REGENERACIÓ CARDÍACA: SOBRE DOGMES, PROVES DE CONCEPTE I NOUS HORITZONS

Bioimpressió 3D

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Unit of Biophysics and Bioenginnering

Març 2019

CardioNet
Grup de Treball en Recerca Bàsica i Translació Clínica de la Societat Catalana de Cardiologia

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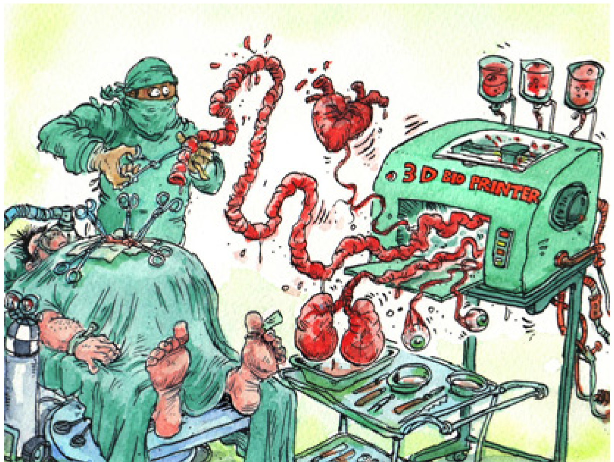
3D bioprinting for cardiac regeneration



>BIOCIENCIA

Más cerca de generar corazones bioartificiales

Una investigación en la que participa el Instituto de Bioingeniería de Cataluña consigue crear injertos de corazón funcionales a partir de células madre. Por **Lidia Montes**

EL FUTURO DE LA BIOINGENIERÍA

Las bioimpresoras abren el camino a la creación de órganos en 3D

Investigadores del IBEC en Barcelona crean tejidos cardiacos a partir de células madre

Los cultivos se pueden transformar en estructuras con formas variadas

¿Y SI TODOS TUVIÉRAMOS UN CORAZÓN DE REPUESTO?

Algunos órganos en 3D podrían estar disponibles en 3 años

http://www.ibecbarcelona.eu/category/ibec-in-the-media/

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3D bioprinting for cardiac regeneration

1. Myths:
   - 3DBP is a very complex technique
   - 3DBP technology is very expensive
   - ECM bioinks are not idoneous
   - Cells damage in the BP process
2. Proof of concepts:
   - Cardiac patches
   - Blood vessels
3. New horizons:
   - Bionics
4. Take-home messages

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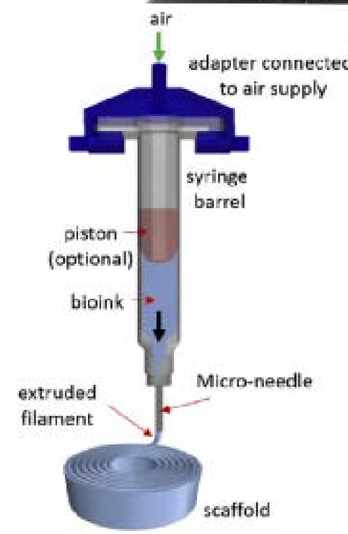
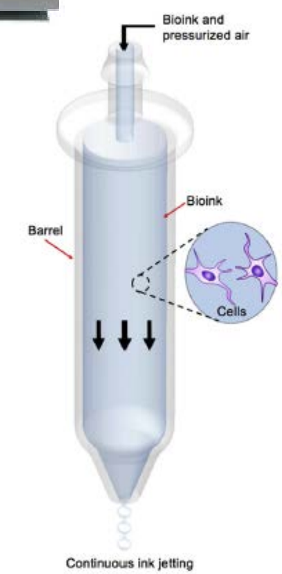
Myth 1: 3DBP is a very complex technique





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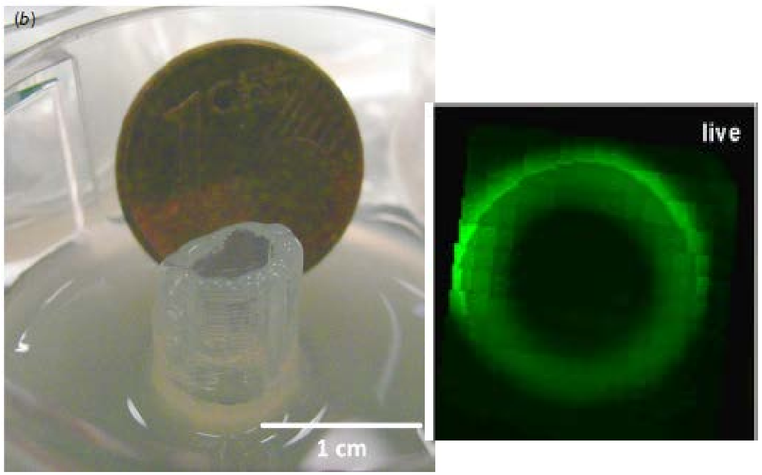
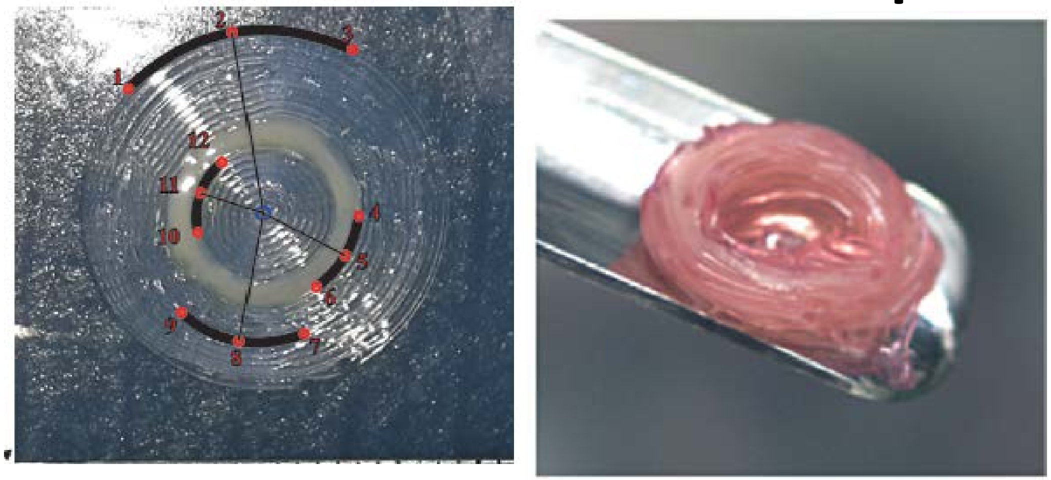


Cells encapsulated



Direct cell printing

Advanced Drug Delivery Reviews 132 (2018) 252–269

Contents lists available at ScienceDirect

Advanced Drug Delivery Reviews

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

ELSEVIER

3D bioprinting for cardiovascular regeneration and pharmacology☆

Haitao Cui [a], Shida Miao [a], Timothy Esworthy [a], Xuan Zhou [a], Se-jun Lee [a], Chengyu Liu [b], Zu-xi Yu [b], John P. Fisher [c,d], Muhammad Mohiuddin [e], Lijie Grace Zhang [a,f,g,h,*]

