Advanced Technologies for Heart Tissue Engineering

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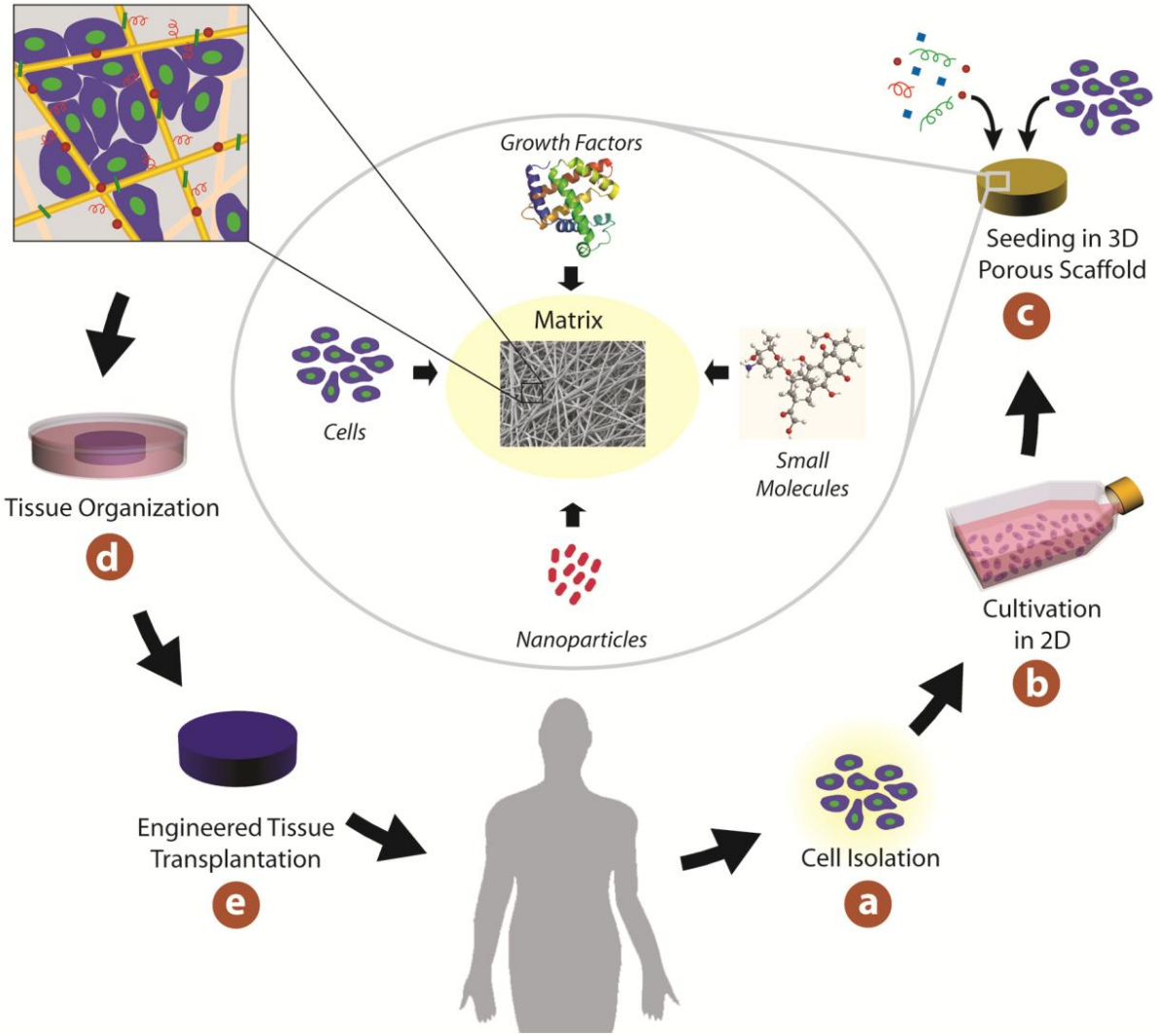
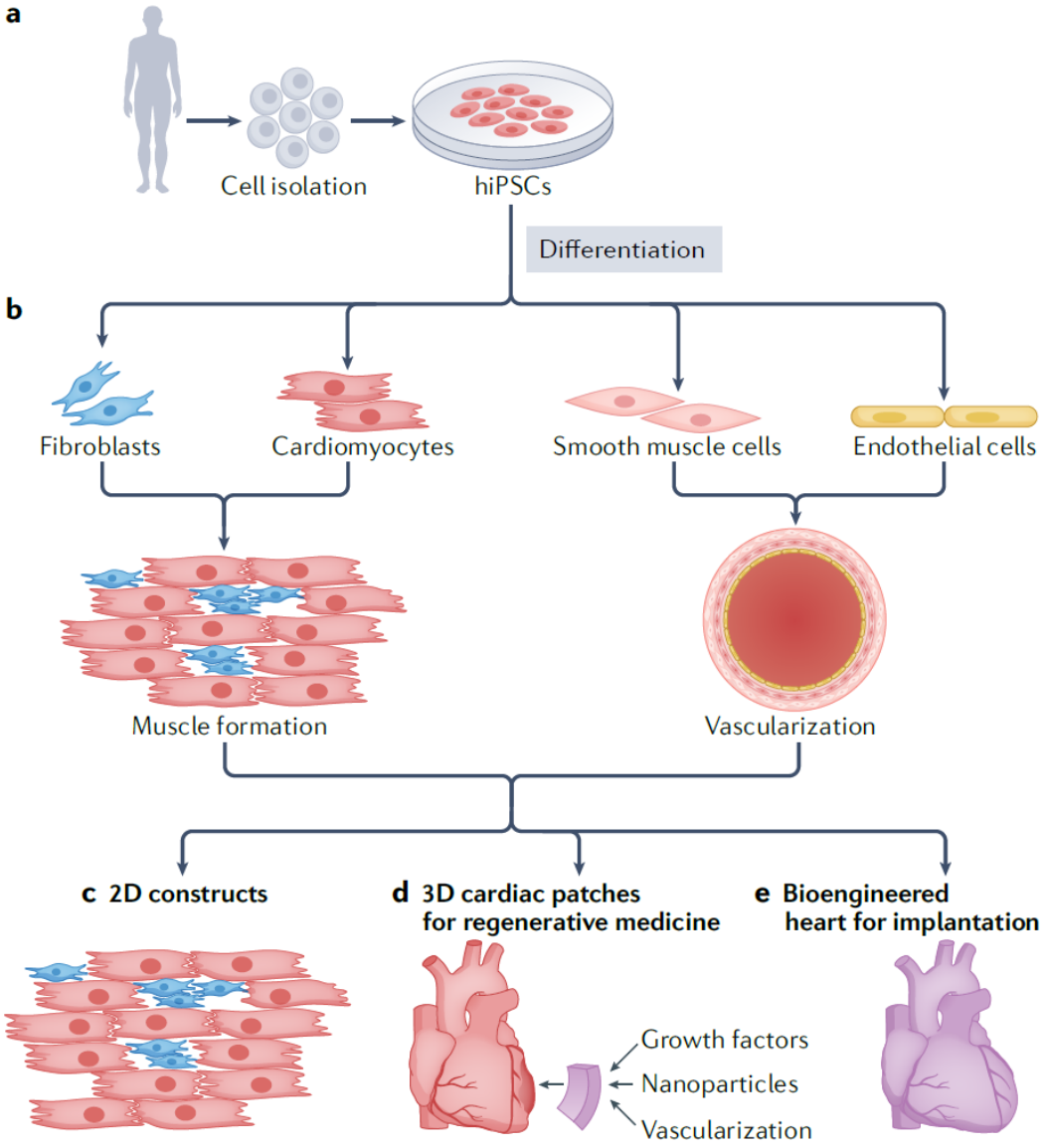
CRS 2025

Tissue engineering- the concept



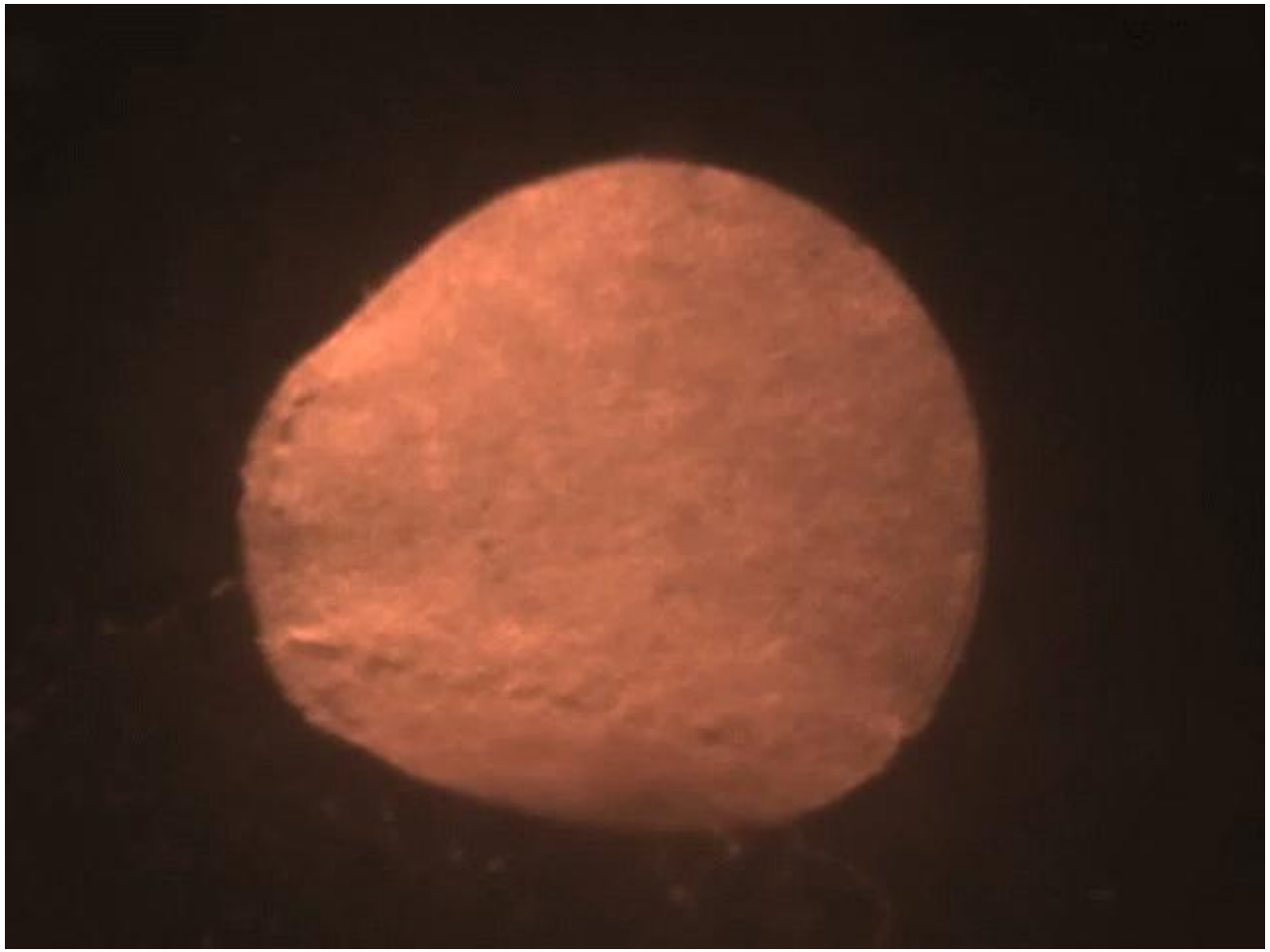
Dvir T., Timko BP., Kohane DS., Langer R. *Nature Nanotechnology*. 2010

Cardiac tissue engineering



Yadid M., Oved H., Silberman E., Dvir T. *Nature Reviews Cardiology*. 2021

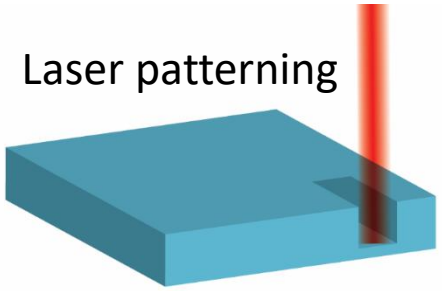
Engineered heart tissues



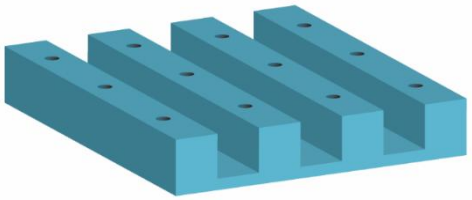
Fleischer et al. *Biomaterials.* 2013
Fleischer et al. *Biotechnol. Bioeng.* 2014
Fleischer et al. *Nanotechnology*. 2015
Shevach et al. *J. Mater. Chem B*. 2013
Fleischer*,Shevach*, Feiner*, Dvir. *Nanoscale*. 2014
Shevach et al. *Nano Letters*. 2014
Fleischer et al. *PNAS*. 2017

Bottom-up approach to assemble thick cardiac patches

Laser patterning

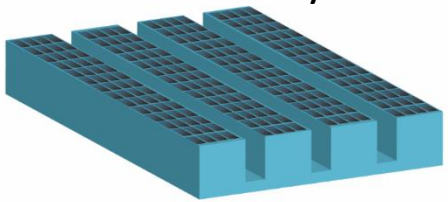


Grooved layer



Cardiac cells

Channel+ Honeycomb



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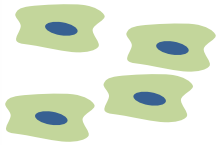
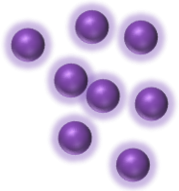
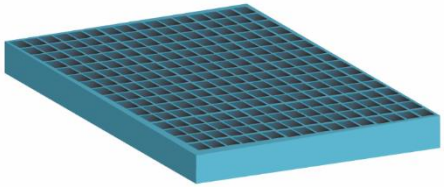


