
MDS	Medical systems design			■	■	■
EChem	Electrochemistry					■
EPhys	Electrophysiology	■	■	■	■	
Biophys	Biophysics					■
microFl	Microfluidics	■		■		

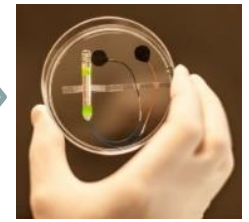
Matrix 2 : Person-to-Expertise	Nano Tech	Micro Tech	BioMem	Polym	Chem	CMB	Physiol	MDS	EChem	EPhys	Biophys	MicroFl
ALCARAZ, Jean-Pierre	■	■	■	■		■	■					
BARLETTI, Beatrice	■		■								■	
BEAUJEAN, Céline						■	■					
CASALI, Veronica	■	■										■
CINQUIN, Philippe							■	■				
MACCARINI, Marco	■		■								■	
MARTIN, Donald	■	■	■	■						■		
TRONEL, Alexandre				■		■						
VAN DER SANDEN, Boudewijn	■	■					■				■	
ZEBDA, Abdelkader	■	■		■	■			■	■			■

SymDis: Symbiotic Medical Devices ⇨ implementation / project structure



Symbiotic ion channel-based systems

Symbiotic enzyme-based systems



valorisation

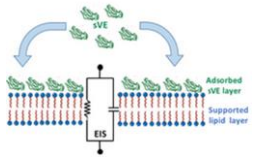
fundamental research

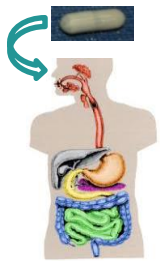
cell-culture and animal models

ethics & human factors

biological engineering

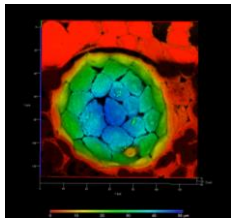
interfaces for biocompatibility





Bioinspired diagnostic systems

Bioinspired therapeutic systems



Biotechnology Journal
Systems & Synthetic Biology · Nanobiotech · Medicine

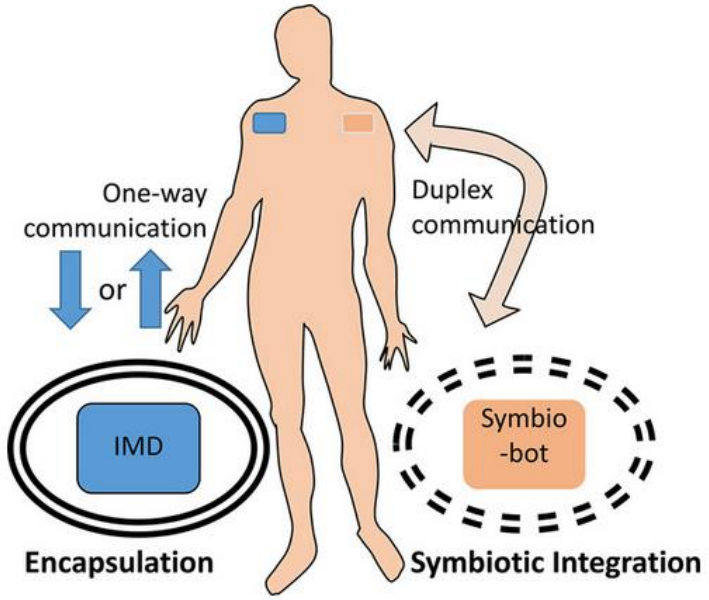
Volume 13, Issue 12
Biomimetic and Bioinspired Biotechnology
December 2018

Review

Tackling the concept of symbiotic implantable medical devices with nanobiotechnologies*