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Myth 2: 3DBP is very expensive

regenHU BIOSYSTEM ARCHITECTS

200-300k€

IBEC shared equipment

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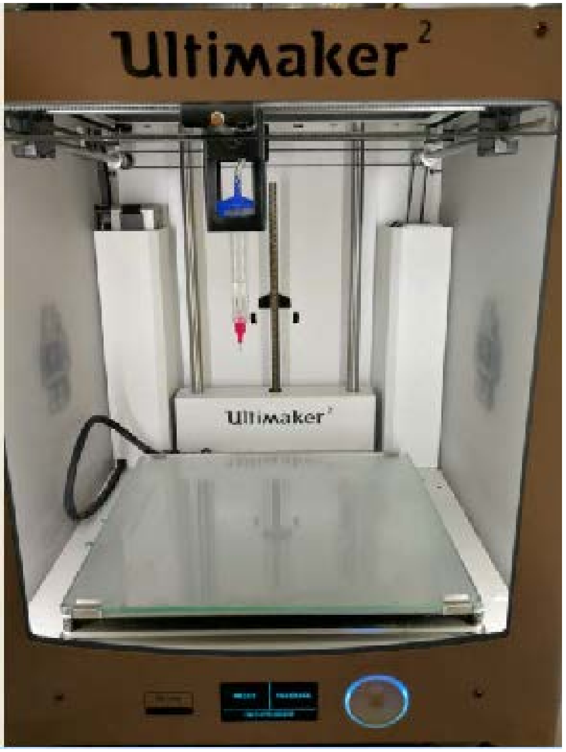

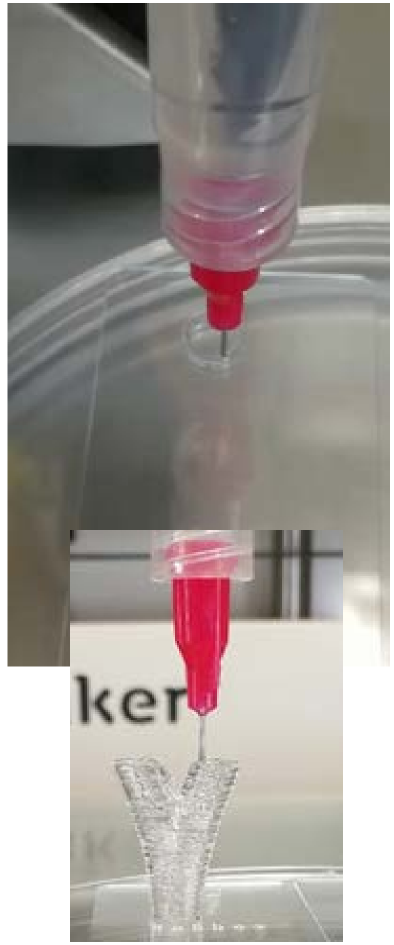

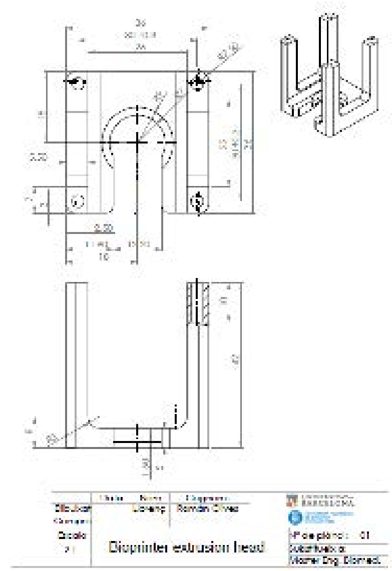


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;TYPE:WALL-OUTER
G11
G1 F450 X111.568 Y108.996 Z0.253 E0.65356
G1 X112.04 Y109.05 Z0.258 E0.68207
G1 X112.225 Y109.103 Z0.26 E0.69361
G1 X112.552 Y109.221 Z0.263 E0.71447
G1 X112.918 Y109.427 Z0.267 E0.73967
G1 X113.241 Y109.691 Z0.271 E0.7647
G1 X113.502 Y109.979 Z0.275 E0.78803
G1 X113.732 Y110.34 Z0.279 E0.81371
G1 X113.882 Y110.7 Z0.283 E0.83711
G1 X113.908 Y110.783 E0.84233
G1 X113.988 Y111.118 Z0.287 E0.863
.
.
.
G1 X115.693 Y111.158 E227.42026
G1 X115.692 Y111.157 E227.42035
G0 F900 X115.662 Y111.551
G0 X115.716 Y111.983
G0 X115.833 Y112.349
G0 X115.867 Y112.414
G10
G0 X115.097 Y112.656
G0 X107.927 Y110.394
G0 X107.079 Y110.48
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M107
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;End of Gcode
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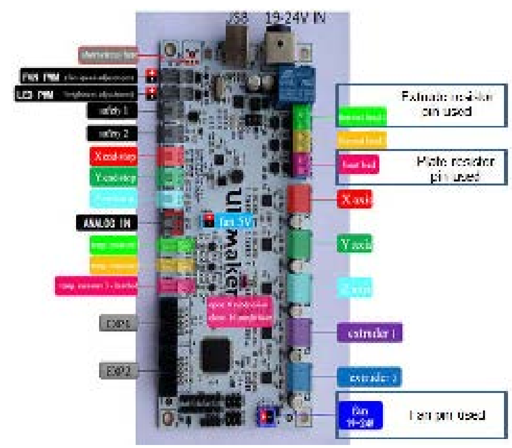

3D printer -> bioprinter
- Ultimaker 2 (2k€)
- Syringe extruders (1k€)
- HW and SW adaption

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Myth 2: 3DBP is very expensive

- Commercial 3D bioprinter:
  - Ready-to-use bioprinter from start
  - Official help/support* (spin-offs)
  - Medium to high effort to customize
  - Expensive
- Open source 3D printer adaption:
  - Initial time-consuming development
  - No official help/support
  - Geek community -> huge help
  - Easier to customize
  - Cheaper solution* (initial time inversion)