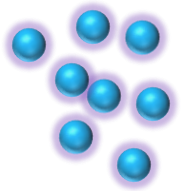
VEGF particles



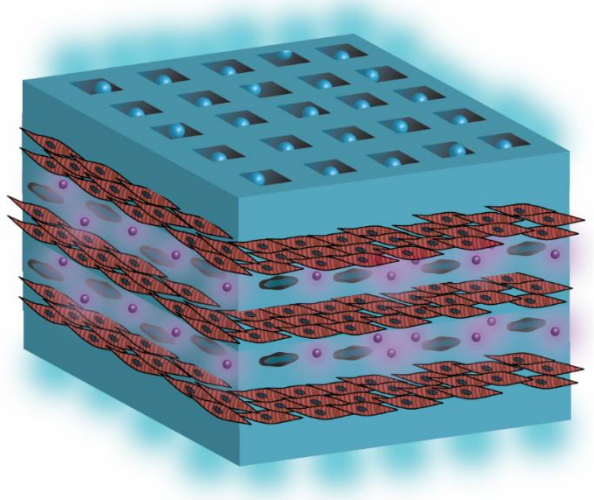
Honeycomb

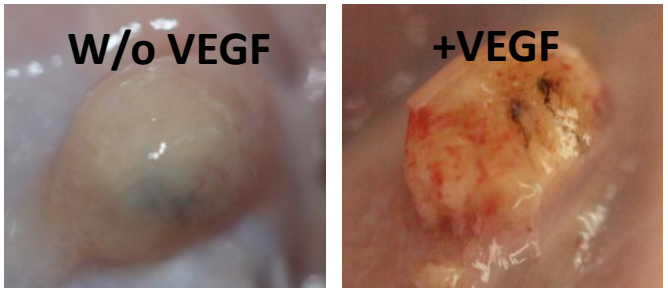


DEX particles



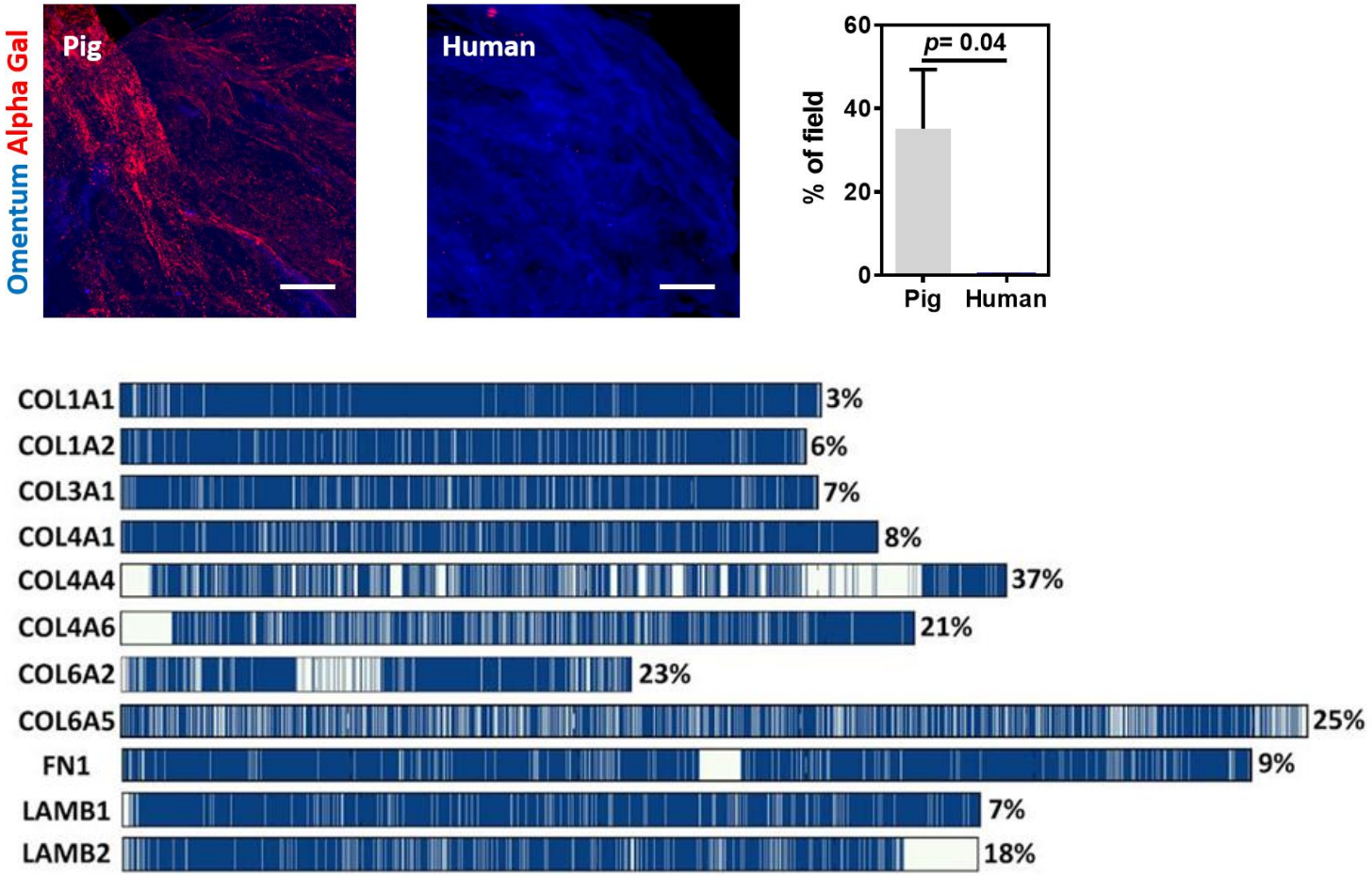
Assembly just prior to transplantation





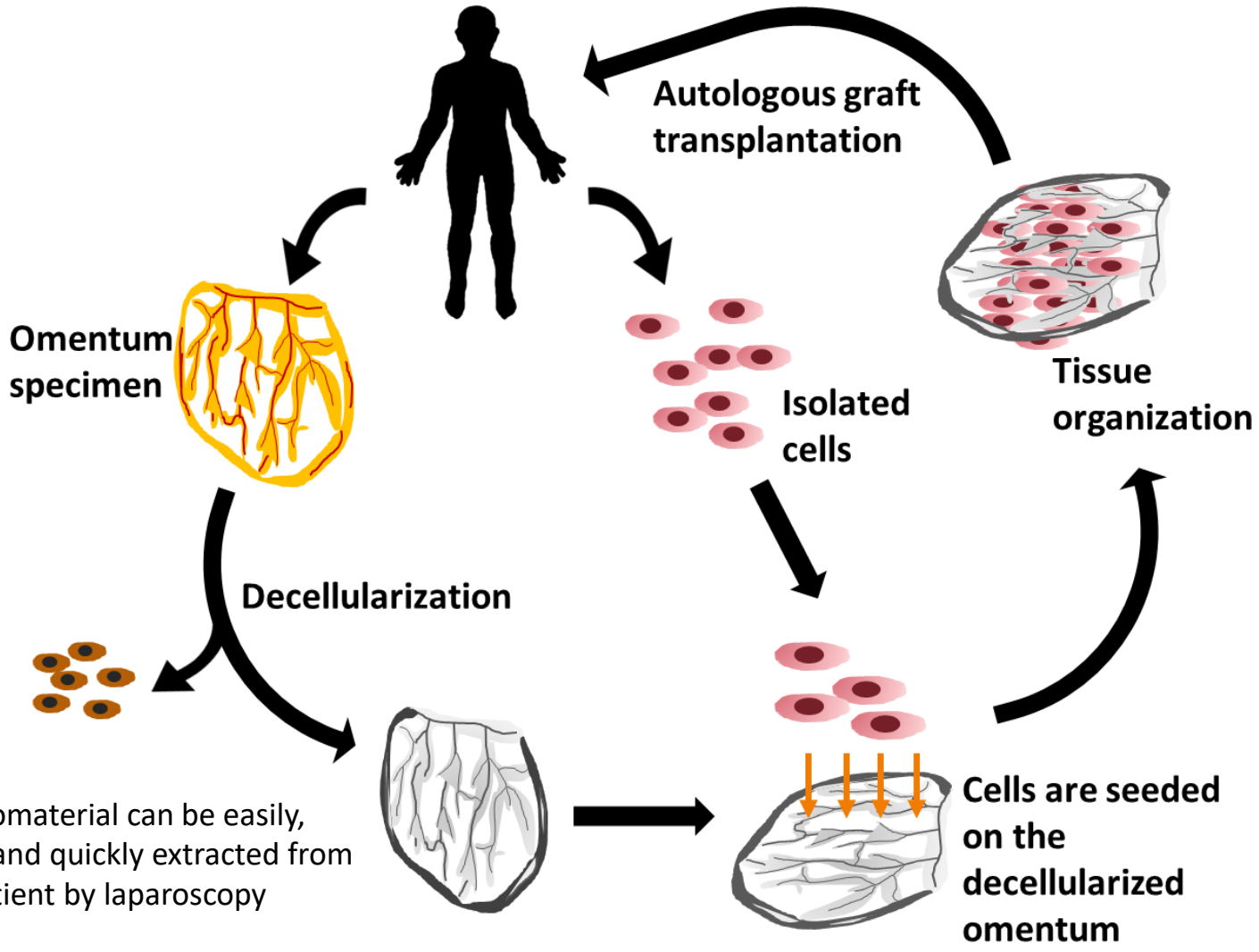
Fleischer et al. *PNAS.* 2017

Immune response to pigs' matrices



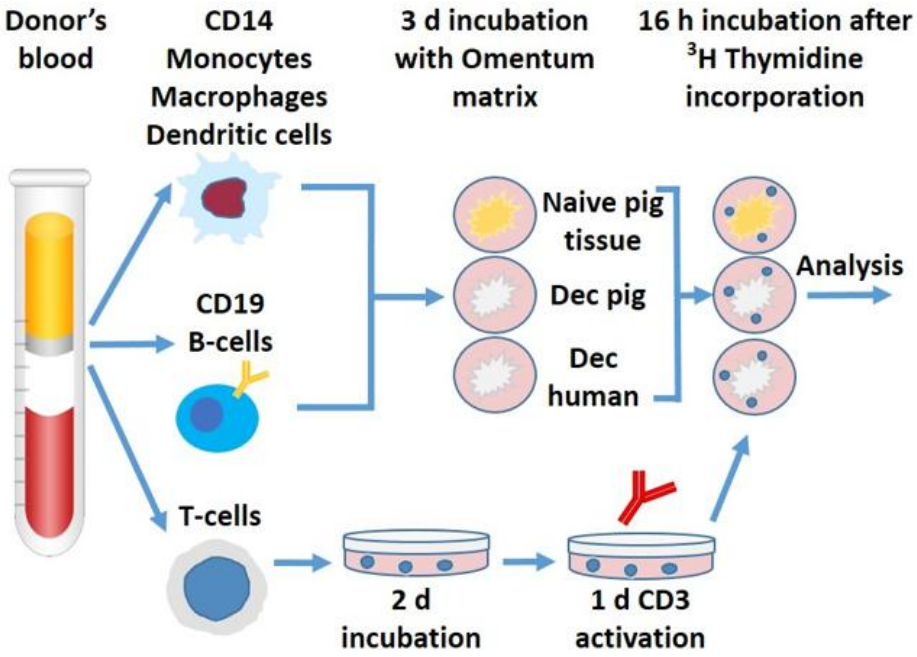
Edri et al. *Advanced Materials*. 2018

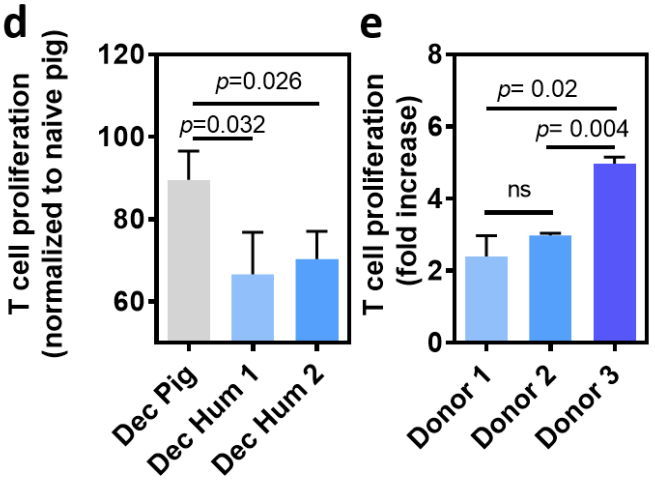
Autologous matrix- The concept



Shevach et al. *Biofabrication*, 2014
Soffer-Tsur et al. *Biofabrication.* 2014

Immune response to matrices

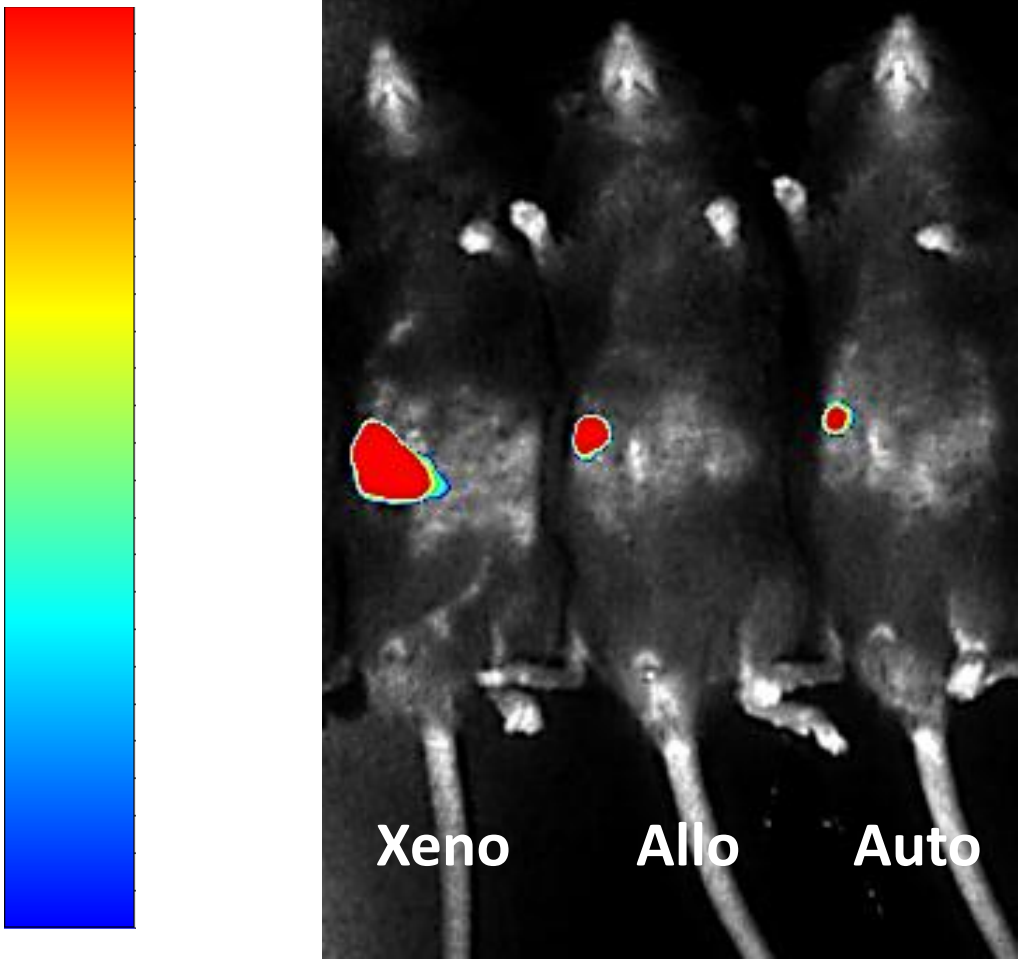




W Dan Peer, TAU

Edri et al. *Advanced Materials*. 2019

In vivo immune response

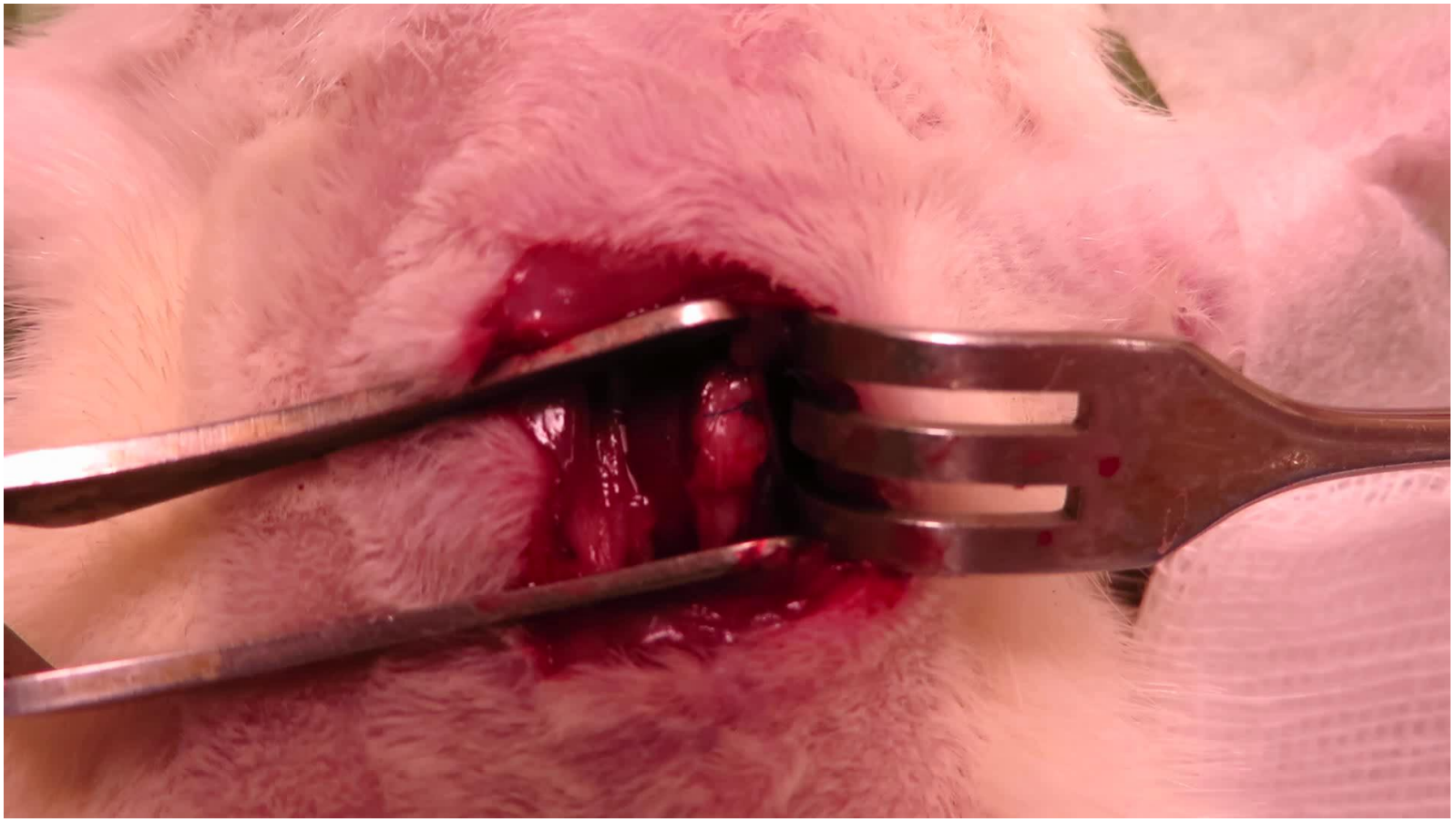


ROS production

W Doron Shabat, TAU

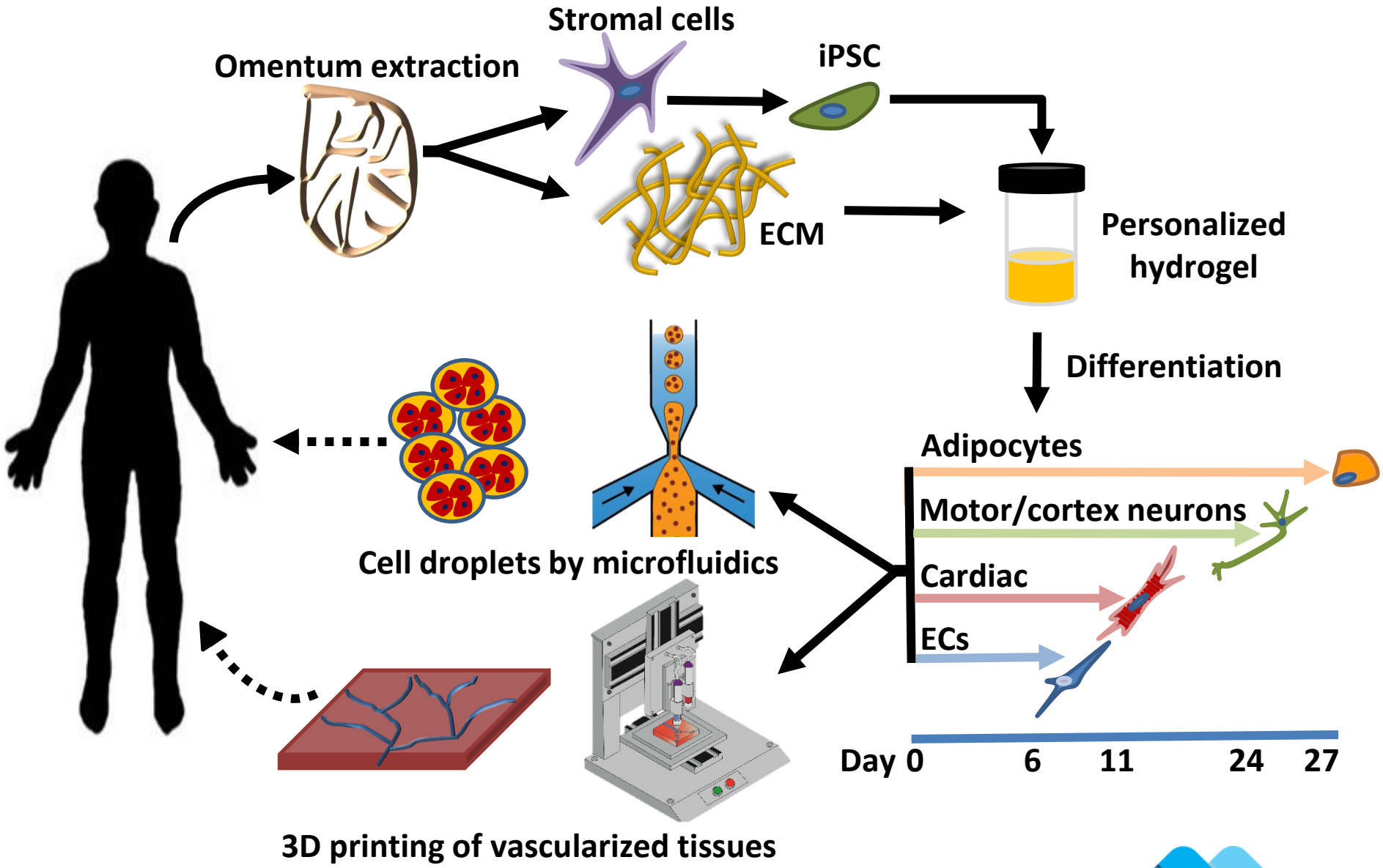
Edri et al. *Advanced Materials*. 2019

Patch needs an open chest surgery



Thermoresponsive hydrogel

Shevach et al. *Biomedical Materials*. 2015
Arvatz and Wertheim et al. *Nanomaterials*. 2019

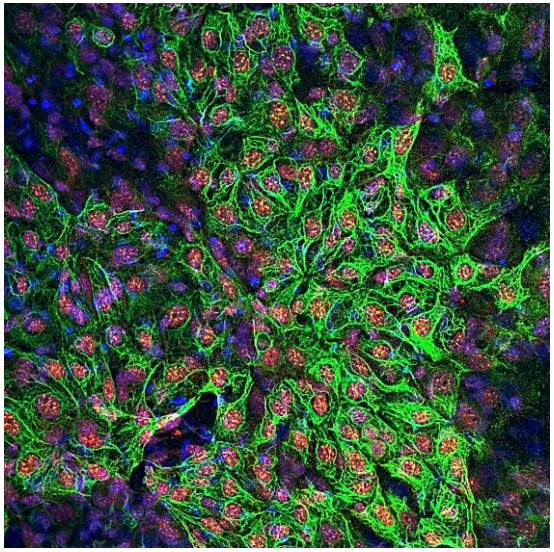


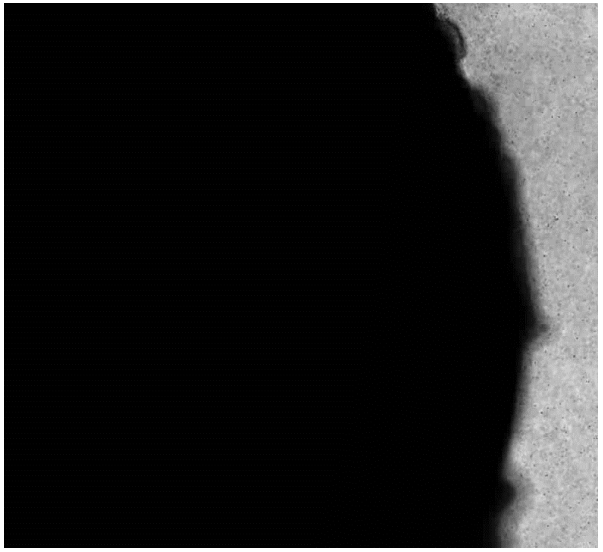
Disclosure: Matricelf was formed based on this platform technology