Jean-Pierre Alcaraz, Philippe Cinquin, Donald K. Martin

First published: 26 October 2018 | https://doi.org/10.1002/biot.201800102



Bioelectrochemistry 124 (2018) 57–72

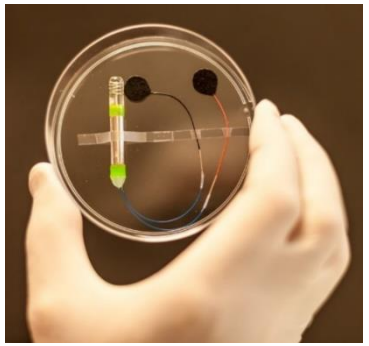
Contents lists available at ScienceDirect

Bioelectrochemistry

journal homepage: www.elsevier.com/locate/bioelechem

Challenges for successful implantation of biofuel cells

Abdelkader Zebda [a], Jean-Pierre Alcaraz [a], Pankaj Vadgama [b], Sergey Shleev [c], Shelley D. Minteer [d], François Boucher [a], Philippe Cinquin [a], Donald K. Martin [a,*]



main challenge is biocompatibility ⇨ eliminate biofouling to ensure stable supply of substrates

(stable supply of substrates = stable level of sufficient power)

Materials Science & Engineering C 108 (2020) 110359

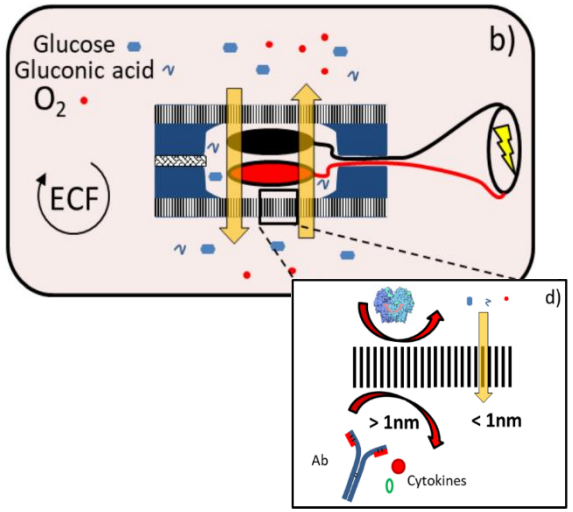
Contents lists available at ScienceDirect

Materials Science & Engineering C

journal homepage: www.elsevier.com/locate/msec

Long duration stabilization of porous silicon membranes in physiological media: Application for implantable reactors

Abdoullatif Baraket[a,1], Jean-Pierre Alcaraz[b,1], Chantal Gondran[c], Guillaume Costa[d], Guillaume Nonglaton[d], Frédéric Gaillard[d], Philippe Cinquin[b], Marie-Line Cosnier[d], Donald K. Martin[b,*]



Energy & Environmental Science

ROYAL SOCIETY OF CHEMISTRY

PAPER

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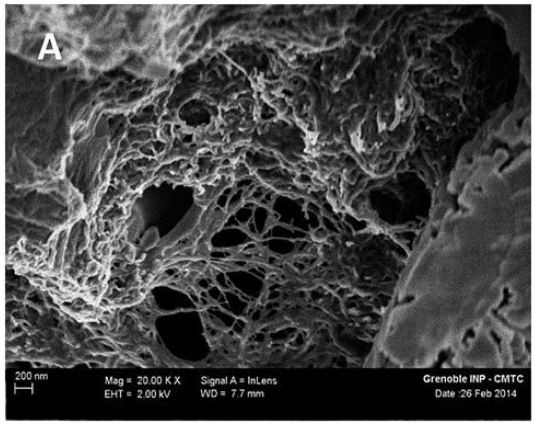
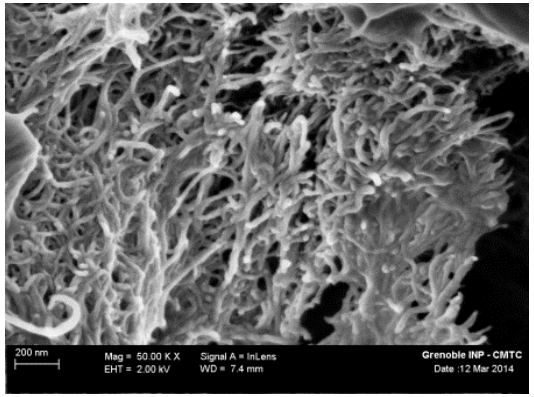
Cite this: *Energy Environ. Sci.*, 2015, 8, 1017