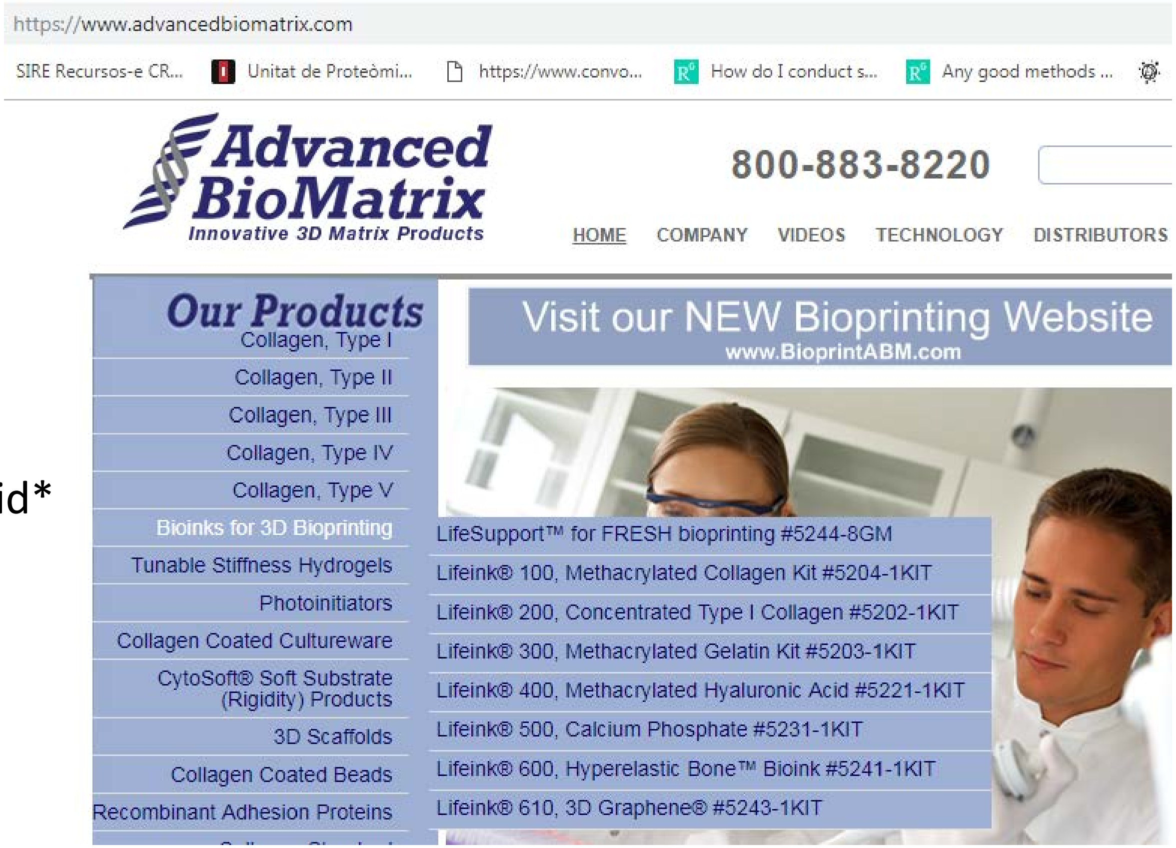
Myth 3: ECM bioinks are not idoneous

Natural bioinks:

- Alginate
- Gellan gum
- Silk
- Agarose
- Chitosan
- Gelatin*
- Collagen*
- Hyaluronic acid*

Synthetic bioinks:

- PCL
- PEG
- Pluronic



Gungor-Ozkerim. *Bioinks for 3D bioprinting.* Biomater Sci. 6. 2018

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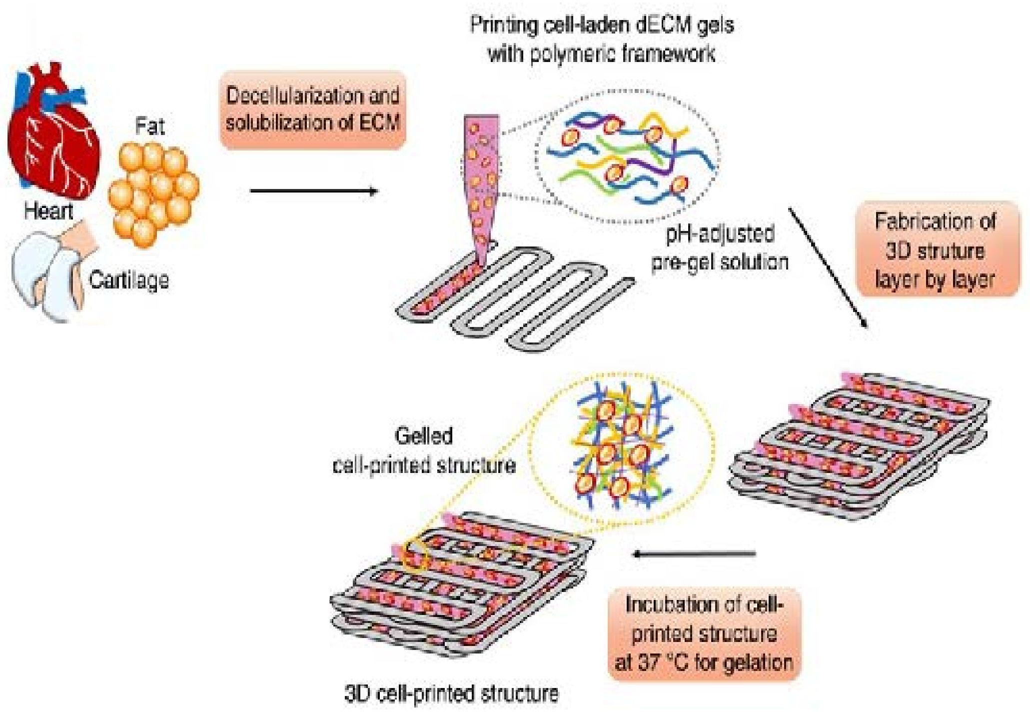
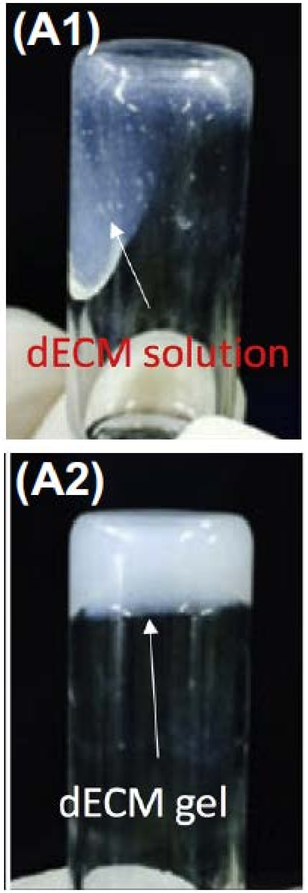


Zhang. 3D Bioprinting for Tissue and Organ Fabrication. Annals of Biomedical Engineering, 2017



Pati. *Printing three-dimensional tissue analogues with decellularized extracellular matrix.* Nat. Comm. 5. 2014.

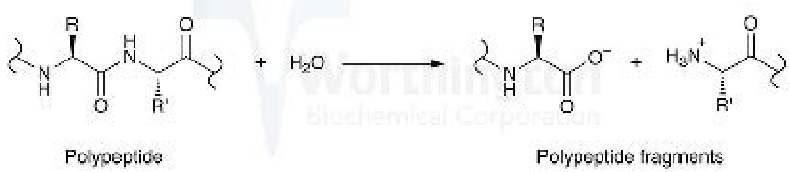
Myth 3: ECM bioinks are not idoneous

Published in final edited form as:
Methods Mol Biol. 2014 ; 1181: 69–81. doi:10.1007/978-1-4939-1047-2_7.

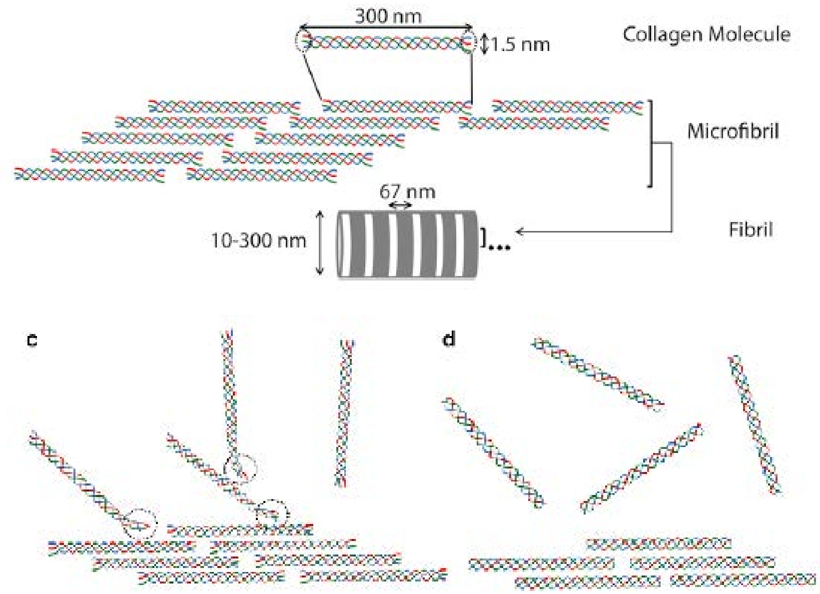
Native Cardiac Extracellular Matrix Hydrogels for Cultivation of Human Stem Cell-Derived Cardiomyocytes

Donald O Freytes[1,2], **John D O'Neill**[1], **Yi Duan-Arnold**[1], **Emily Wrona**[2], and **Gordana Vunjak-Novakovic**[1,#]
[1]Columbia University, Department of Biomedical Engineering, New York, NY 10032
[2]New York Stem Cell Foundation, New York, NY 10023

4. After lyophilization, mix the ECM powder with pepsin in a ratio of 10:1 w/w per 100 mL 0.01 N HCl. Otherwise, for long-term storage at room temperature, wrap the cap of the tube containing the lyophilized cardiac ECM powder with parafilm.
5. Digest the solution for 48 hrs at room temperature under constant stirring using a magnetic stir bar and plate until the solution becomes viscous with no visibly undigested granules.