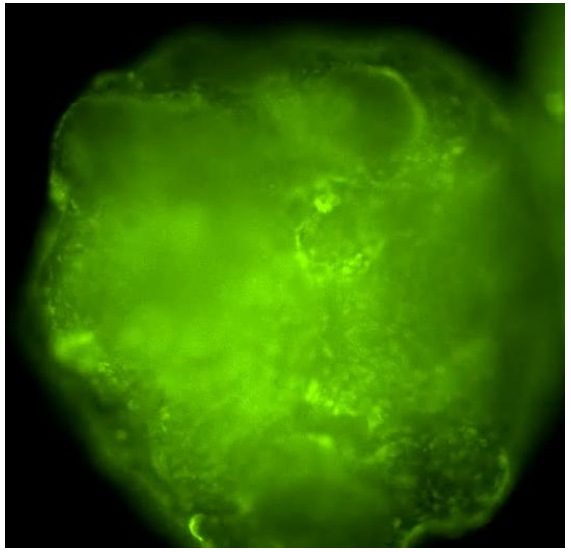
matricelf
Regenerating the future of medicine

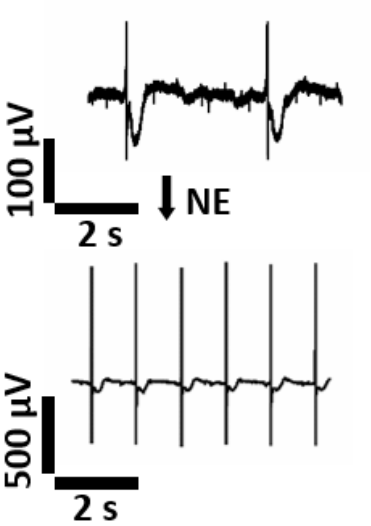
Cardiac implants

HOECHST TROPONIN NKX2-5

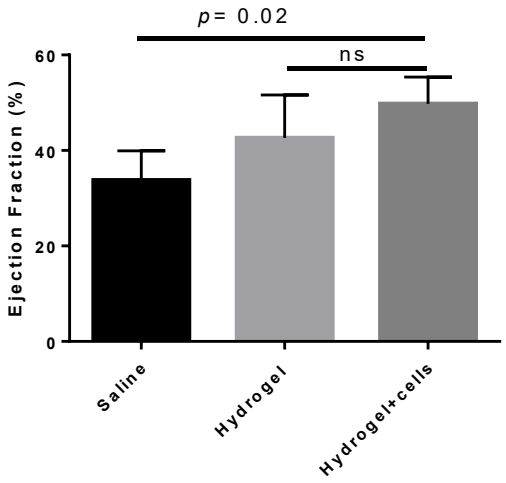




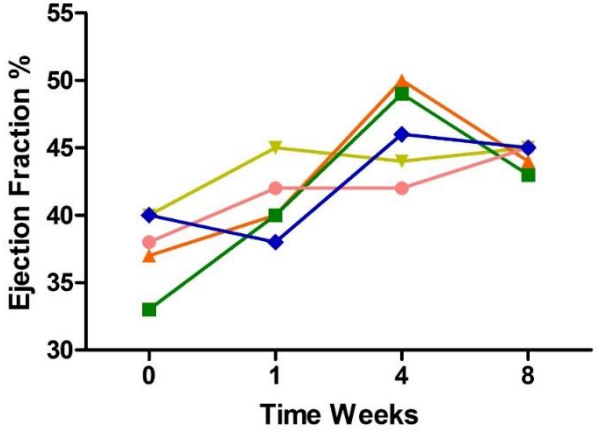




Small animals



Large animals

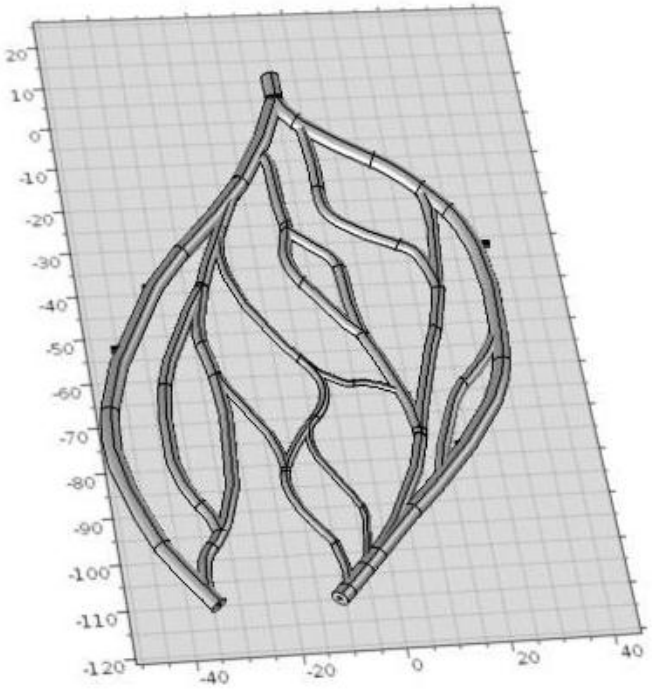


Edri et al. *Advanced Materials*. 2019

3D printing of patient-specific tissues

CT image of the infarcted heart

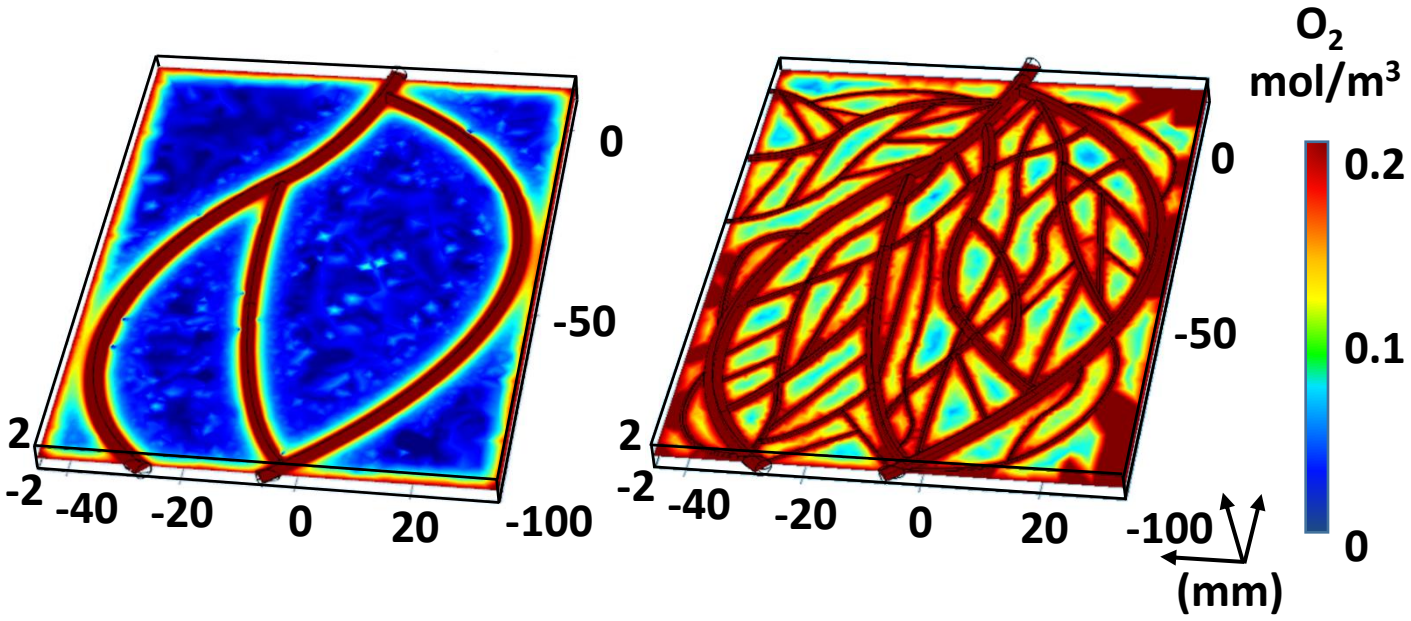
Focus on the vessels



Creating a vasculature model

Noor et al. *Advanced Science.* 2019

Oxygen transfer



Noor et al. *Advanced Science.* 2019

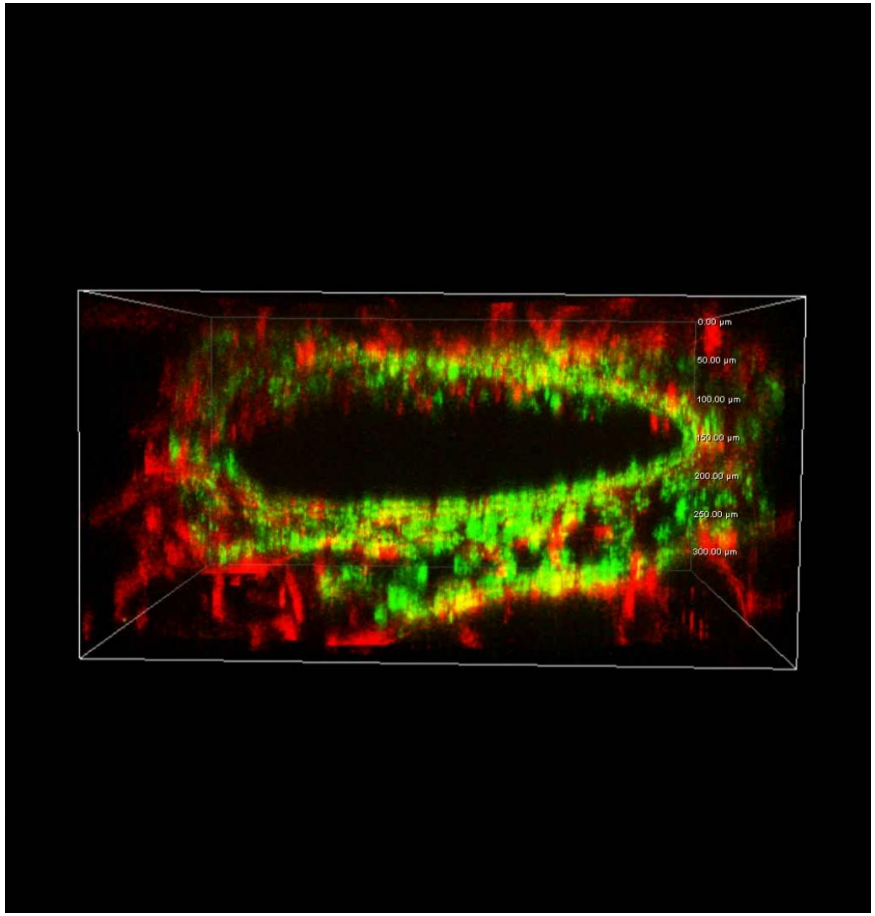
Printing patient-specific vascularized cardiac patches