Bioelectrodes modified with chitosan for long-term energy supply from the body

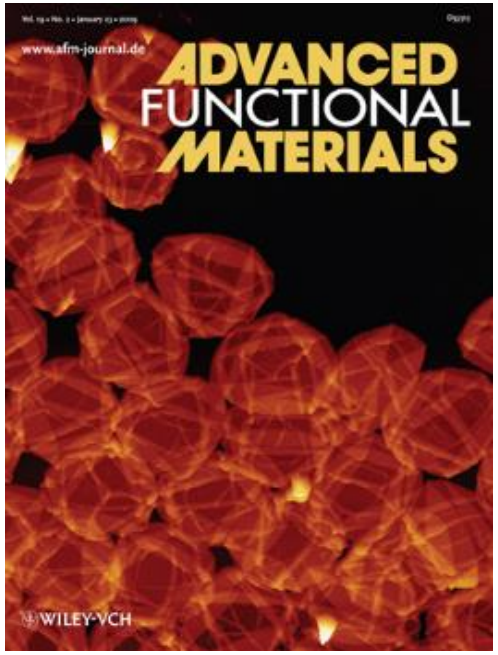
S. El Ichi,[a] A. Zebda,[a] J.-P. Alcaraz,[a] A. Laaroussi,[b] F. Boucher,[a] J. Boutonnat,[c] N. Reverdy-Bruas,[b] D. Chaussy,[b] M. N. Belgacem,[b] P. Cinquin[a] and D. K. Martin*[a]



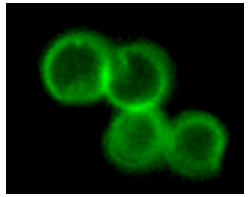
(genepin-crosslinked chitosan) + (MWCNT) + (laccase)



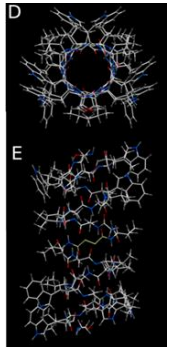
After 167 days of implantation



lipid bilayer



ion channel



19:201-208, 2009

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Cite this: DOI: 10.1039/c9cc05569j

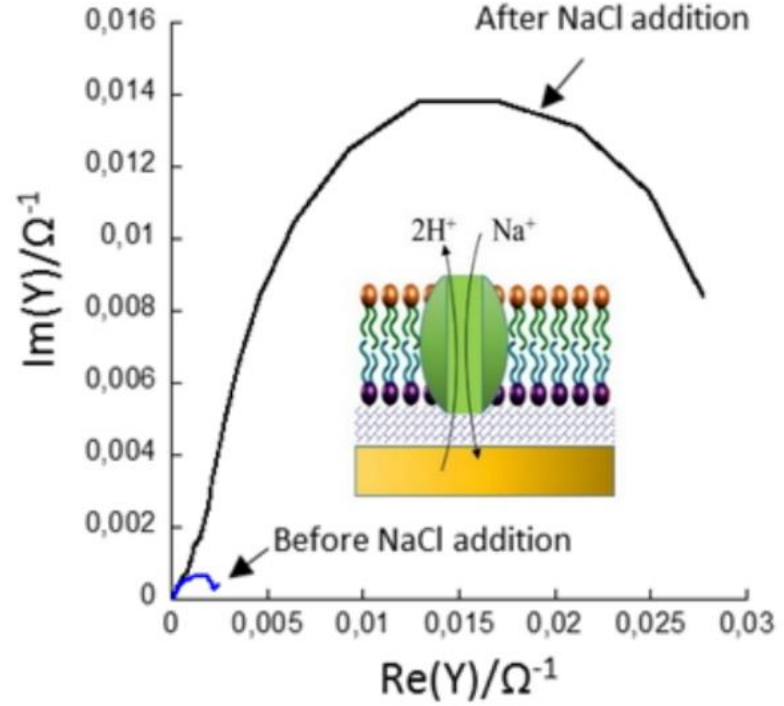
Received 18th July 2019,
Accepted 9th October 2019