R and R' = Leu, Phe, Trp, and Tyr (preferred); also hydrolyzes esters



Biophysical *Journal*
Article

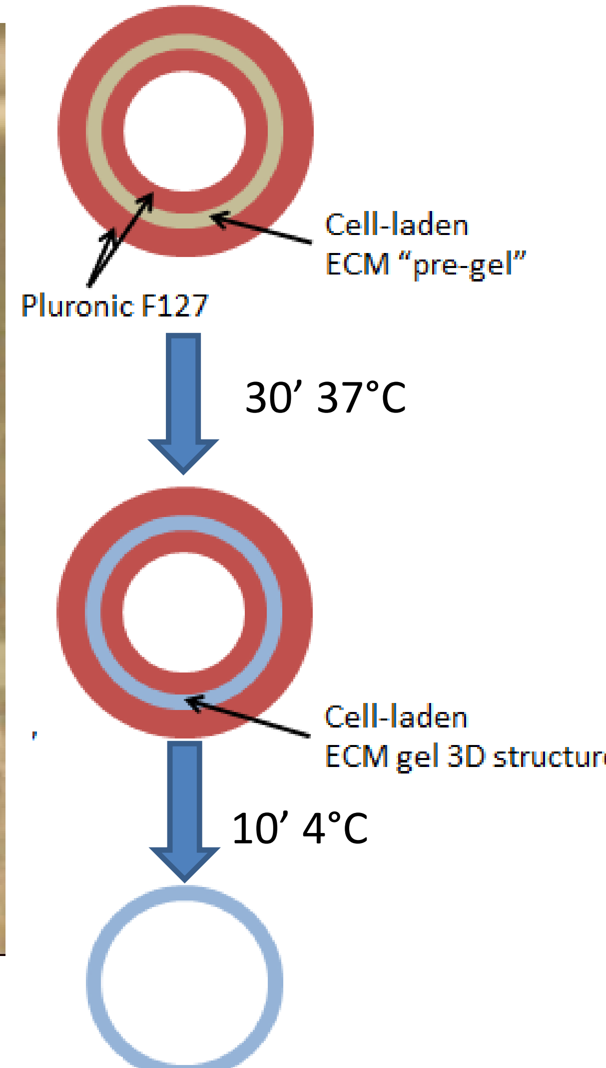
Intact Telopeptides Enhance Interactions between Collagens

Marjan Shayegan,[1] Tuba Altindal,[2,3] Evan Kiefl,[3] and Nancy R. Forde[1,2,3,*]
[1]Department of Chemistry, [2]Department of Molecular Biology and Biochemistry, and [3]Department of Physics, Simon Fraser University, Burnaby, Canada

Myth 3: ECM bioinks are not idoneous

Myth 4: Cells damage in the BP process

dECM bioink printed at atmospheric pressure



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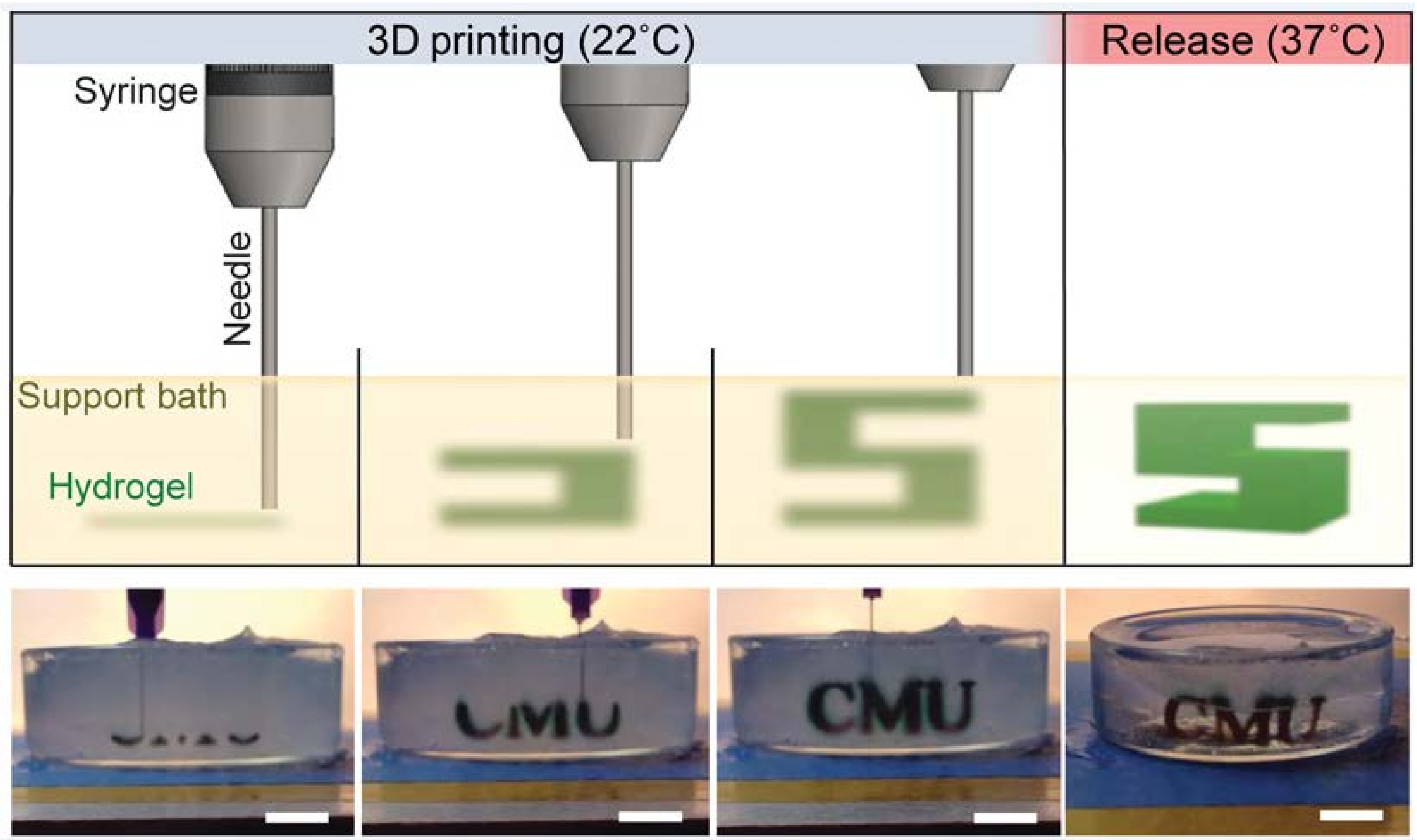

Hinton. *Three-dimensional printing of complex biological structures by freeform reversible embedding of suspended hydrogels.* Sci. Adv. 1. 2015