Noor et al. *Advanced Science.* 2019

Patient-specific printed patch

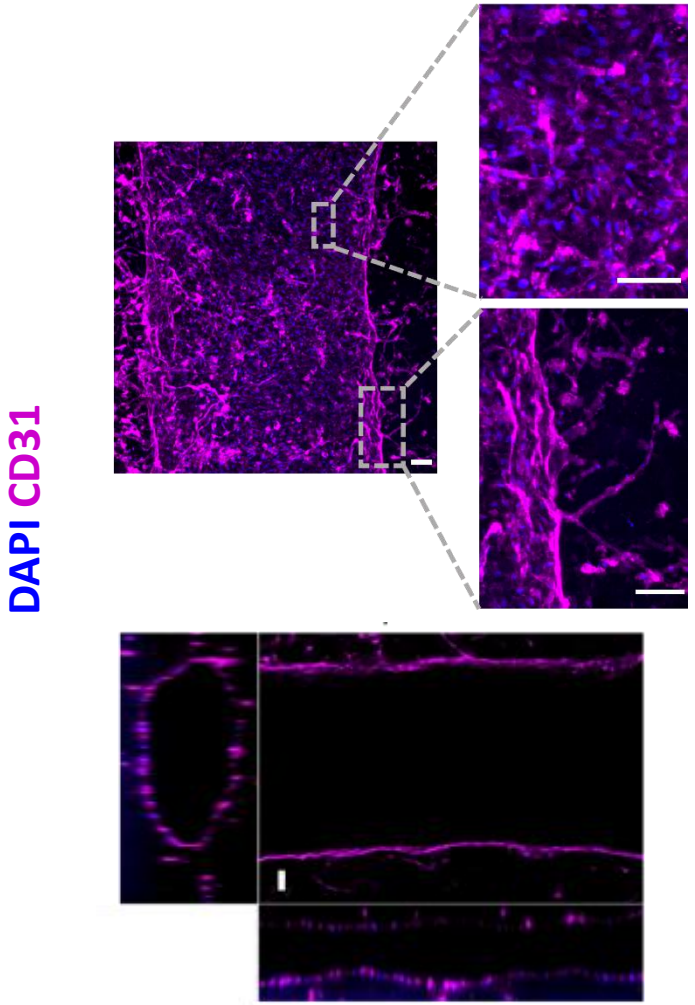
Noor et al. *Advanced Science.* 2019

Blood vessels within the tissue



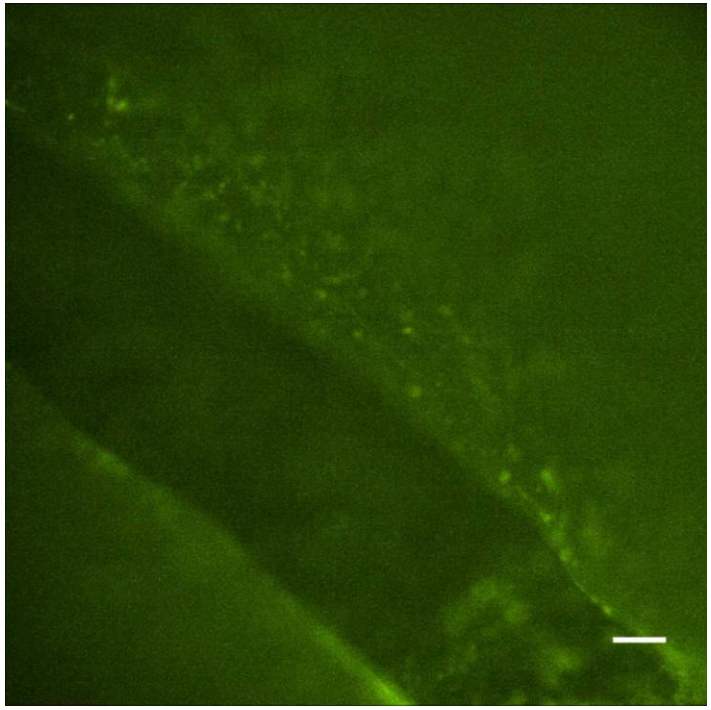
FIBROBLASTS ENDOTHELIAL CELLS

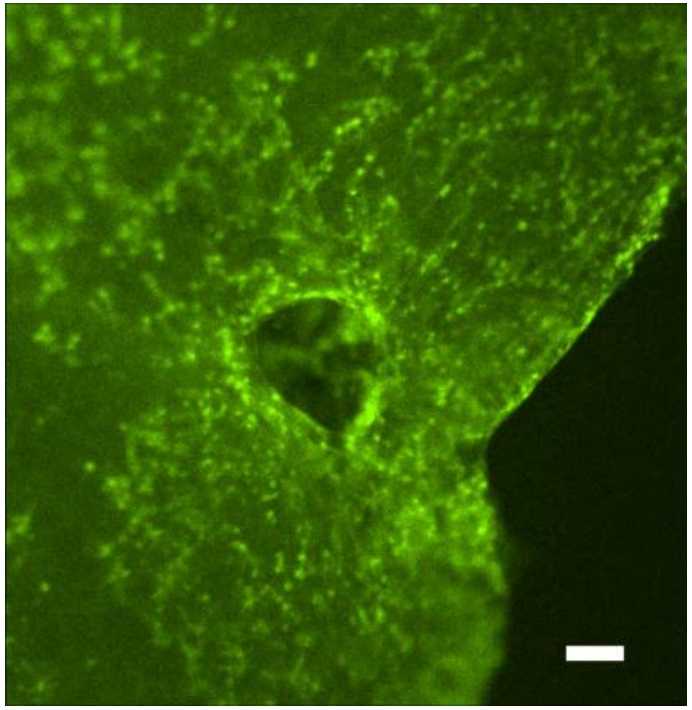
Noor et al. *Advanced Science.* 2019



Cohen et al. *Gels*, 2023

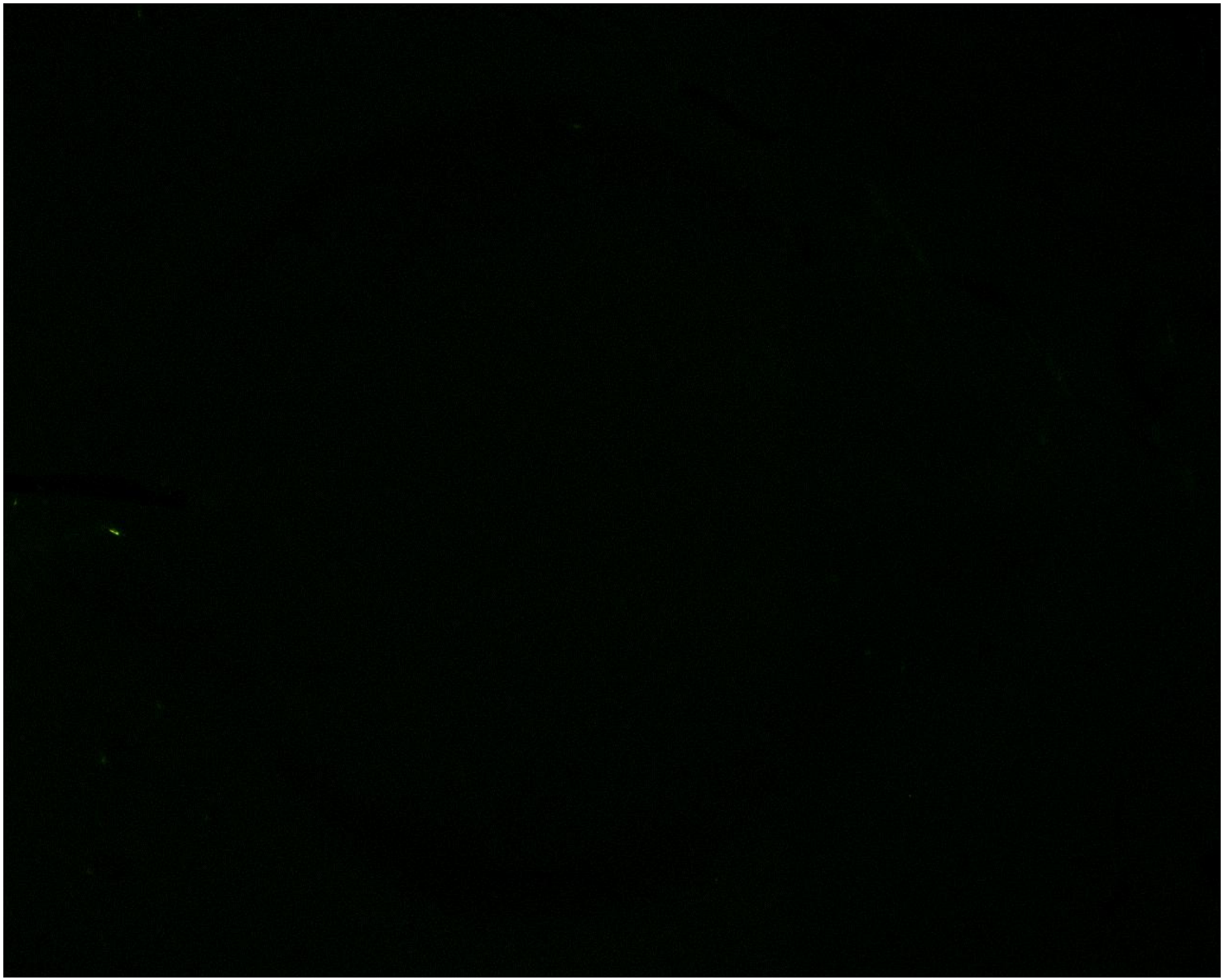
Cardiac patches function



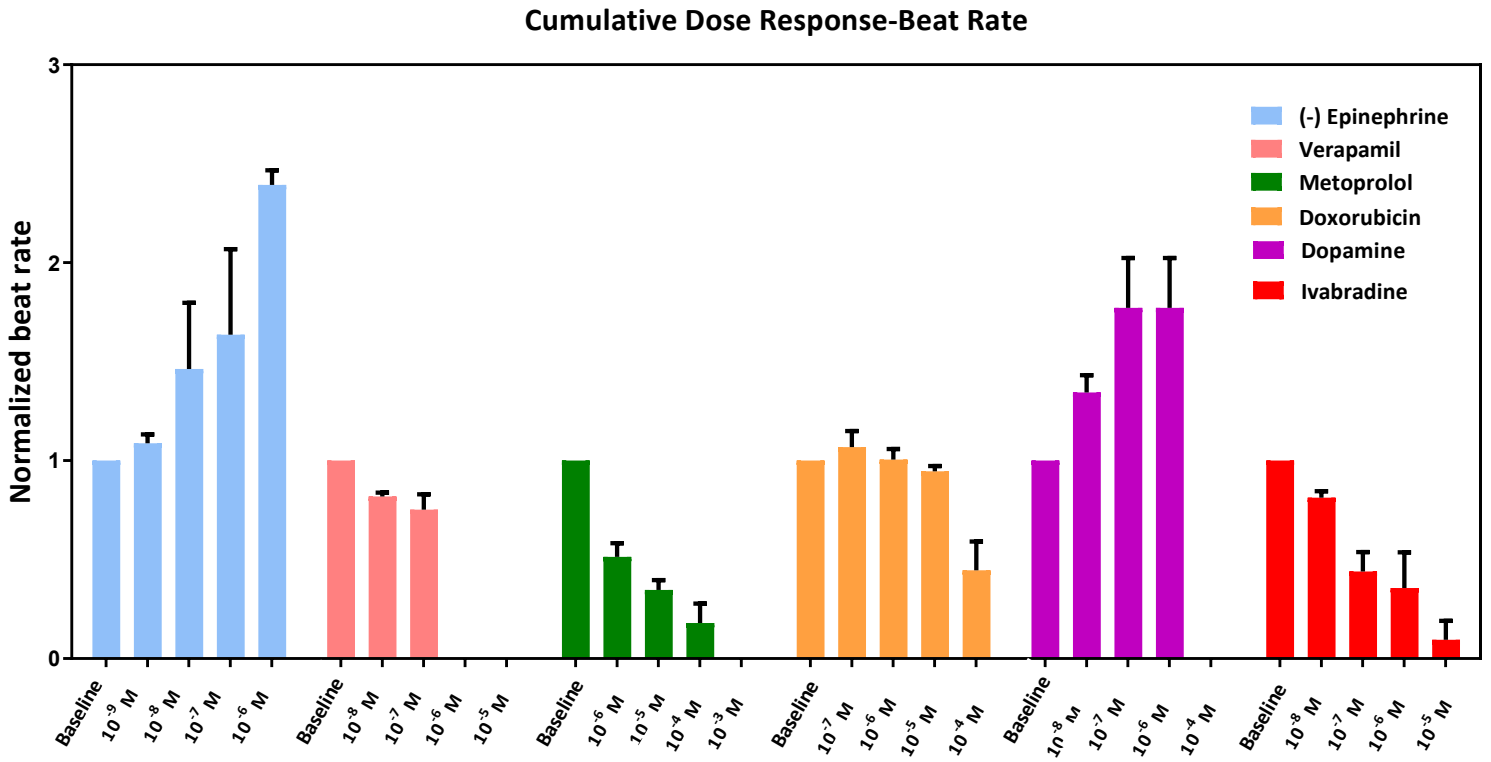


Noor et al. *Advanced Science* 2019

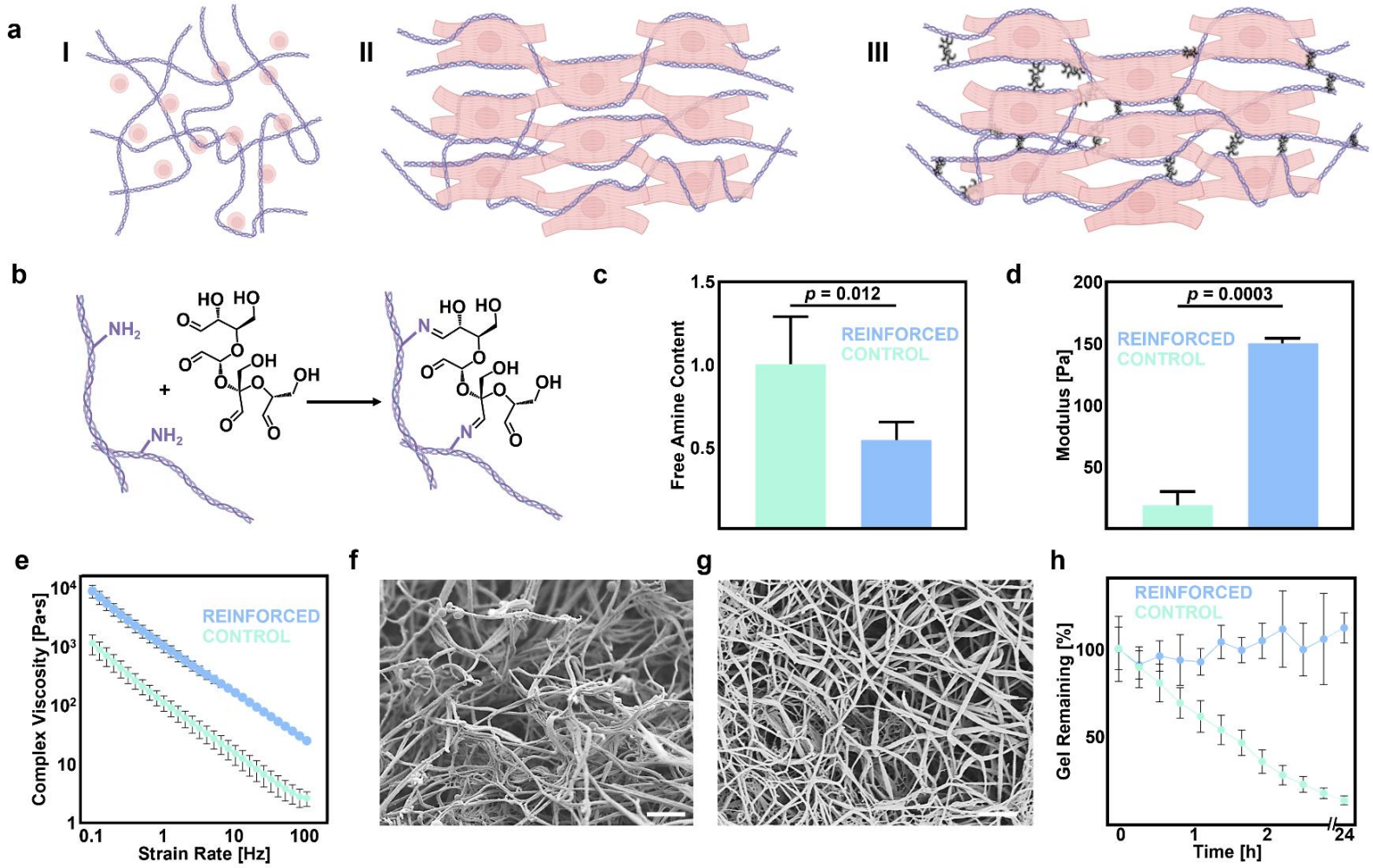
Perfusing through the cardiac patches



Printed patches response to drugs



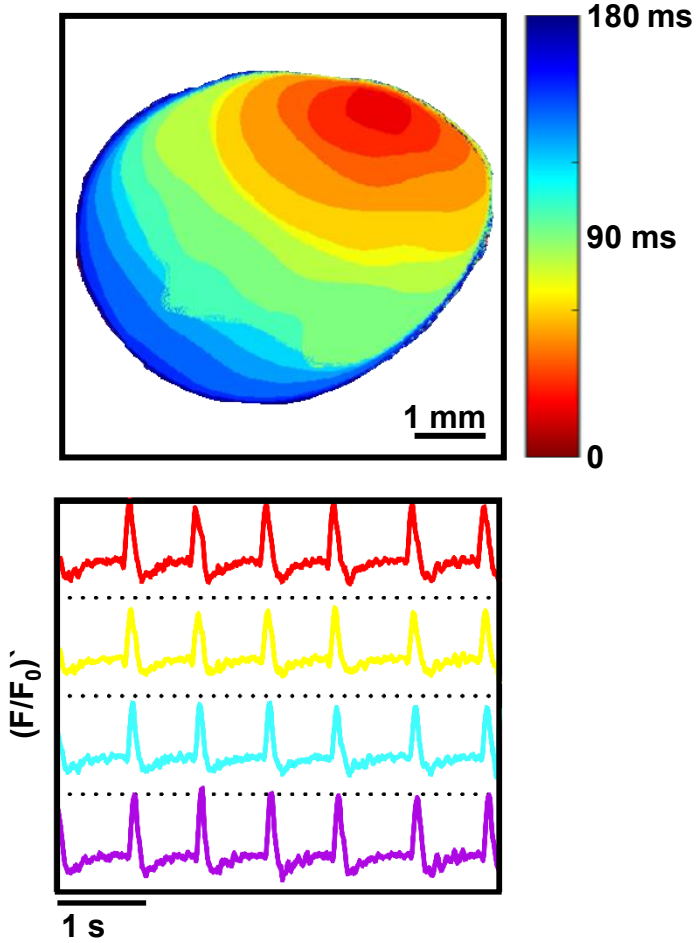
Post-maturation reinforcement of printed tissues



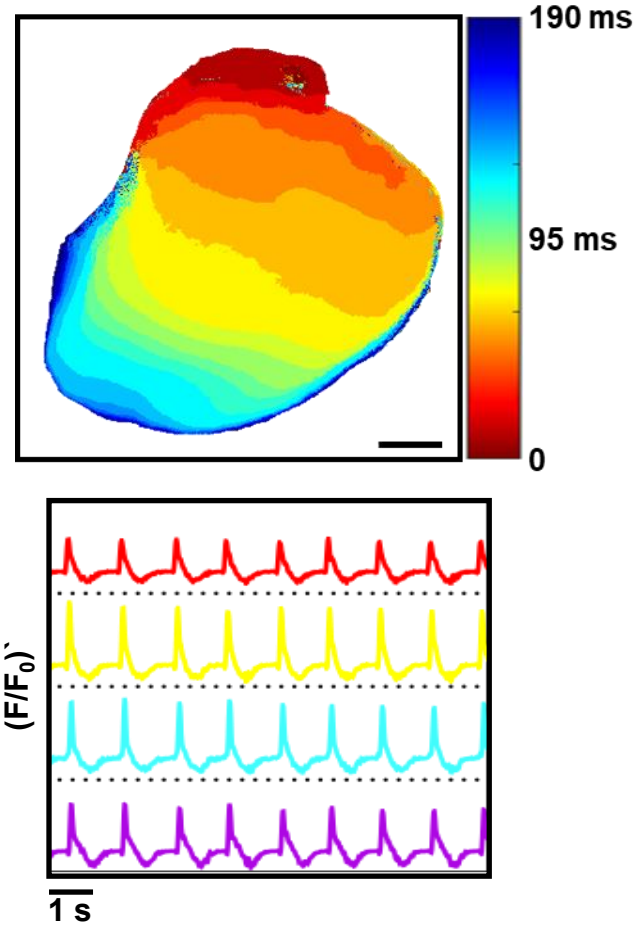
Silberman et al. *Advanced Materials*. 2023

Printing injectable vascularized heart patches

Before injection

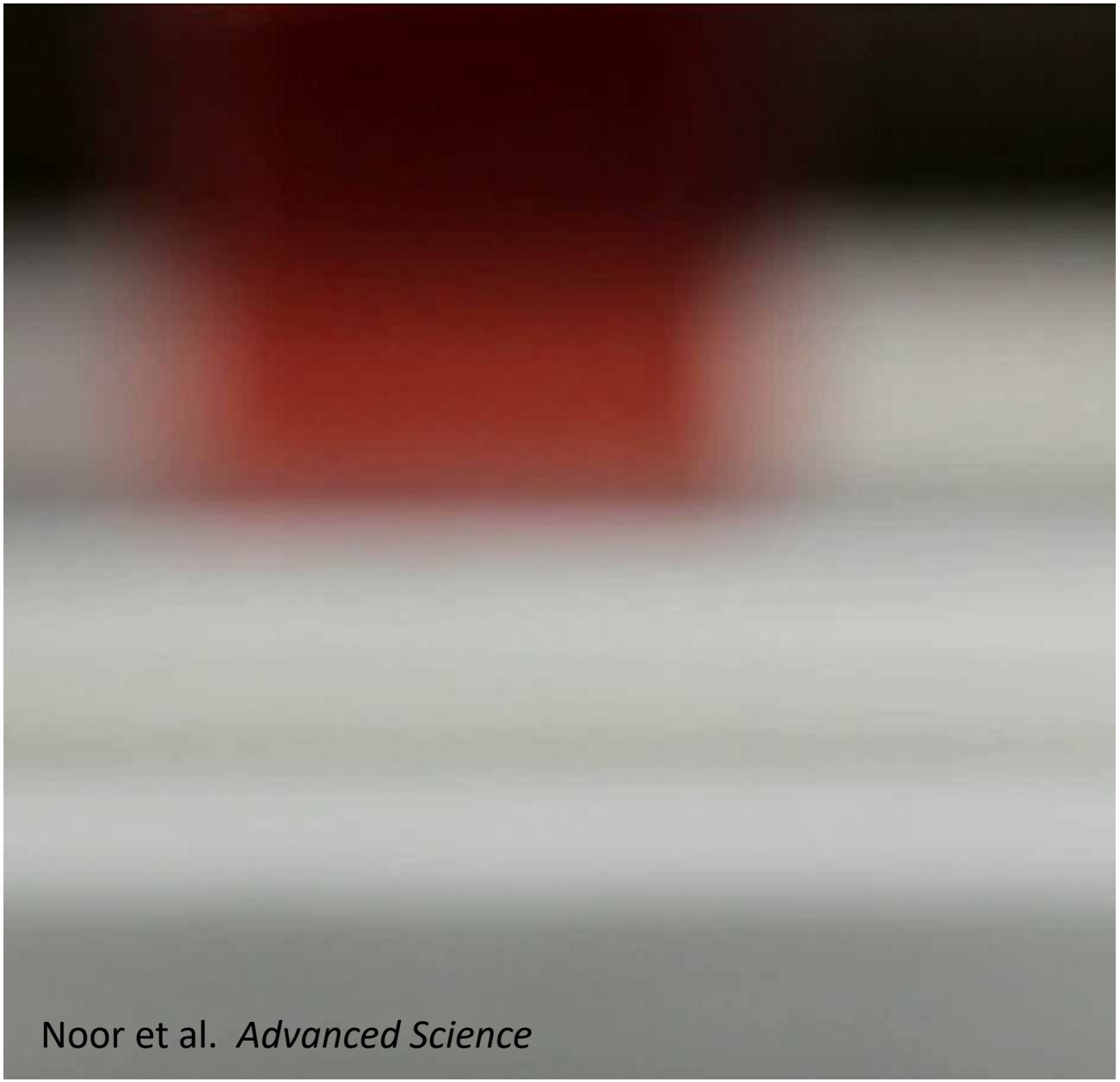


After injection

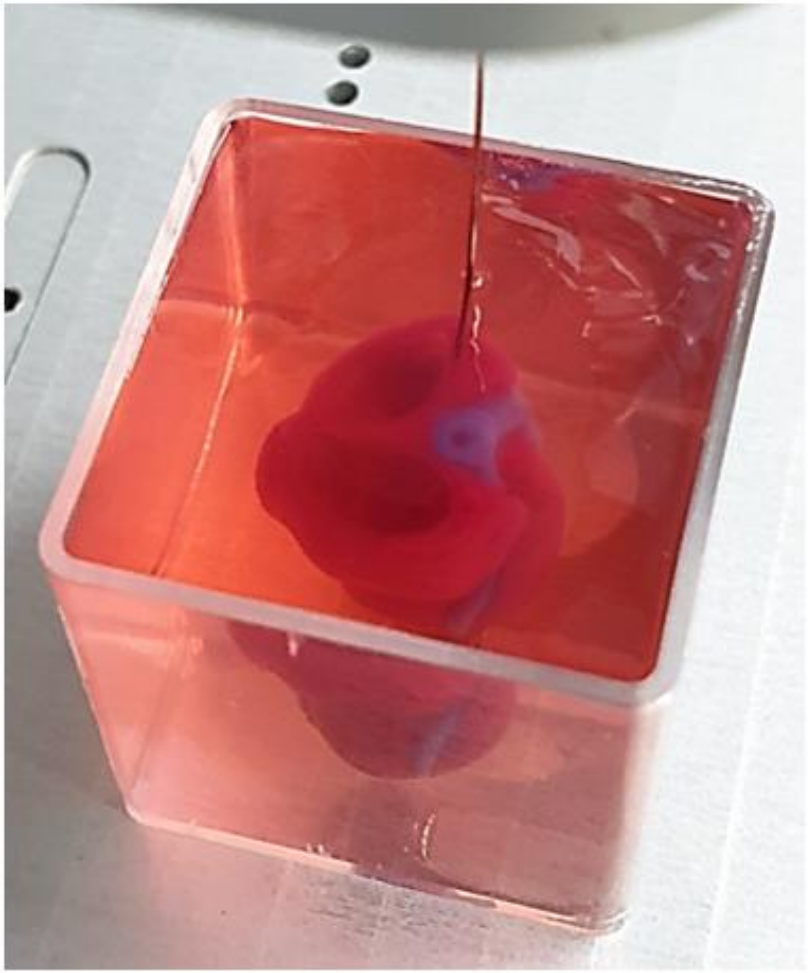


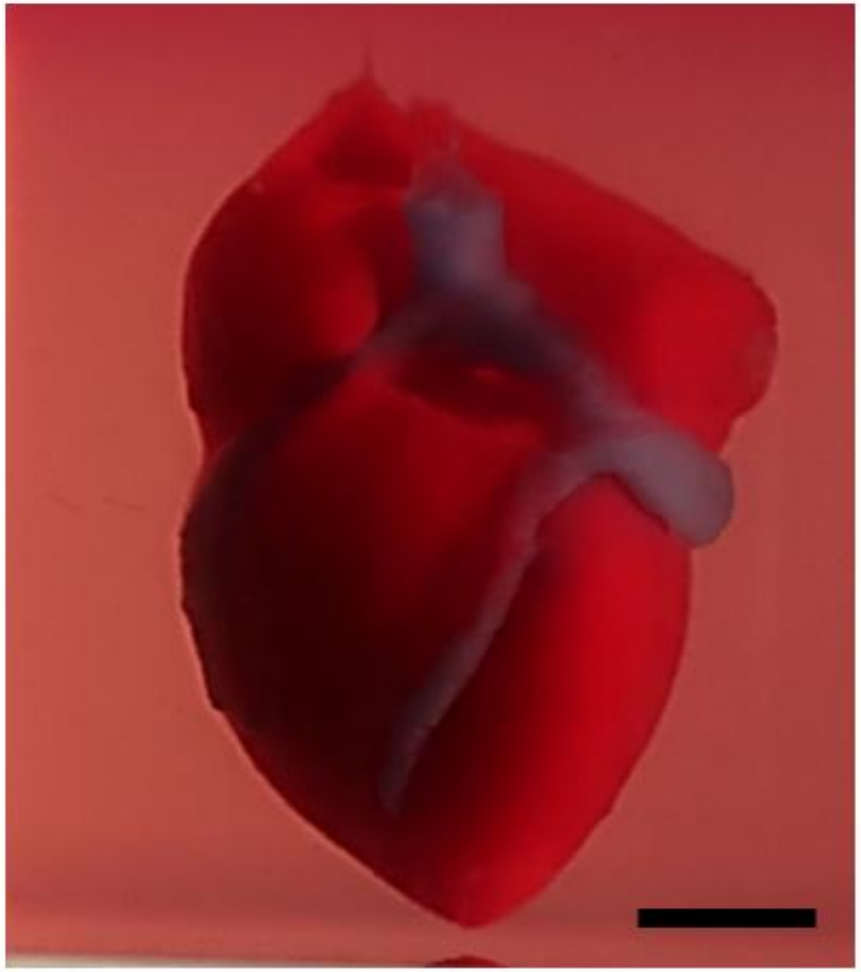
Silberman et al. *Advanced Materials*. 2023