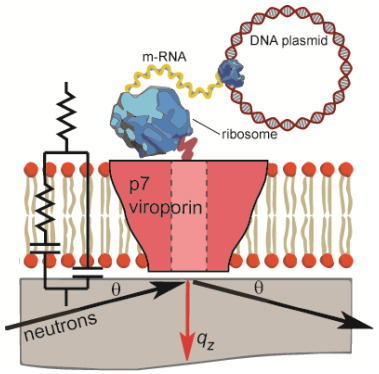
DOI: 10.1039/c9cc05569j

rsc.li/chemcomm

A PANI supported lipid bilayer that contains NhaA transporter proteins provides a basis for a biomimetic biocapacitor†

Awatef Ben Tahar, Abdelkader Zebda,* Jean-Pierre Alcaraz, Landry Gayet, Abderrahim Boualam, Philippe Cinquin and Donald K. Martin *





SCIENTIFIC REPORTS

7: 3399 | DOI:10.1038/s41598-017-03472-8

OPEN

Coupling neutron reflectivity with cell-free protein synthesis to probe membrane protein structure in supported bilayers

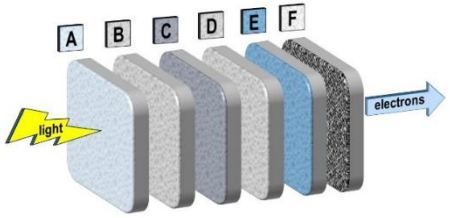
Received: 19 October 2016
Accepted: 16 March 2017
Published online: 13 June 2017

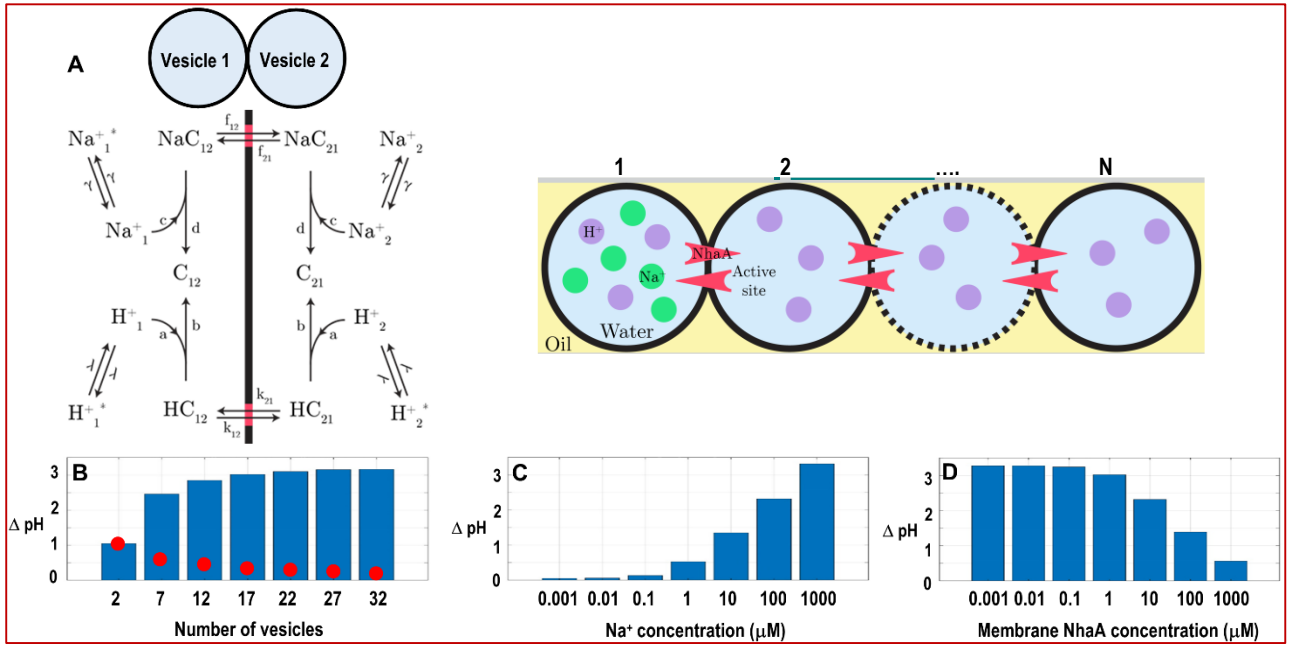
Thomas Soranzo[1,2], Donald K. Martin[3], Jean-Luc Lenormand[2] & Erik B. Watkins[4,5]