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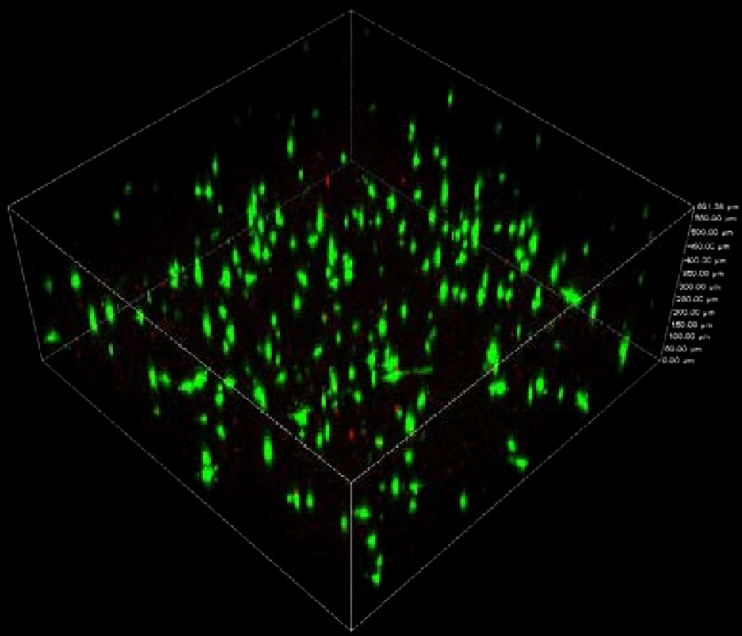

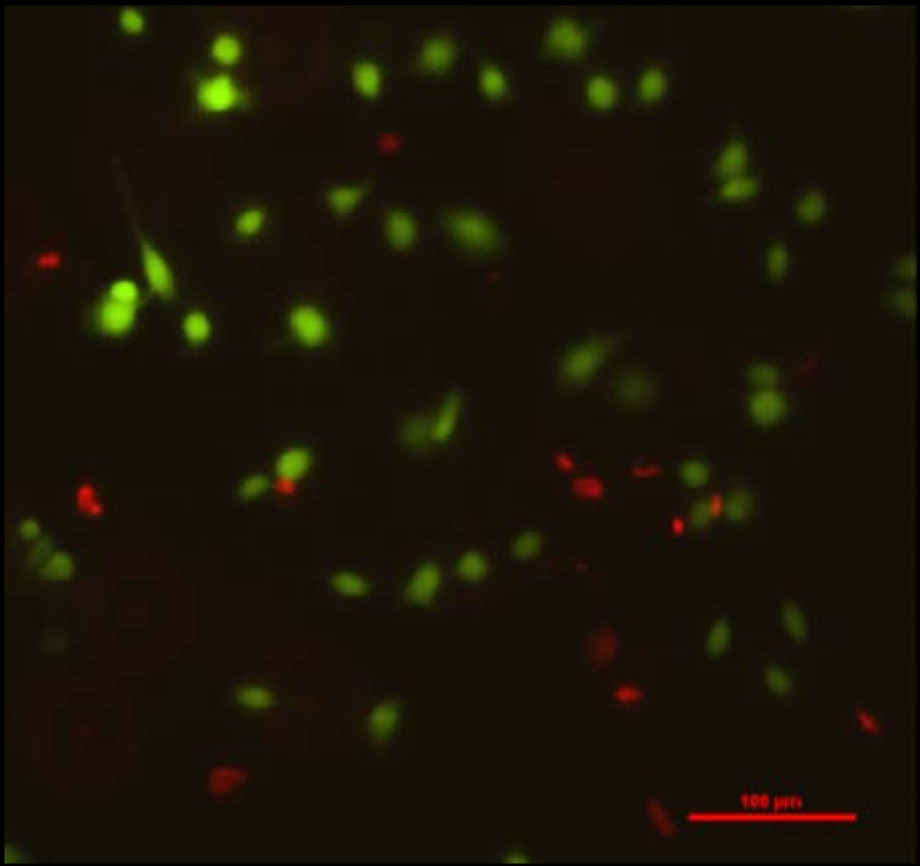

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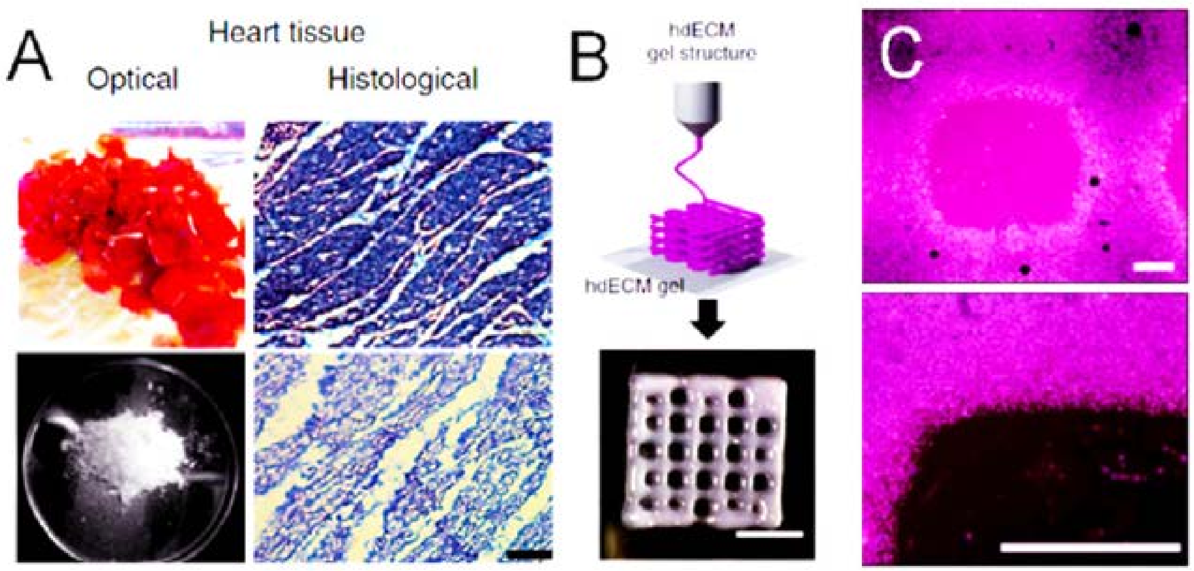
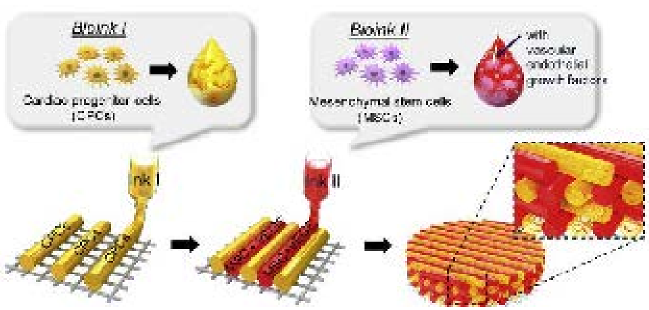
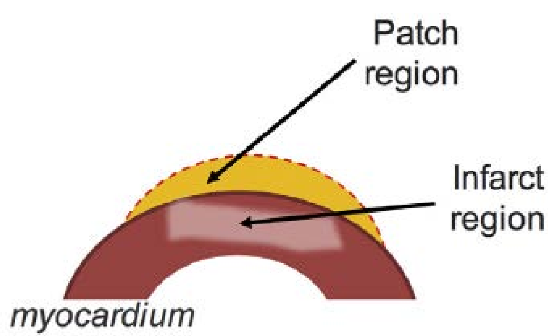
Proof of concepts: Cardiac patches