Printing whole hearts



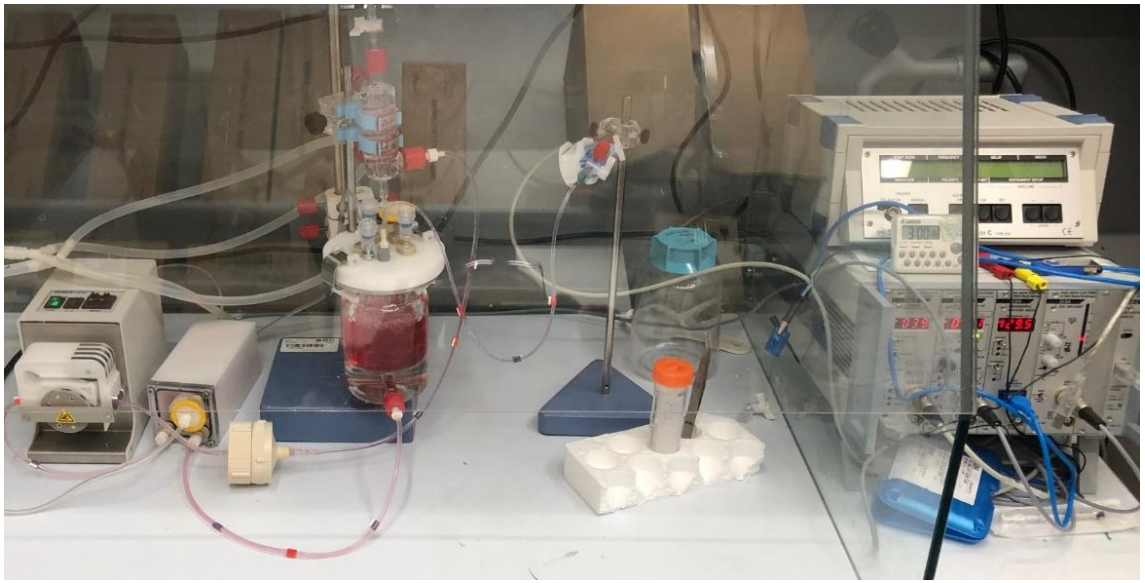
Noor et al. *Advanced Science*





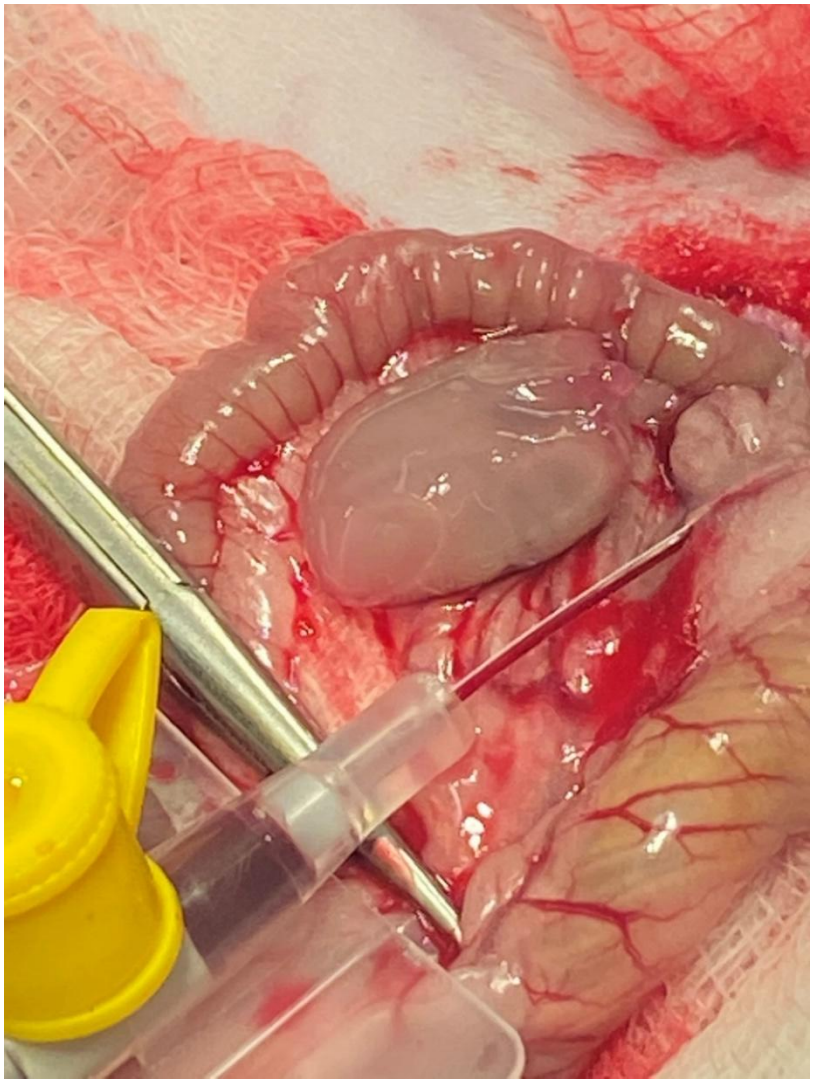
Noor et al. *Advanced Science*

Maturation of hearts



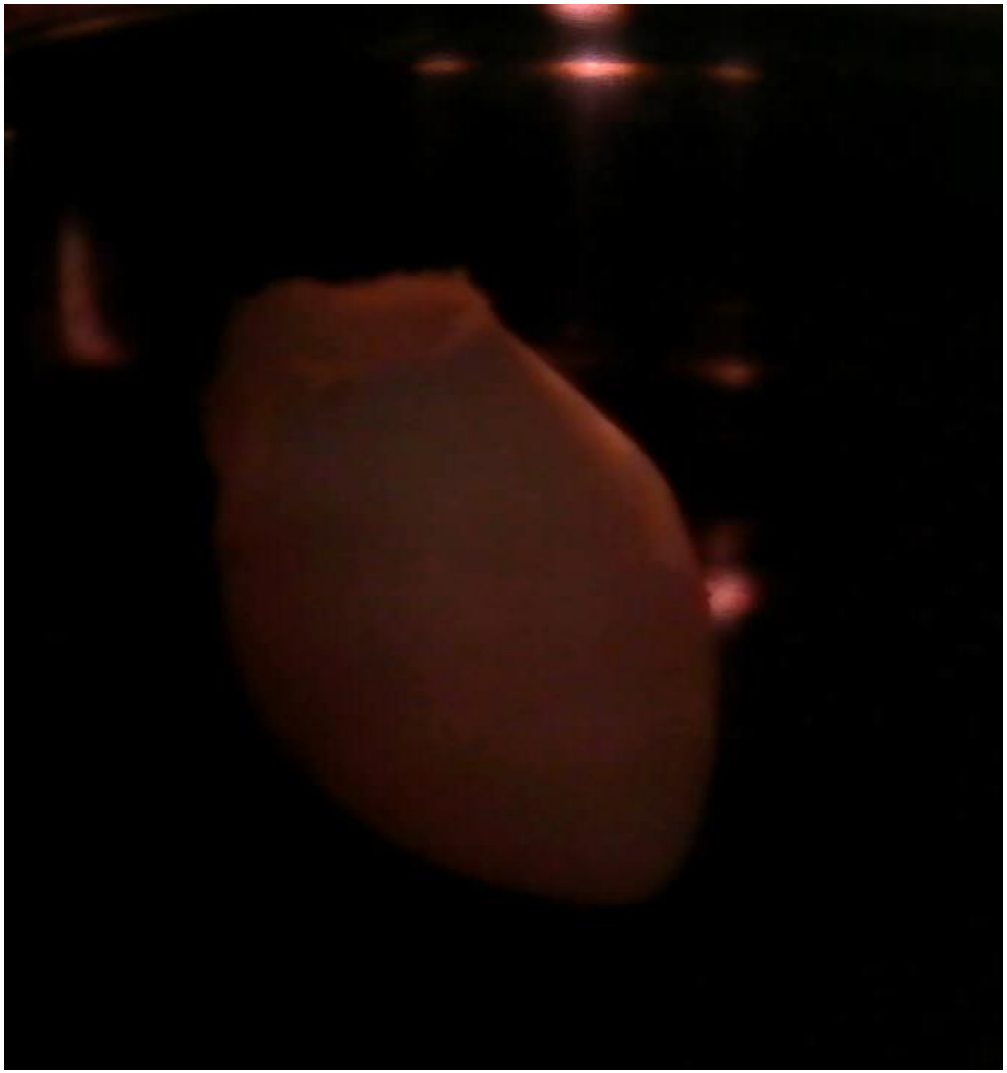
Hadas Oved

Printed heart heterotopic transplantation



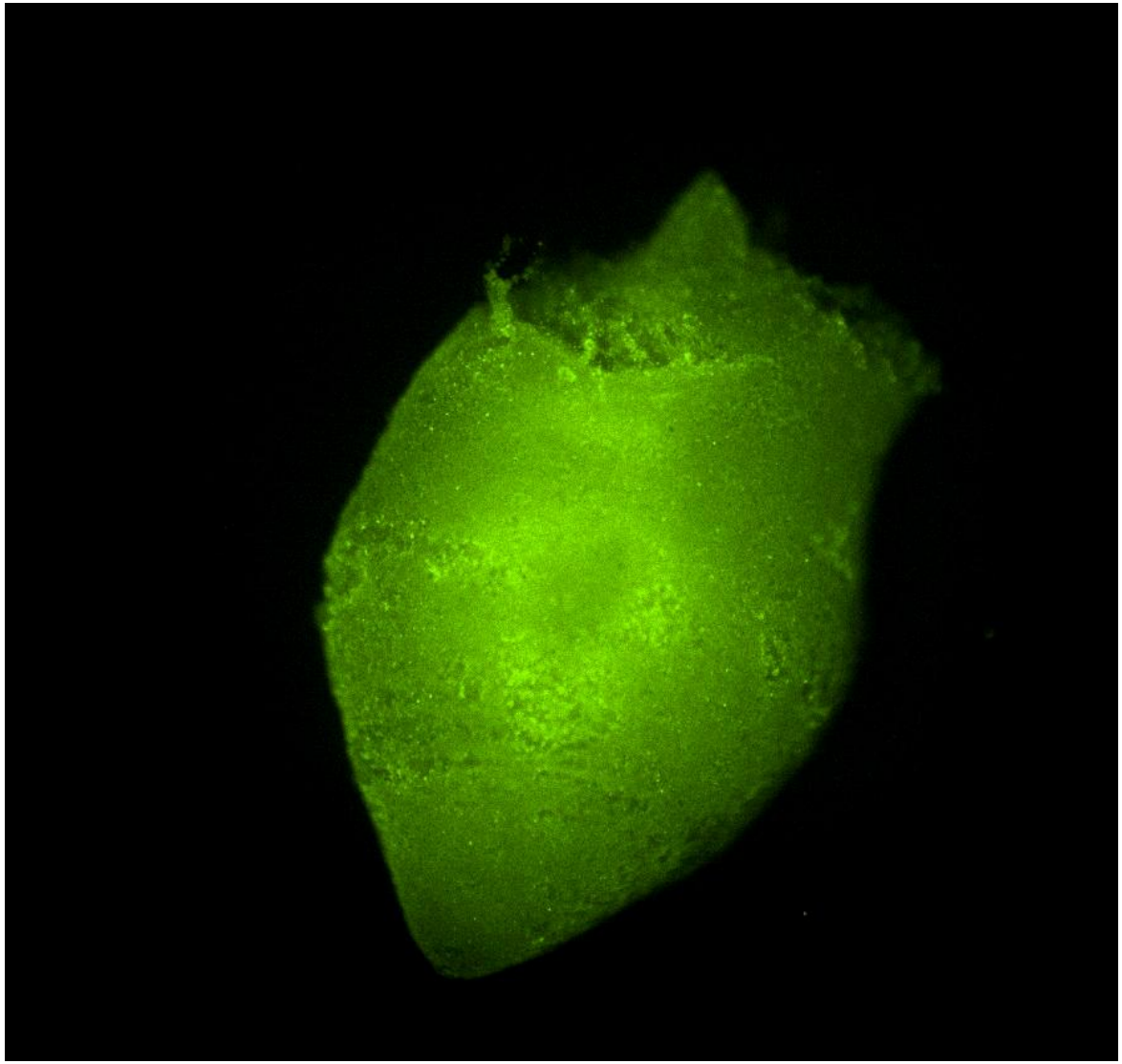
Nadav Noor, Itai Cabilly

Printed heart with a mixed population of CM



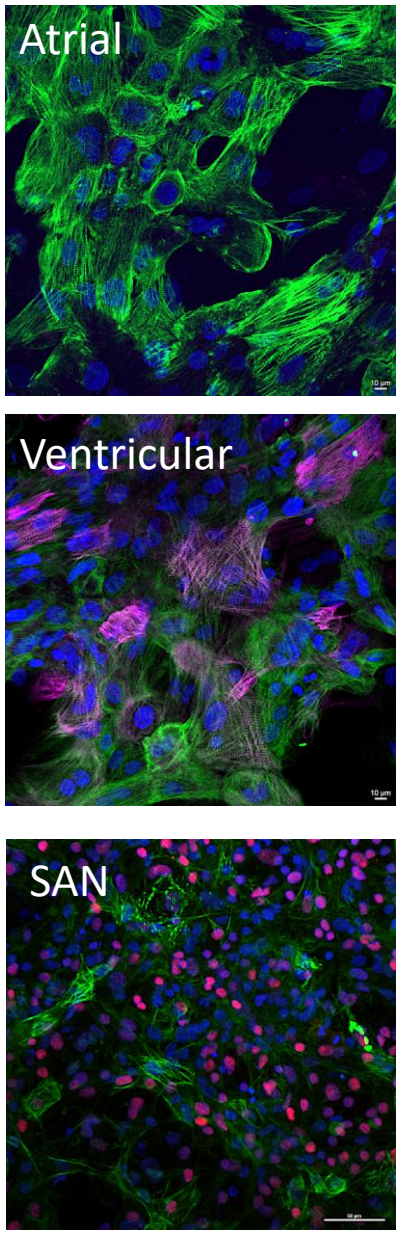
Itai Cabilly, In Preparation

Printed heart electrical activity

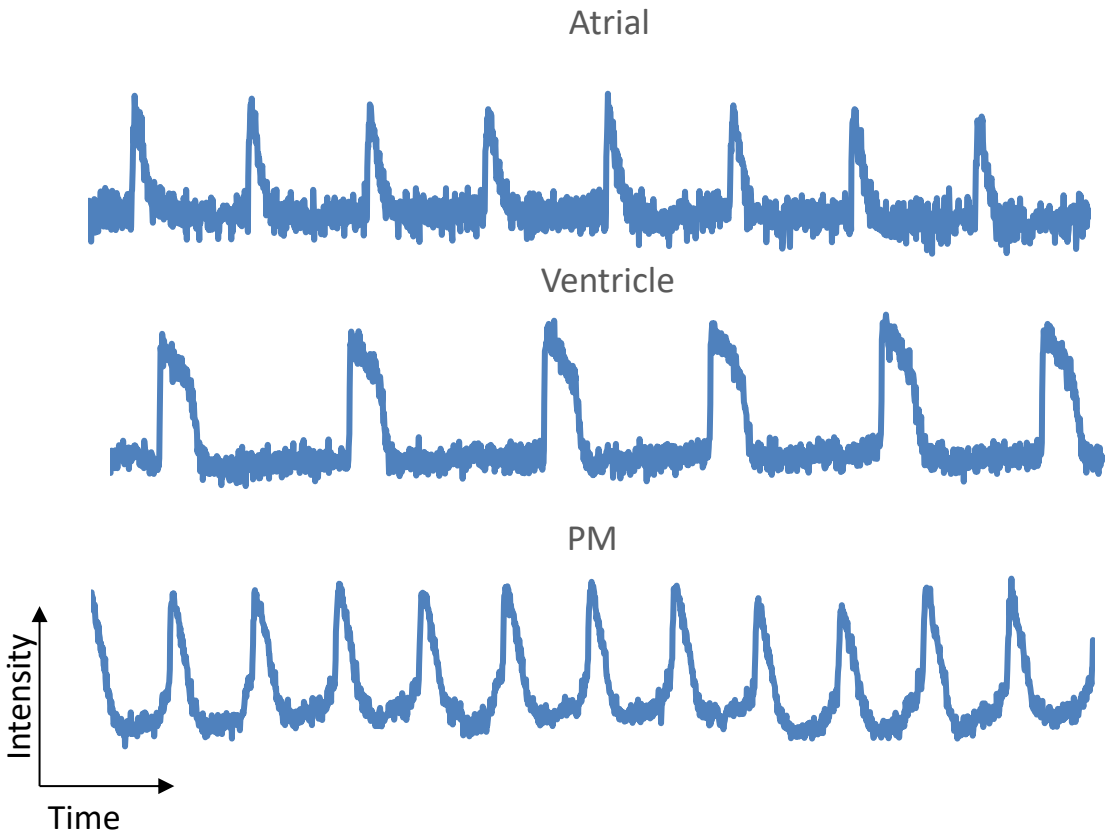


Itai Cabilly, In Preparation

Cardiomyocytes sub-types

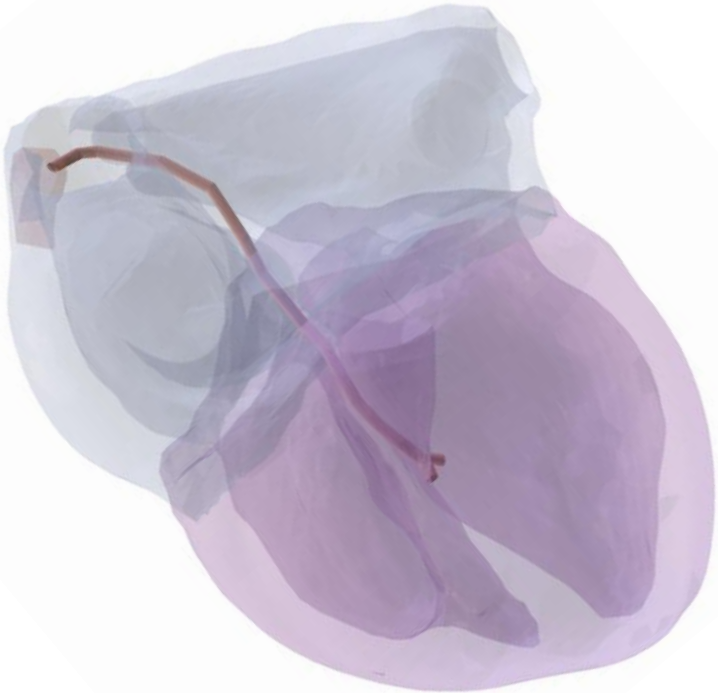


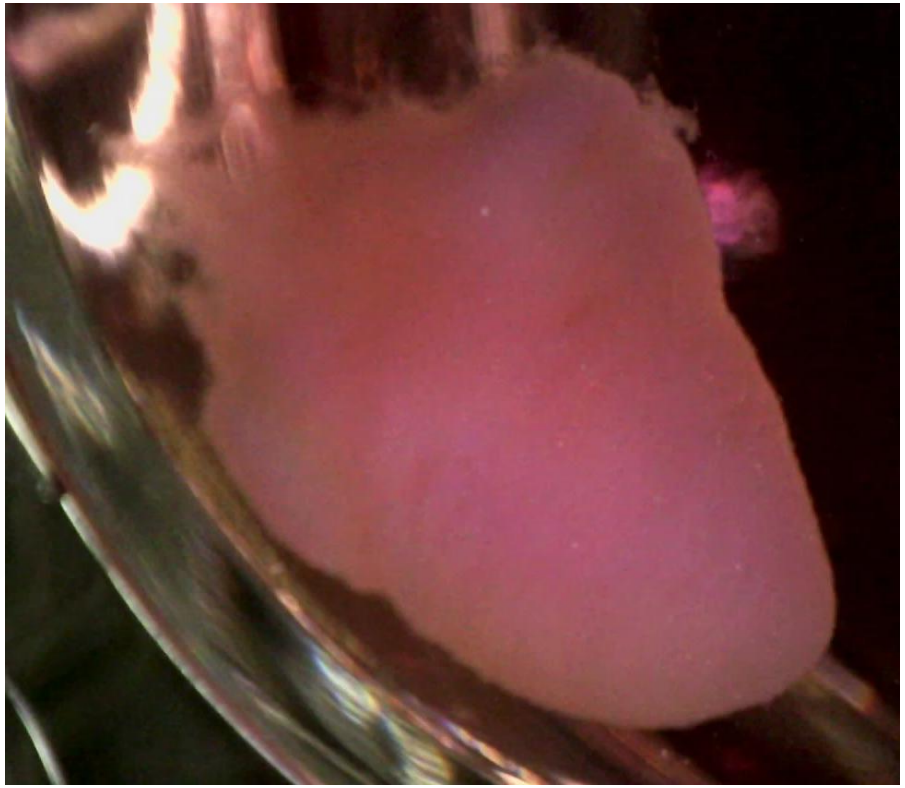