Energy systems

4 mW for a device with a volume of 1 ml (4W/kg)

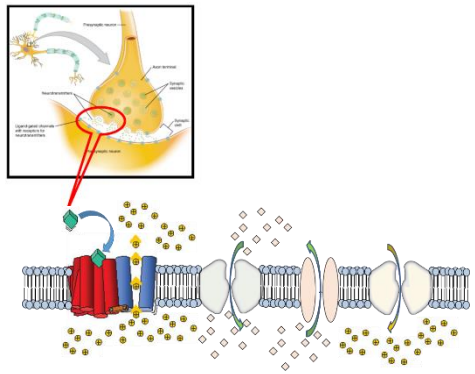
Sensing systems

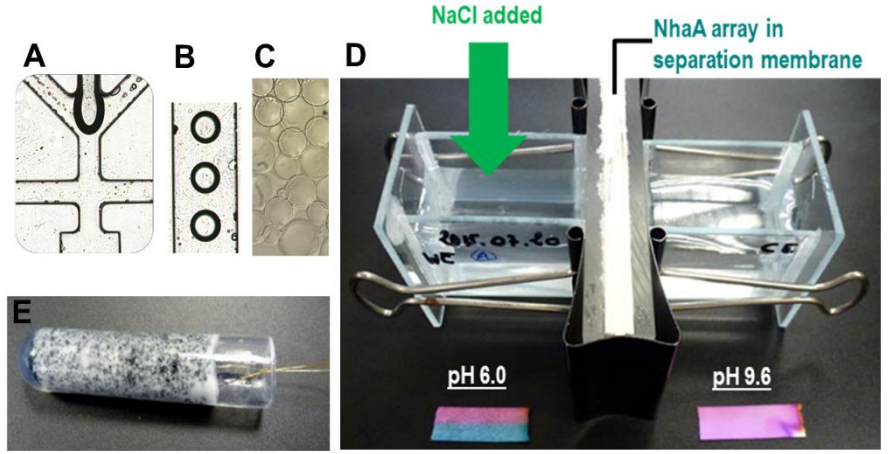




Martin DK, Thelu J, Alcaraz JP, Maccarini M, Zebda A, Cinquin P, Mauri M (2021).
Nanostructured biomimetic neuromorphic system. ***EP21305411***