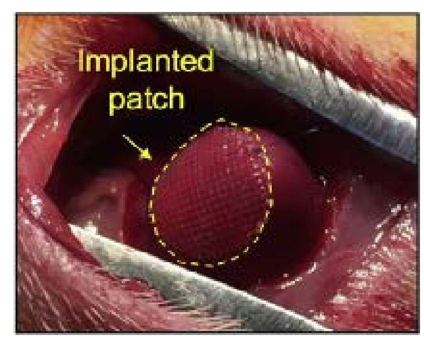


Pati. *Printing three-dimensional tissue analogues with decellularized extracellular matrix bioink.* Nat. Comm. 5. 2014

Jang. *3D printed complex tissue construct using stem cell-laden decellularized extracellular matrix bioinks for cardiac repair.* Biomaterials. 112. 2017







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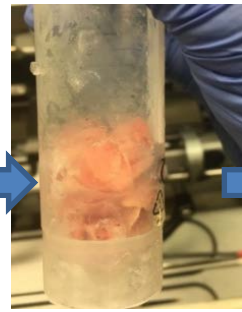
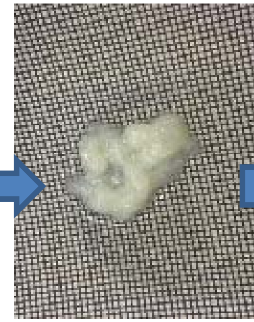
Proof of concepts: Cardiac patches





Decellularization

Powder

Digestion in HCl

pH neutralization

Thermal crosslinking

Hydrogel

Becker. *Processing of Human Cardiac Tissue Towards Extracellular Matrix Self-assembling Hydrogel for In Vitro and In Vivo Applications.* JOVE. 130. 2017

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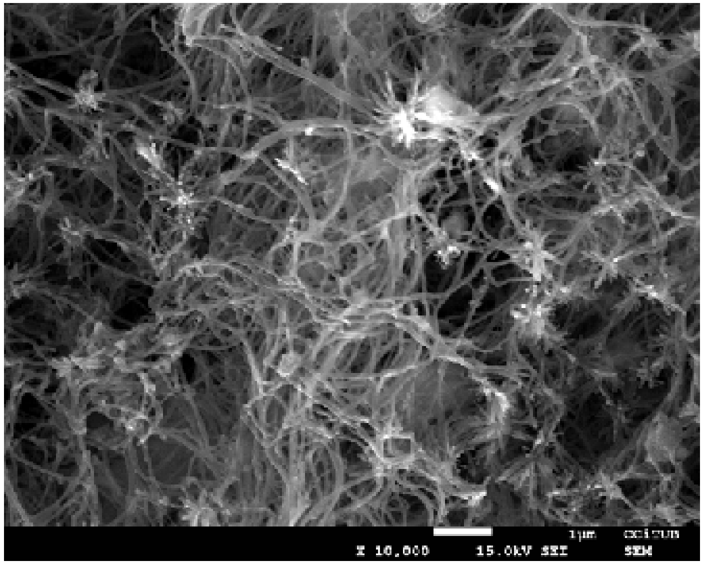
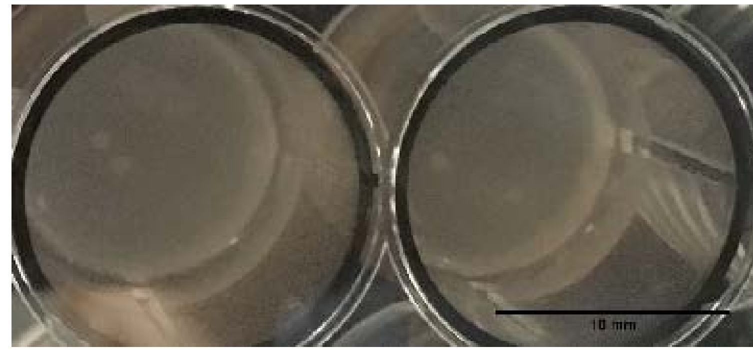
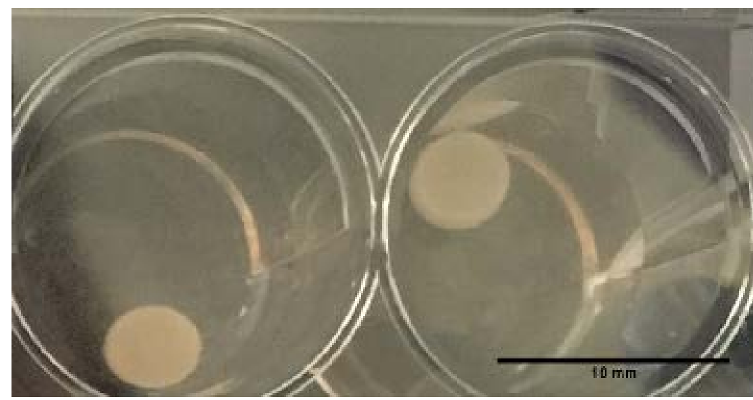


Subcutaneous Adipose Tissue
Mesenchymal Stem Cells (subATMSC)

IGTP
Germans Trias i Pujol Research Institute



48h



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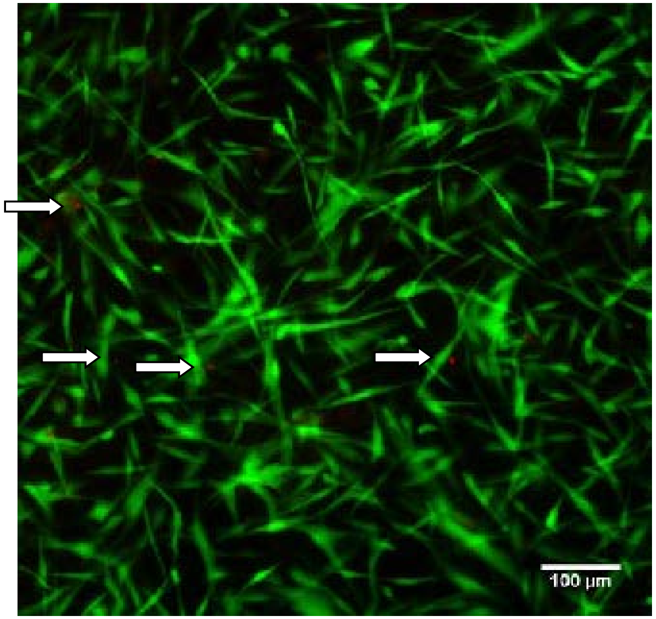
Proof of concepts: Cardiac patches