Optical action potential



Cabilly and Rosner et al. In Prep.

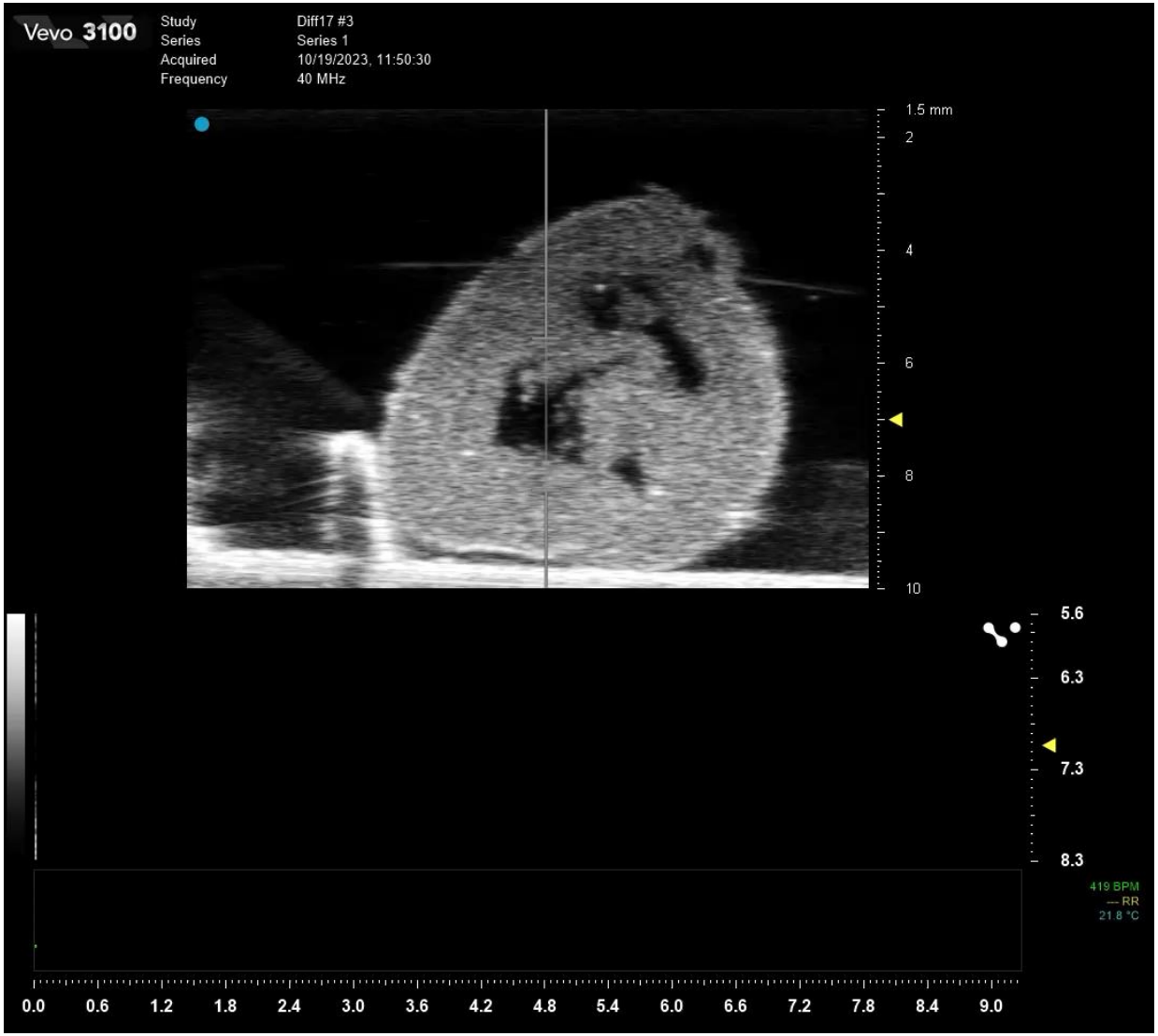
Printing pacemaker, ventricular and atrial cells





Cabilly and Rosner et al. In Prep.

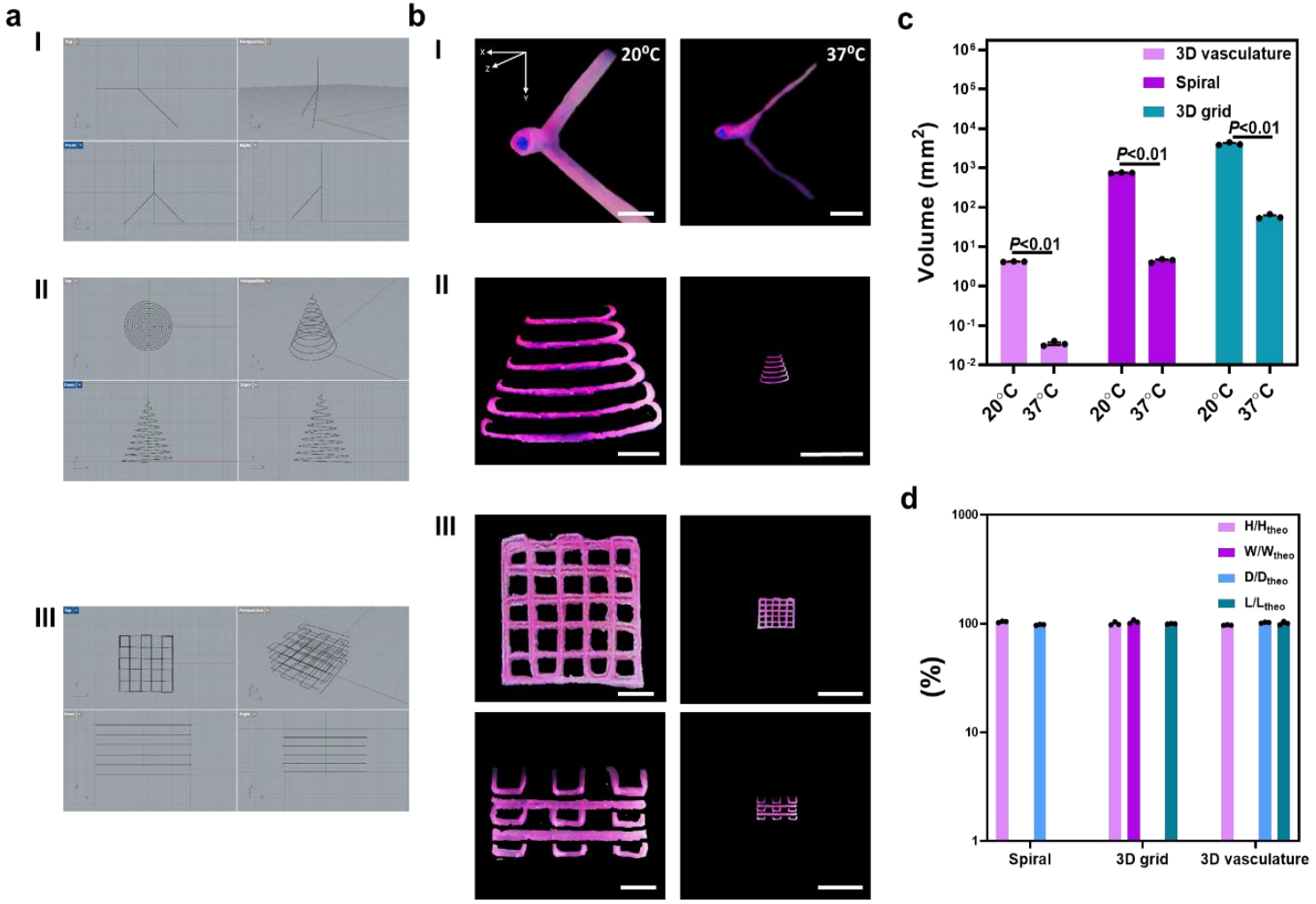
Echocardiography



With Yoram Etzion

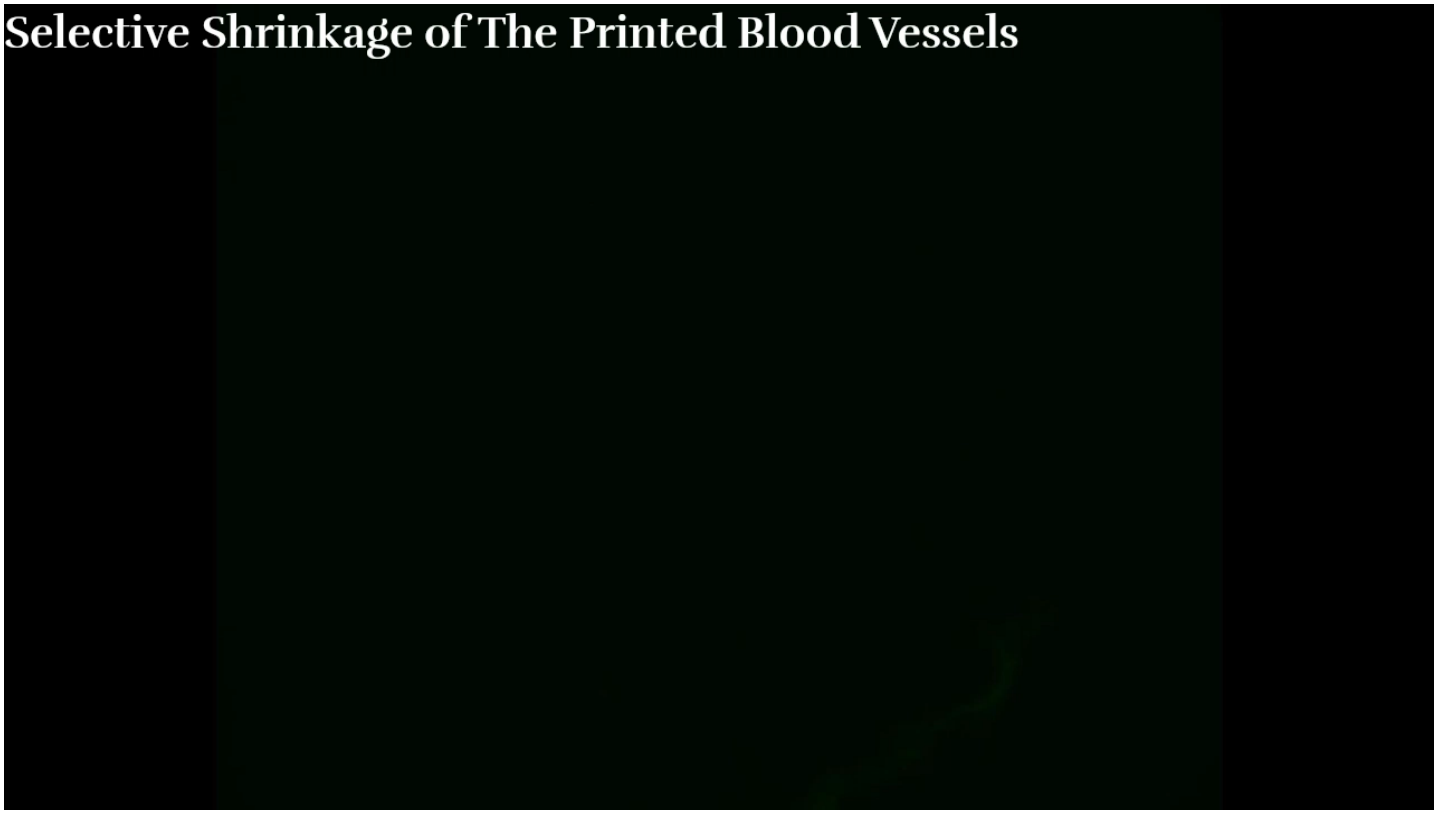
Cabilly and Rosner et al. In Prep.

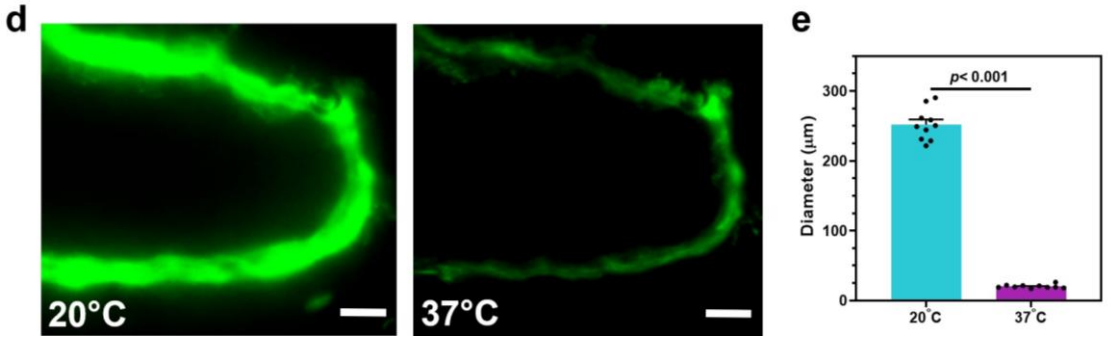
Selective shrinkage of structures in a tissue



Baruch et al. Under revision.

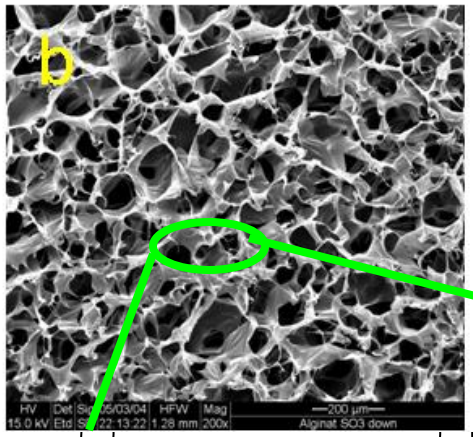
4D printing of small-scale capillaries

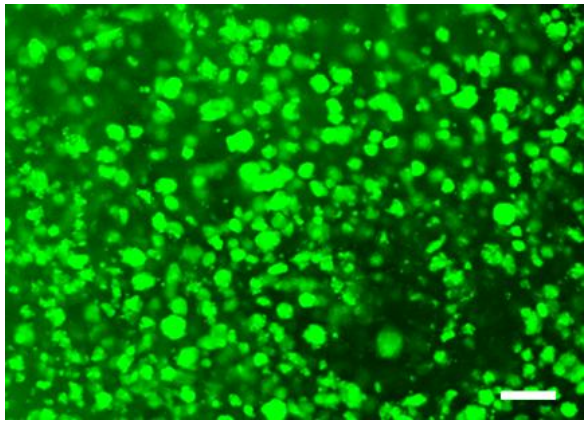


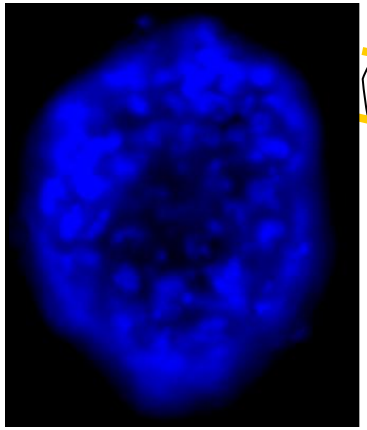


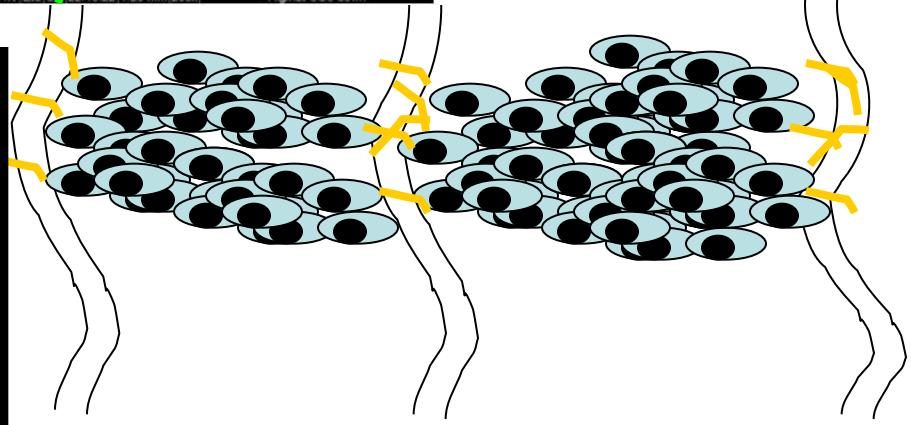
Baruch et al. Under revision.