Therapy systems

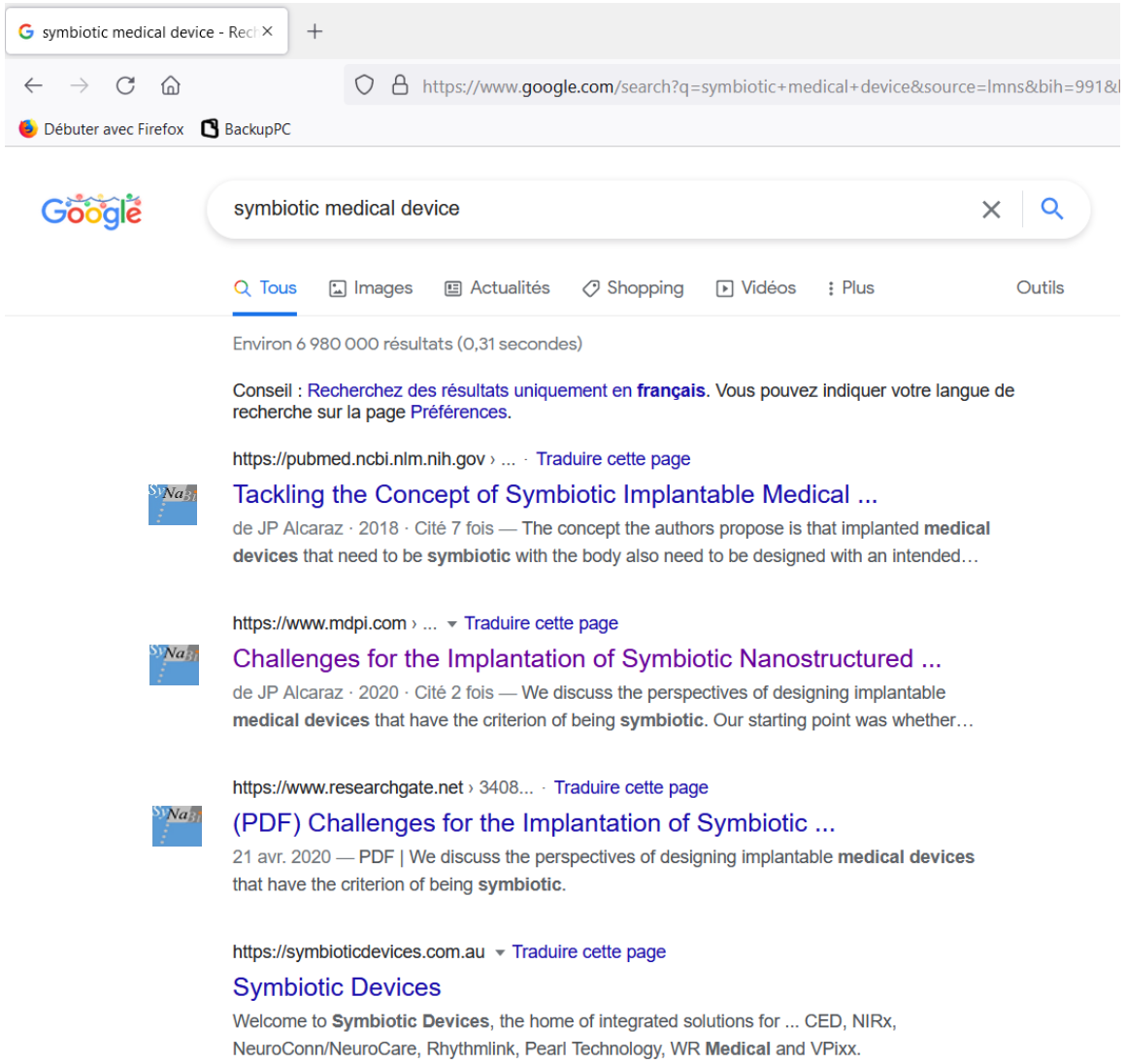


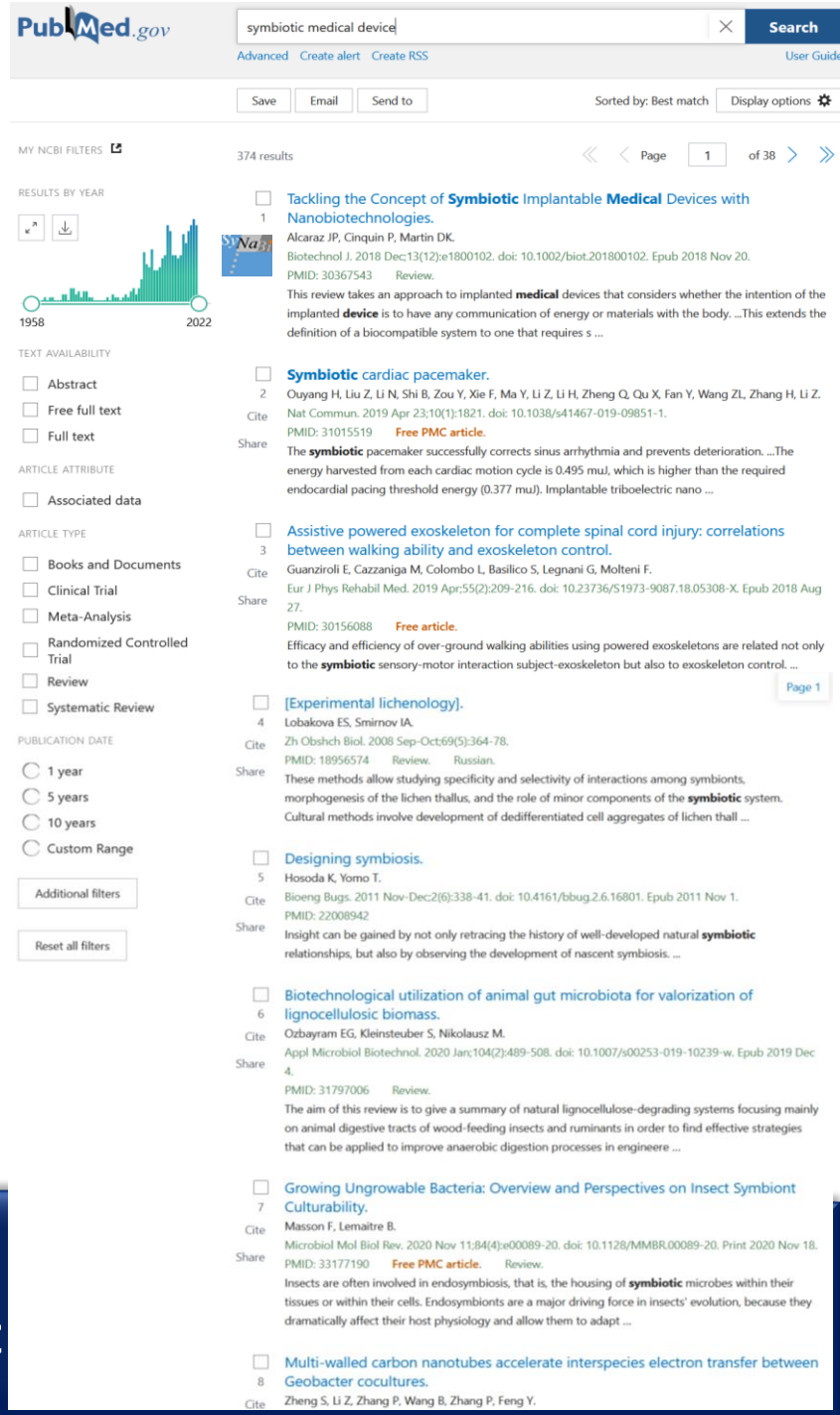


SymDis: Symbiotic Medical Devices ⇨ thematic axes / project examples

… and bioinspired diagnostic and therapeutic systems

- *in vivo* delivery of molecular hydrogen,
- on-chip real-time analysis of secretions from 3D cell cultures





SymDis: Symbiotic Medical Devices ⇨ impact

Current literature is dominated by technology-driven research – there is a need to **re-think** the strategy to solve biocompatibilty and interface problems **by taking** a biological engineering approach to symbiotic medical devices **for addressing** human and ethical needs