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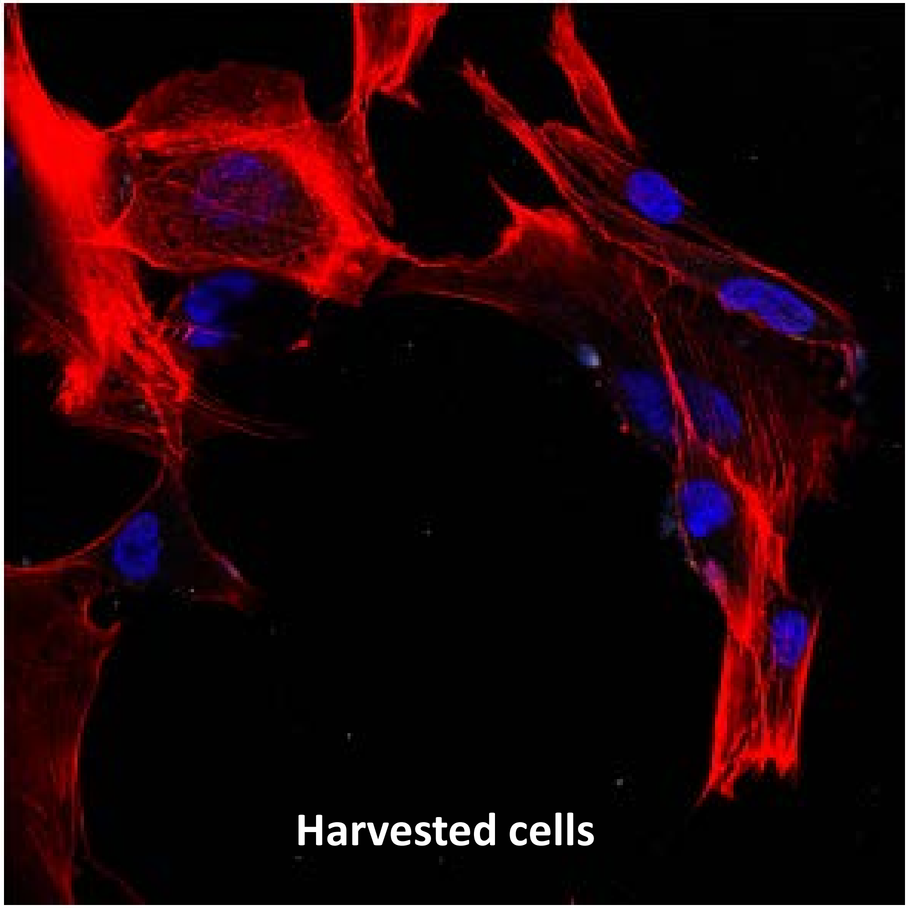

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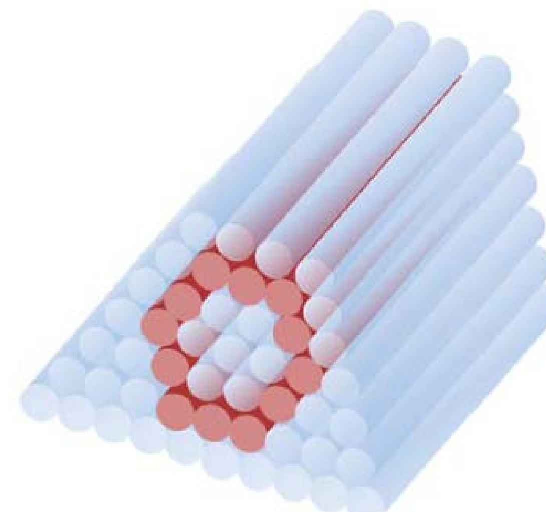
Proof of concepts: Blood vessels

HUMACYTE

Cell Stem Cell. 2018 March 01; 22(3): 340–354. doi:10.1016/j.stem.2018.02.009.

Vascular tissue engineering: progress, challenges, and clinical promise

H-H Greco Song[1,2,3,6], **Rowza T Rumma**[1,4,6], **C Keith Ozaki**[4], **Elazer R Edelman**[1,5], and **Christopher S Chen**[2,3,*]



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Proof of concepts: Blood vessels

High-concentration Rat tail type I collagen

PROTOCOL

Preparation of ready-to-use, storable and reconstituted type I collagen from rat tail tendon for tissue engineering applications

Navneeta Rajan[1], Jason Habermehl[1], Marie-France Coté[1], Charles J Doillon[2–4] & Diego Mantovani[1,4]

Silk fibroin extracted from silkworm cocoons

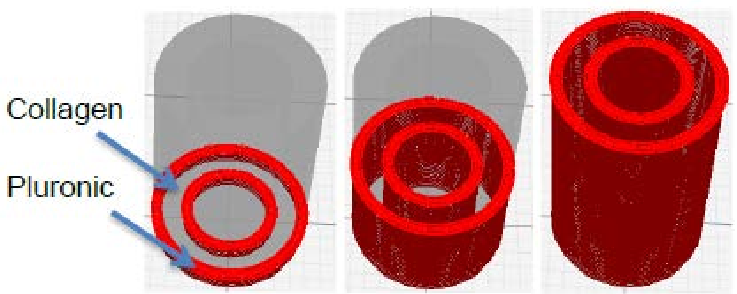
PROTOCOL

Materials fabrication from *Bombyx mori* silk fibroin

Danielle N Rockwood, Rucsanda C Preda, Tuna Yücel, Xiaoqin Wang, Michael L Lovett & David L Kaplan

Nature Protocols

Proof of concepts: Blood vessels



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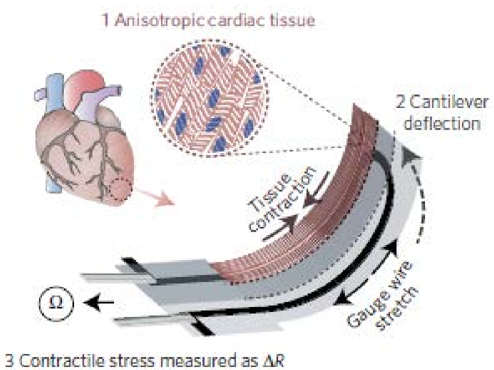
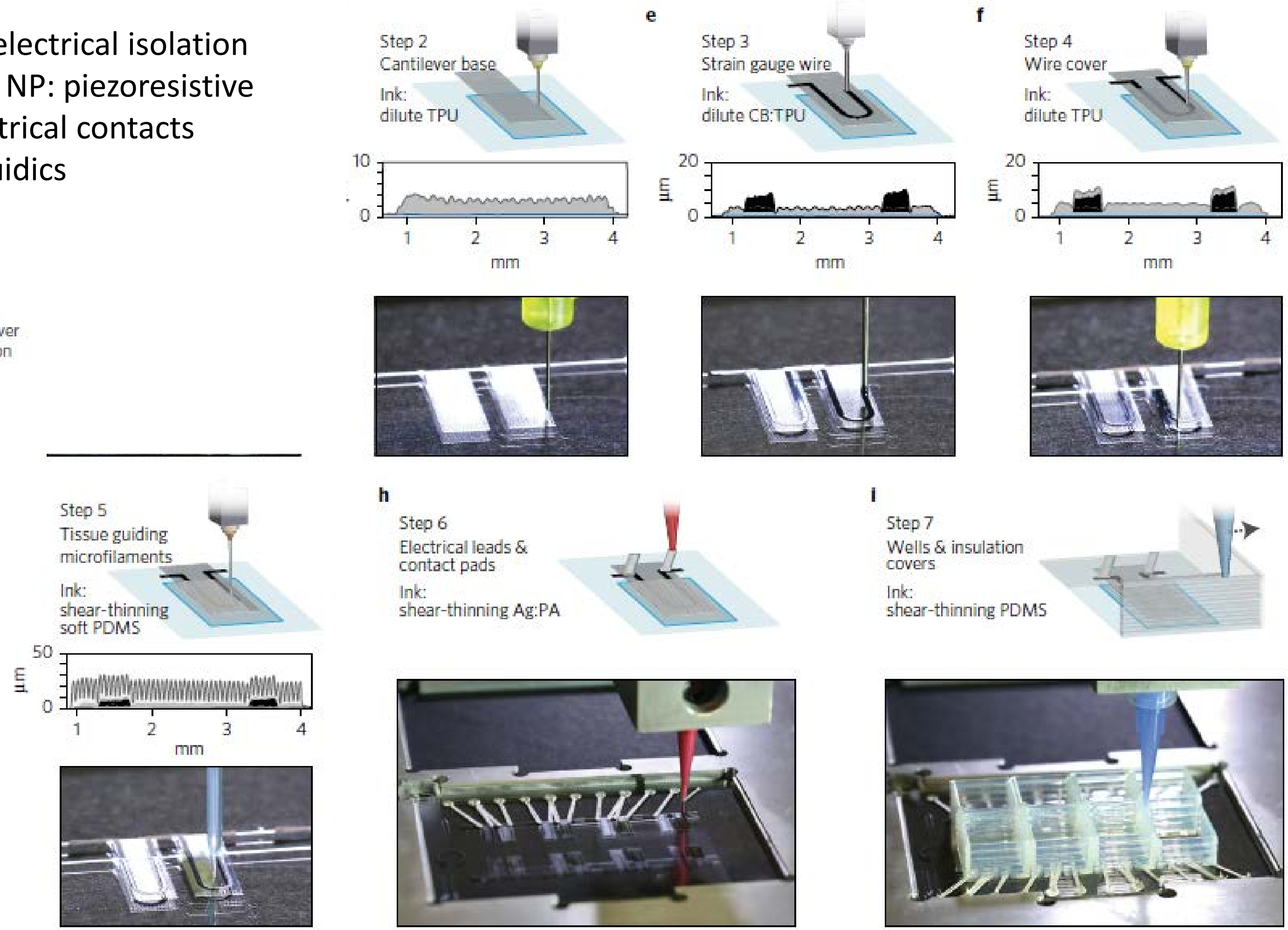
New Horizons: Bionics