Transfer of electrical signal

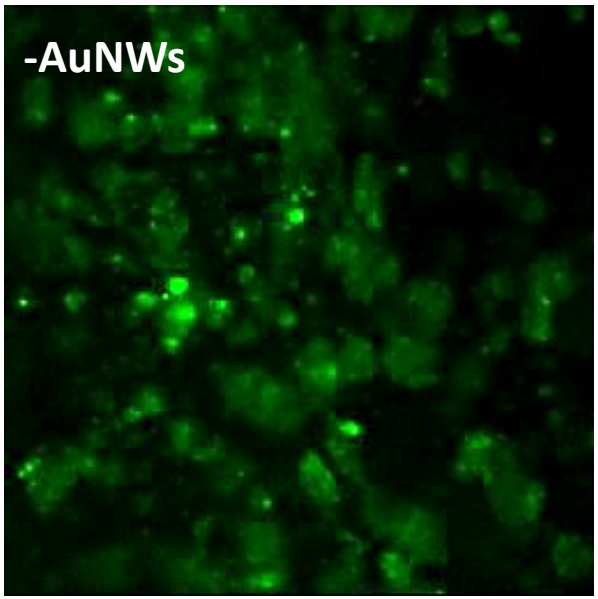


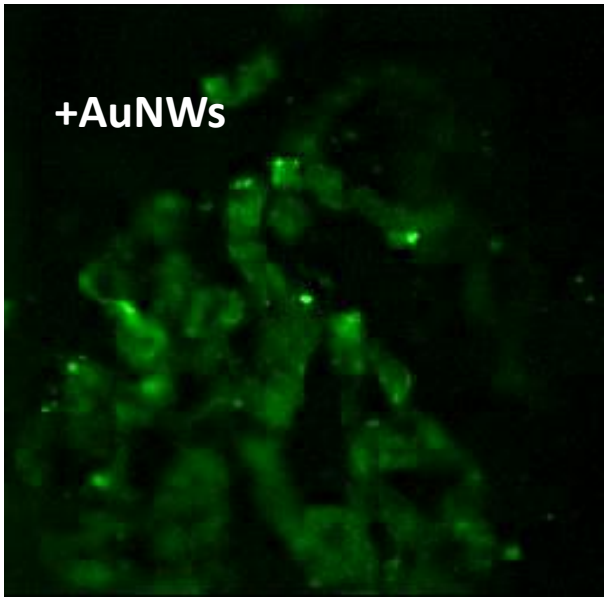


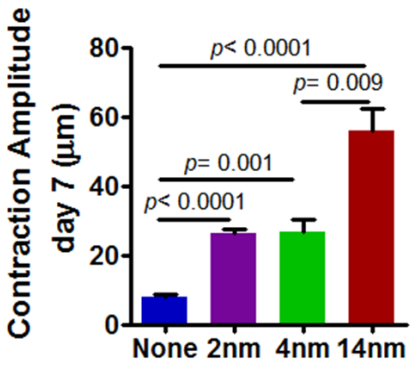


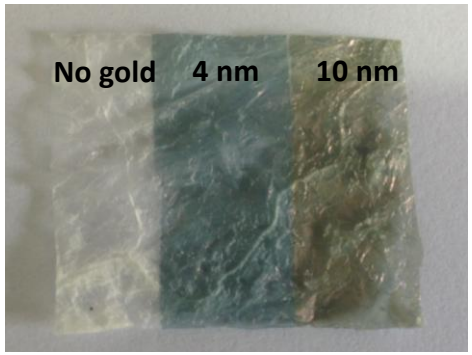


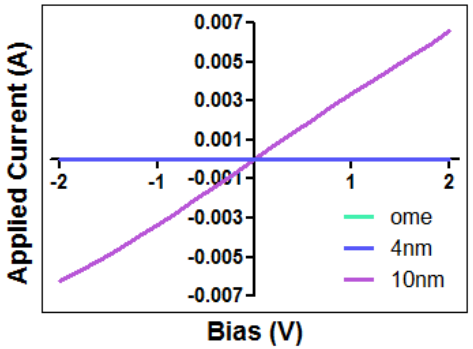
Electrical signal propagation

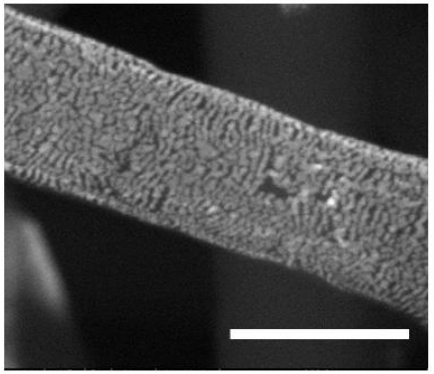


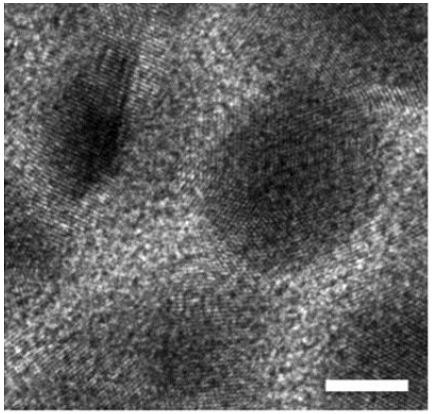






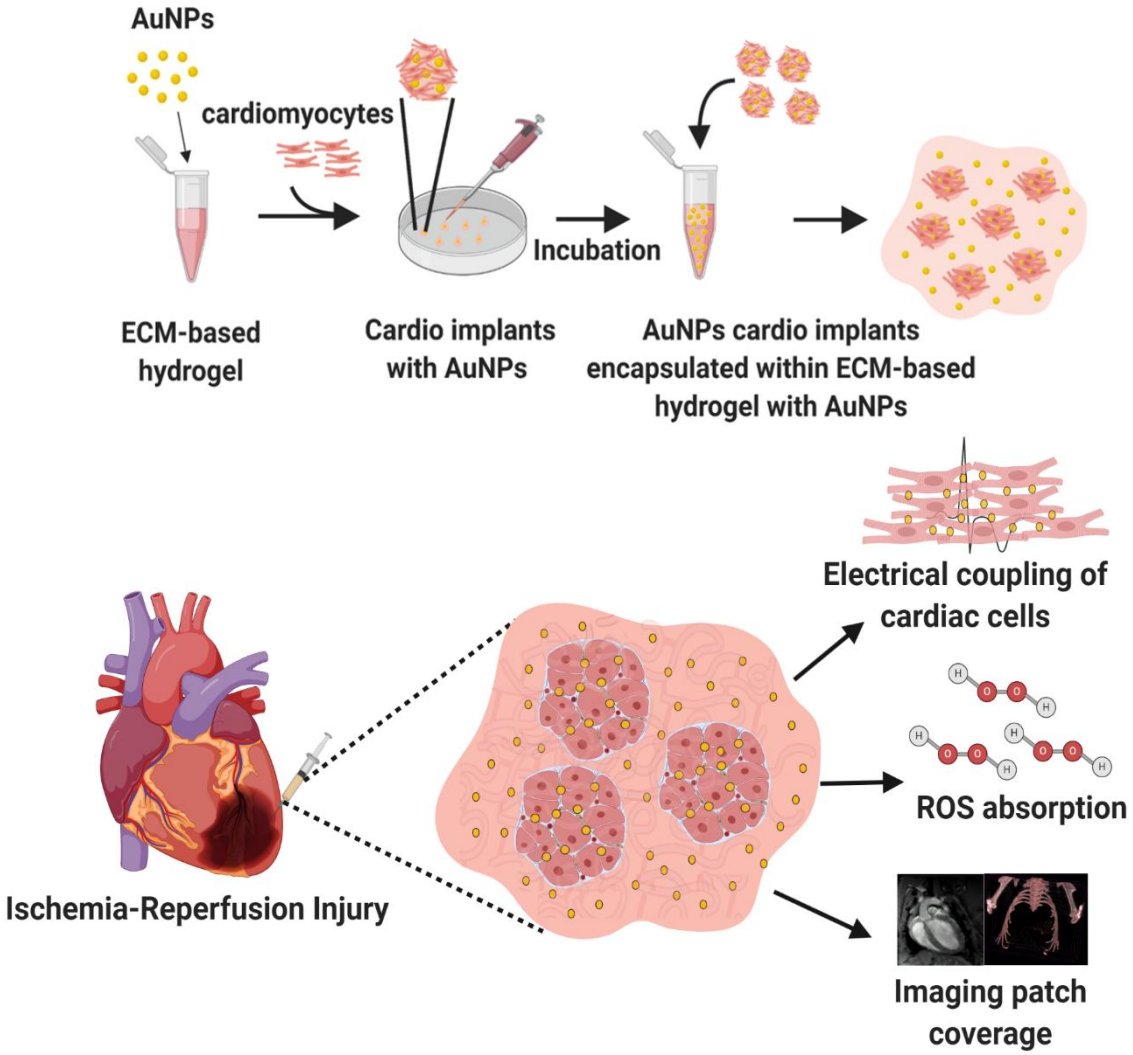






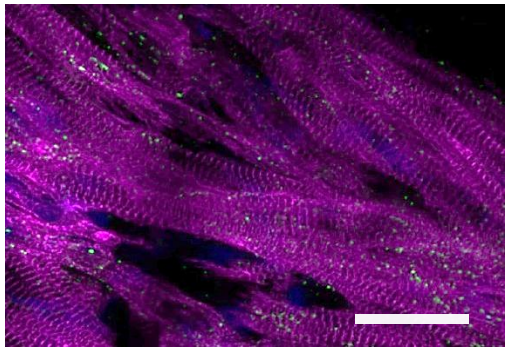
Dvir et al. *Nature Nanotechnology*. 2010
Dvir et al. *Nature Nanotechnology*. 2011
Shevach et al. *J. Mater. Chem B.* 2013
Fleischer*, Shevach*, Feiner*, Dvir. *Nanoscale.* 2014
Shevach et al. *Nano Letters*. 2014
Baranes*, Shevach* et al. *Nano Letters*. 2016

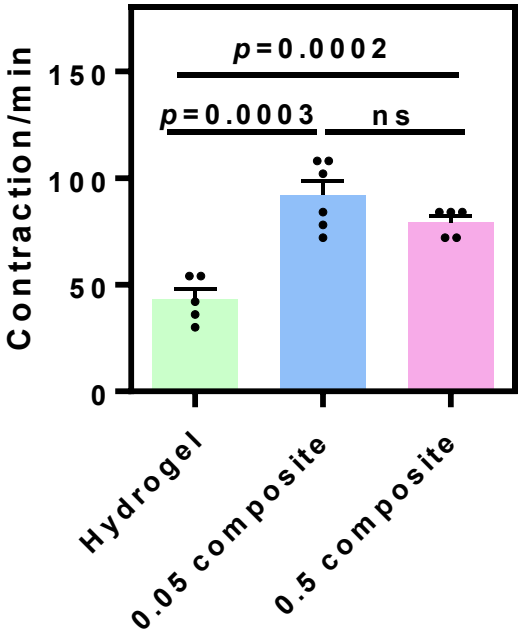
Triple heart combination therapy



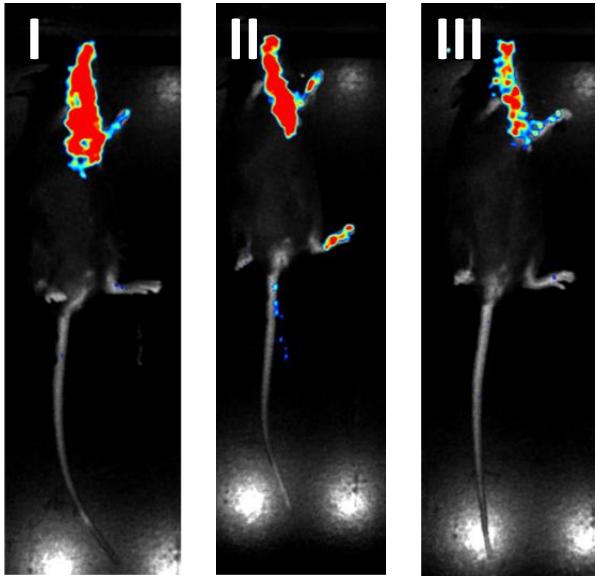
Advanced Science, 2021
Pharmaceutics, 2023

Better contraction

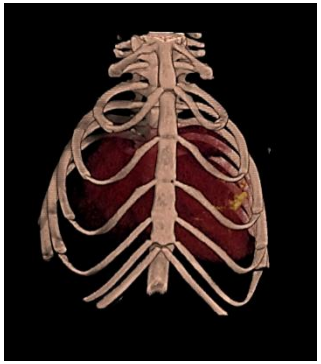


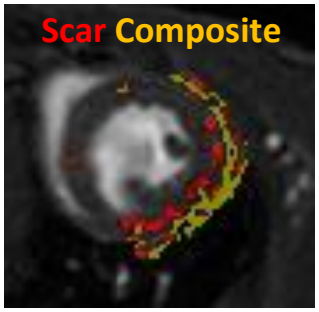


ROS reduction

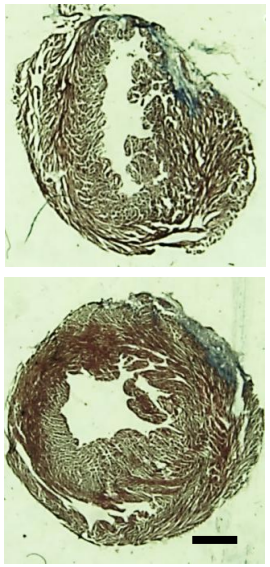


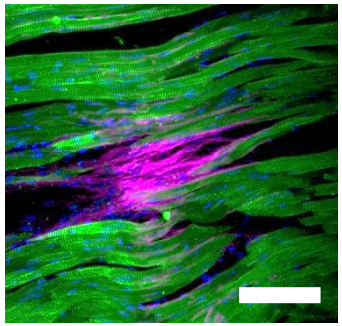
Imaging the treatment/scar

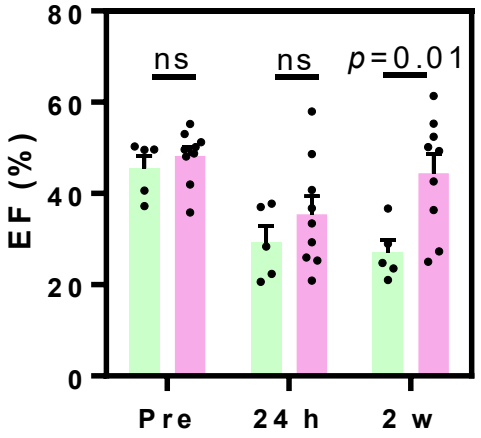




Improving heart function

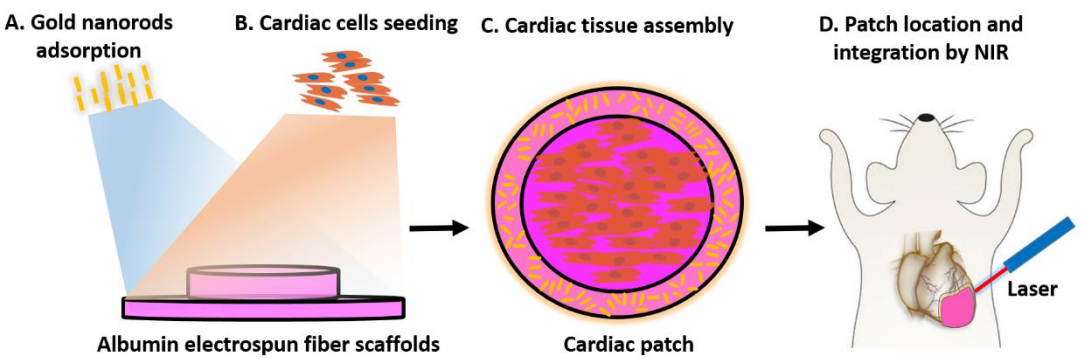


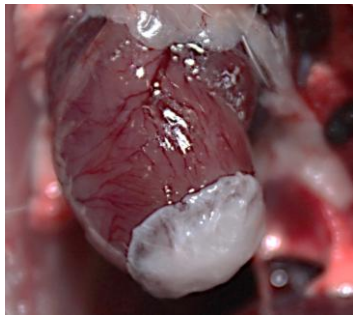




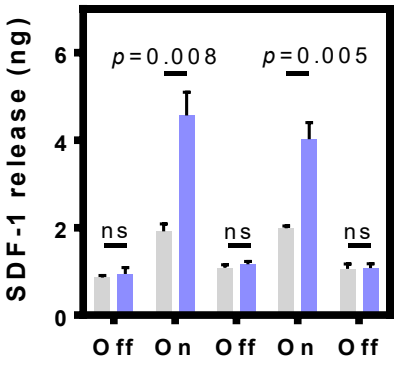
Advanced Science, 2021
Pharmaceutics, 2023

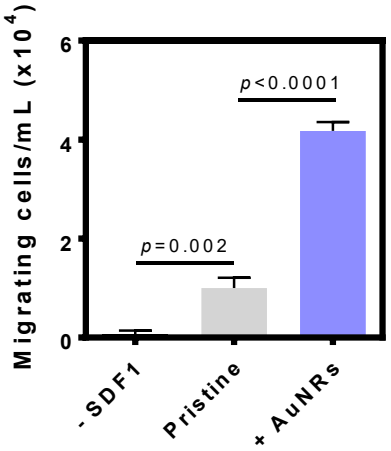
AuNRs for tissue integration and vascularization