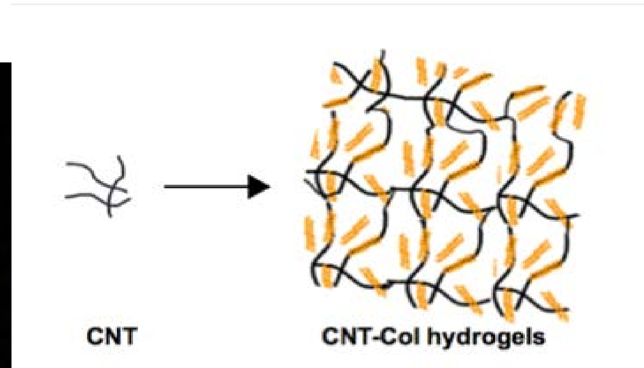
Polyurethane: structural, electrical isolation
Polyurethane with carbon NP: piezoresistive
Polyamide and silver: electrical contacts
PDMS: structural, microfluidics

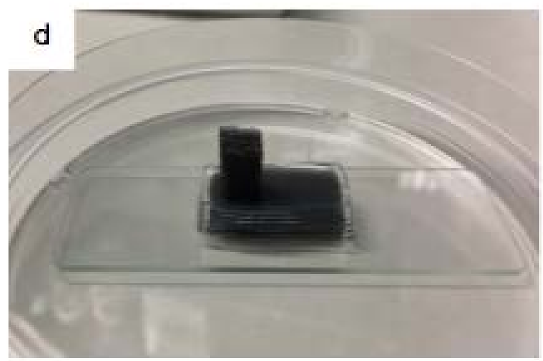




Lind. *Instrumented cardiac microphysiological devices via multimaterial three-dimensional printing.* Nature Materials 16. 2017

New Horizons: Bionics





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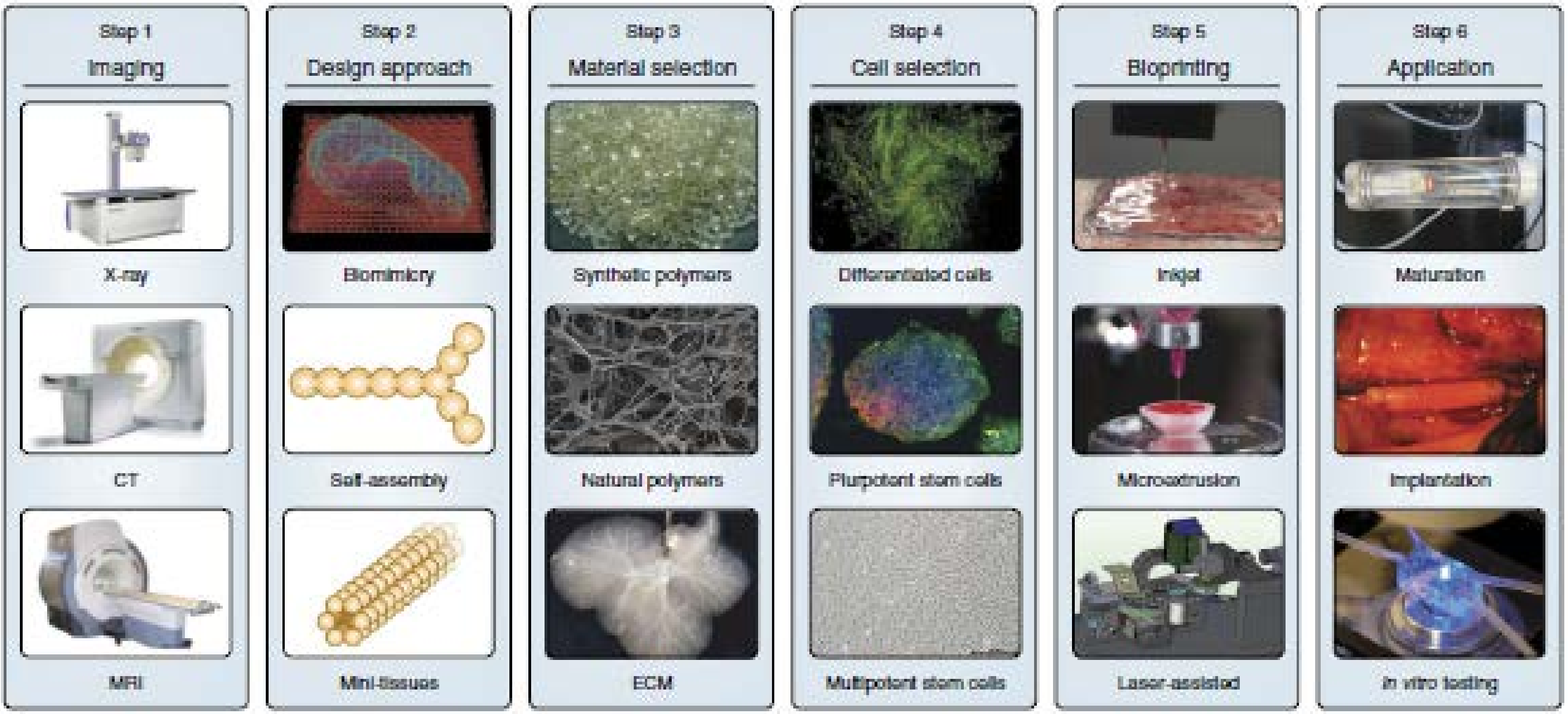
3D Bioprinting could be useful for you



Murphy. *3D bioprinting of tissues and organs.* Nature Biotechnology 32. 2014

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Efforts should be focused on bioinks

https://acell.com/micromatrix/

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MICROMATRIX®

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ACell's Wound Devices:

- Contain epithelial basement membrane and numerous collagens
- Non-crosslinked wound management scaffold
- Complement standard of care

MicroMatrix®

Indications for Use

MicroMatrix® is intended for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, skin tears), and draining wounds. The device is intended for one-time use.

View Instructions for Use

Collaboration and interdisciplinarity

UBB "Bioprinting team"

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REGENERACIÓ CARDÍACA: SOBRE DOGMES, PROVES DE CONCEPTE I NOUS HORITZONS

Bioimpressió 3D

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THANK YOU

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