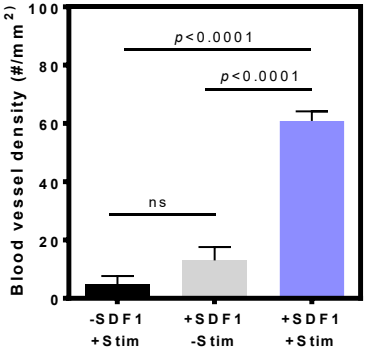




Malki et al. Nano Letters, 2018

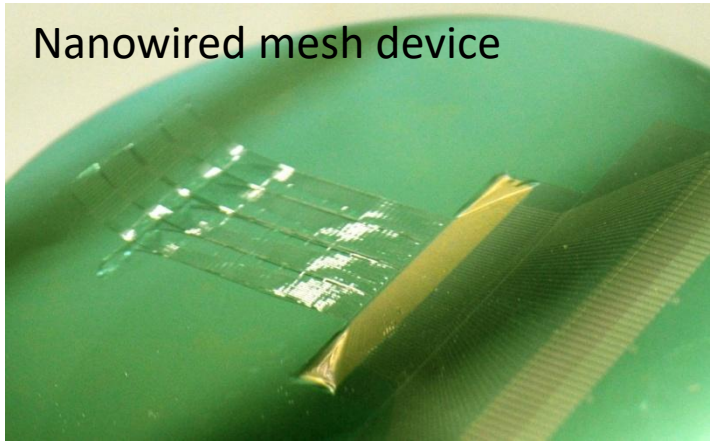


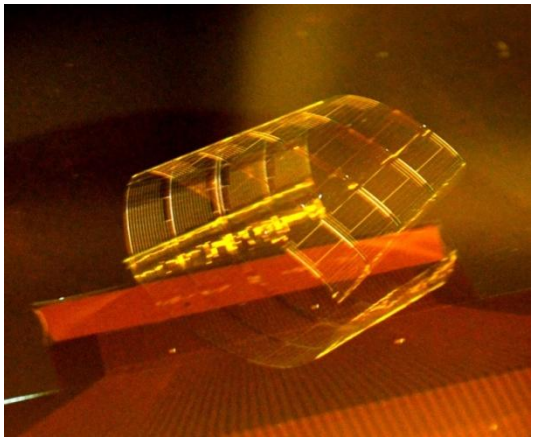


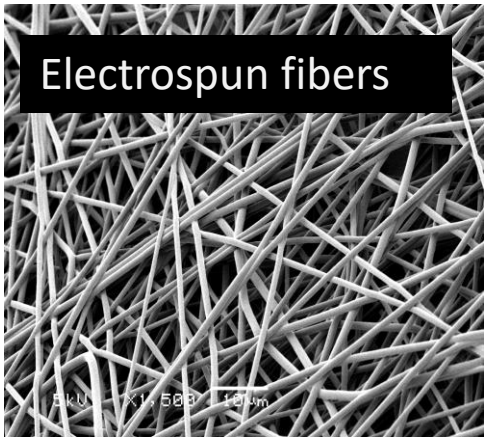


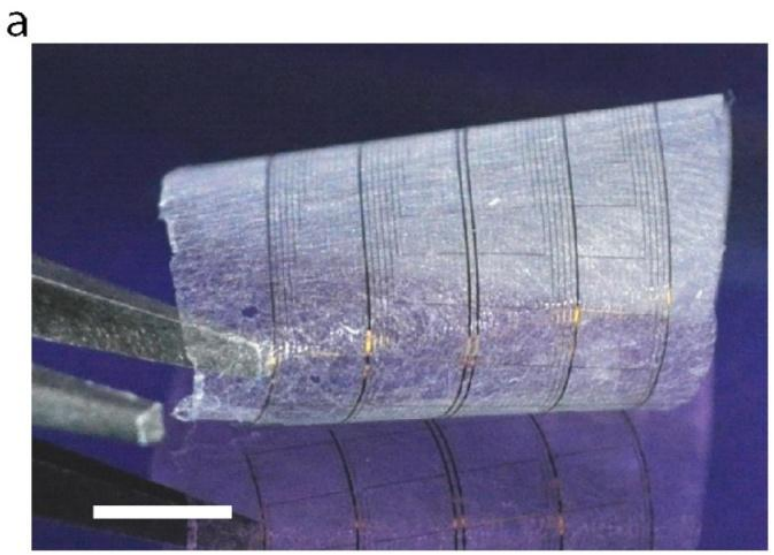
Malki et al. Journal of Nanobiotechnology, 2022

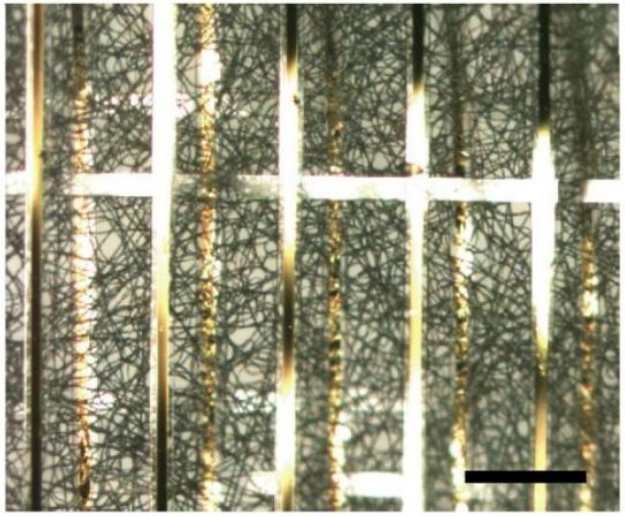
Cyborg tissues- integrating electronics with engineered tissues





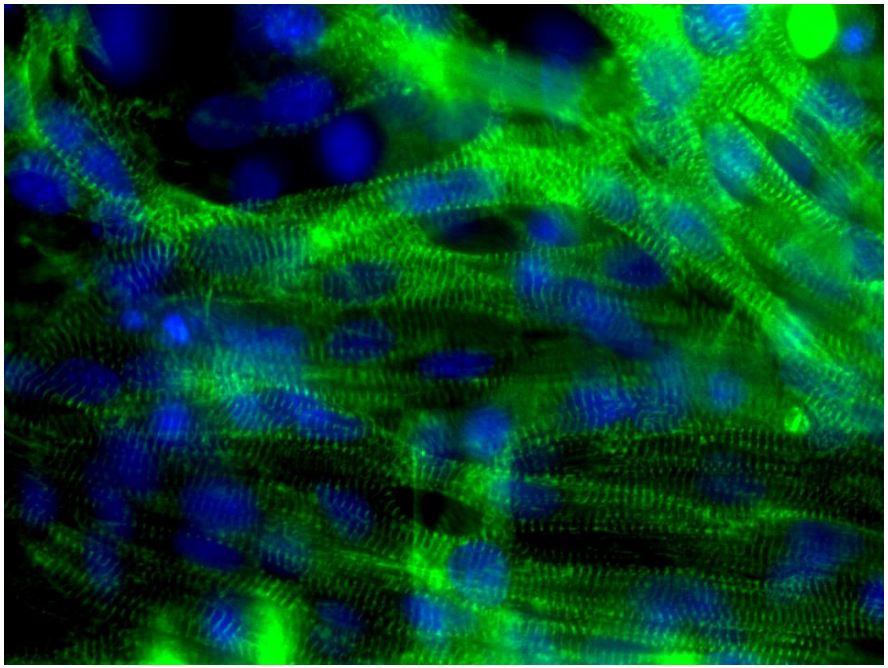


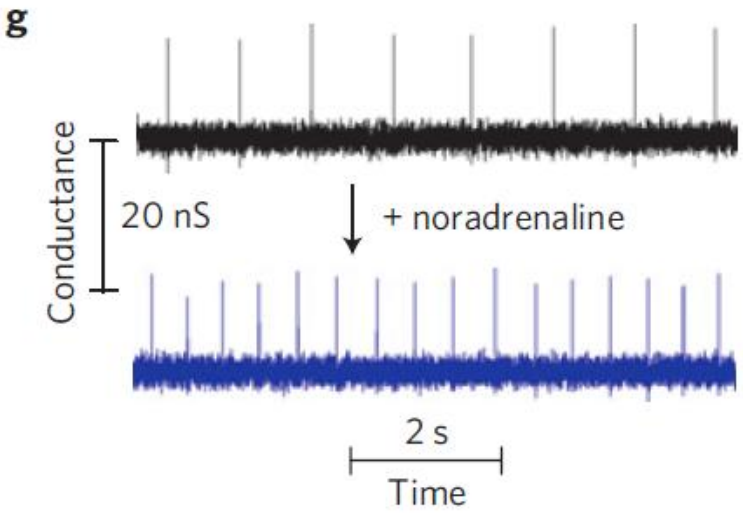




Tian et al. *Nature Materials.* 2012 Nov;11(11):986-94.

On-line monitoring engineered cardiac tissues



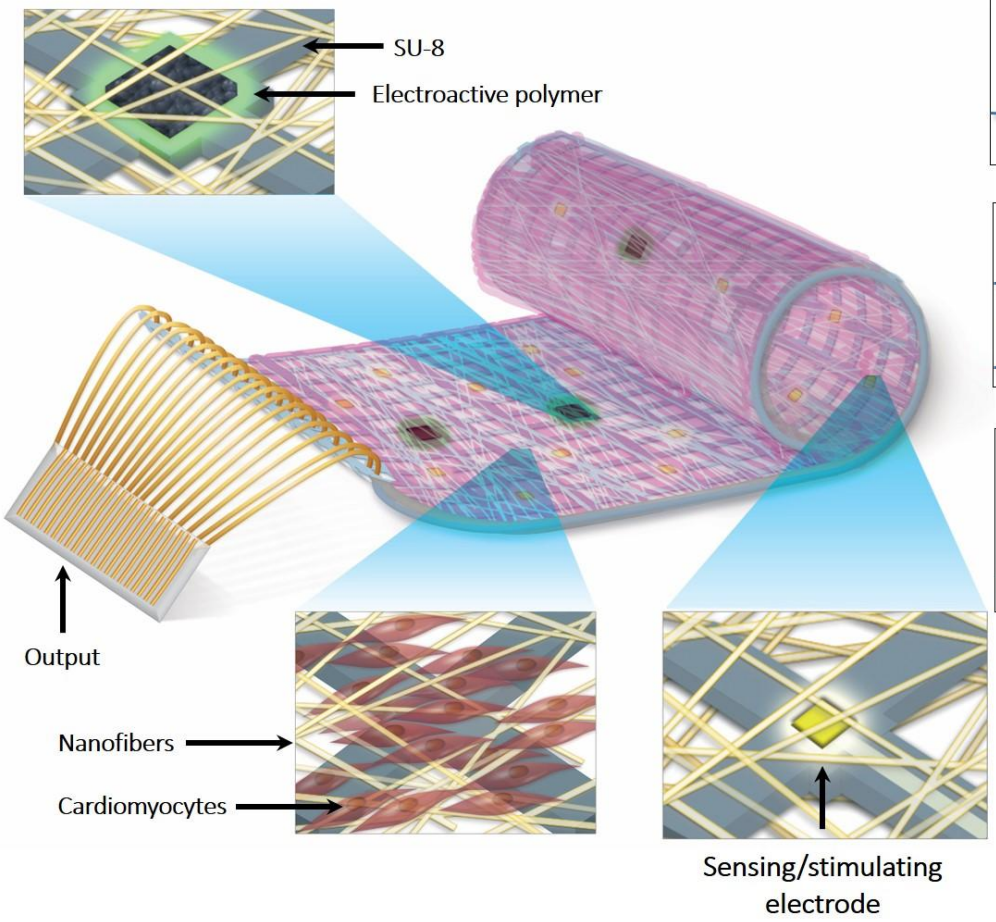


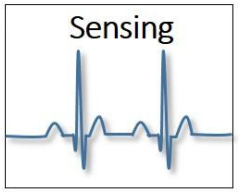
Nature Materials. 2012 Nov;11(11):986-94.

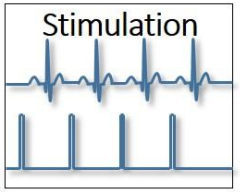
Second generation cyborg tissues

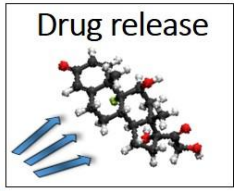
- Flexible
- Wireless
- Robust
- Transplantable

- Recording
- Stimulation
- Release drugs



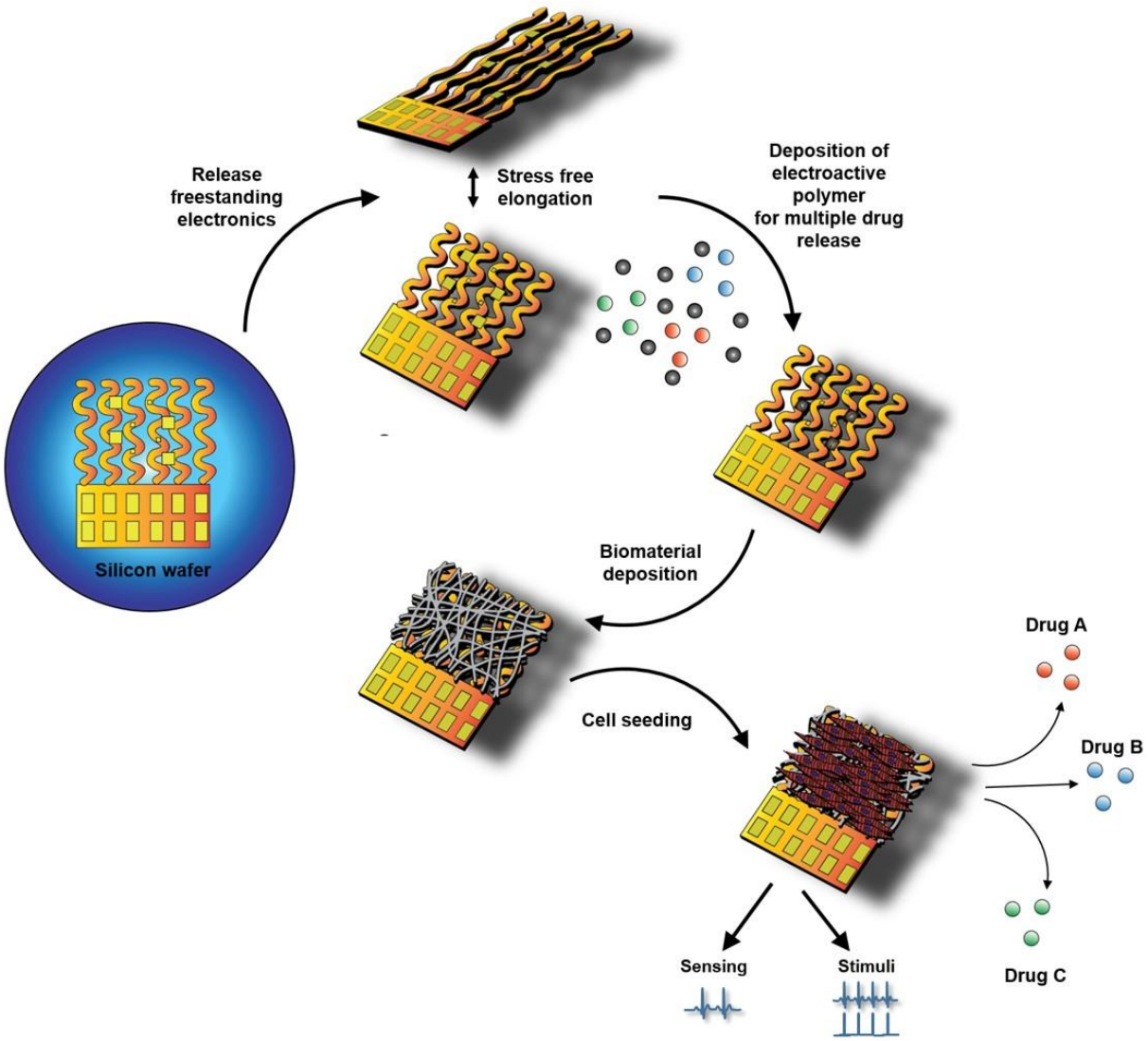






Feiner et al. *Nature Materials. 2016.*

Flexible and stretchable electronics



Feiner et al. *Small*. 2019

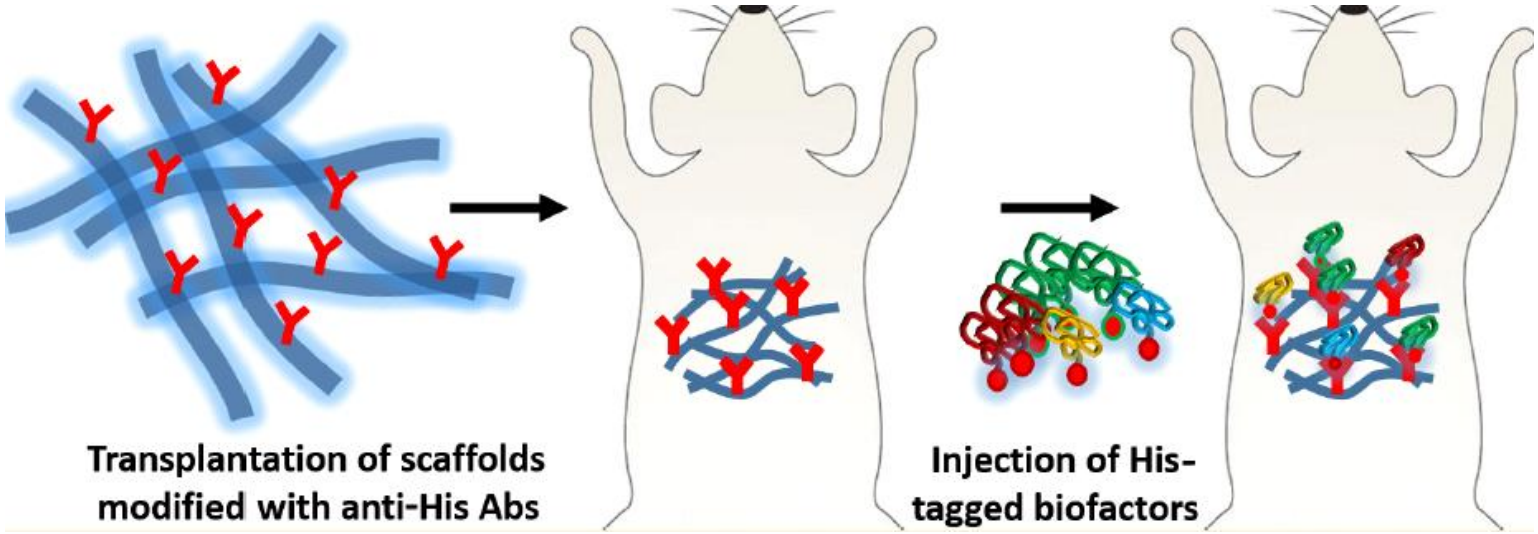
Reloading factors in vivo

NANO LETTERS
Letter
Cite This: *Nano Lett.* XXXX, XXX, XXX–XXX
pubs.acs.org/NanoLett

Universal Biofactor-Releasing Scaffold Enabling in Vivo Reloading

LeeRon Shefet Carasso,[†] Itai Benhar,*[,†,‡] and Tal Dvir*[,†,‡,§,∥]

[†]The School for Molecular Cell Biology and Biotechnology, The George S. Wise Faculty of Life Sciences, [‡]The Center for Nanoscience and Nanotechnology, [§]Department of Materials Science and Engineering, Faculty of Engineering, and [∥]Sagol Center for Regenerative Biotechnology, Tel Aviv University, Tel Aviv 69978, Israel

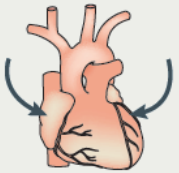


Shefet-Carasso et al. *Nano Letters*. 2019

Design consideration

a Organ dynamics

- Pressure and force generated
- Anisotropic and isotropic dynamics
- Length and volume changes

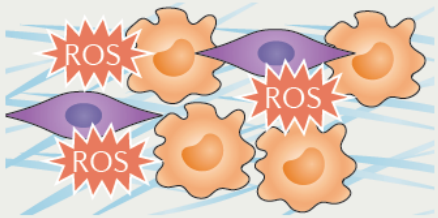


b Mechanical properties

- Elastic moduli of tissues ranging from 1 kPa to > 1 GPa
- Matching of device and tissue stiffness

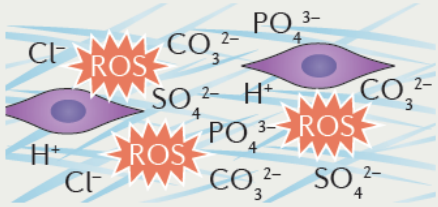
c Immune response

- Immune cell infiltration
- Foreign body response – fibrotic capsule formation
- Complement system
- Compromised local immune system



d Chemical environment

- Degradative enzymes
- Changes in local pH
- High concentration of ions
- ROS production

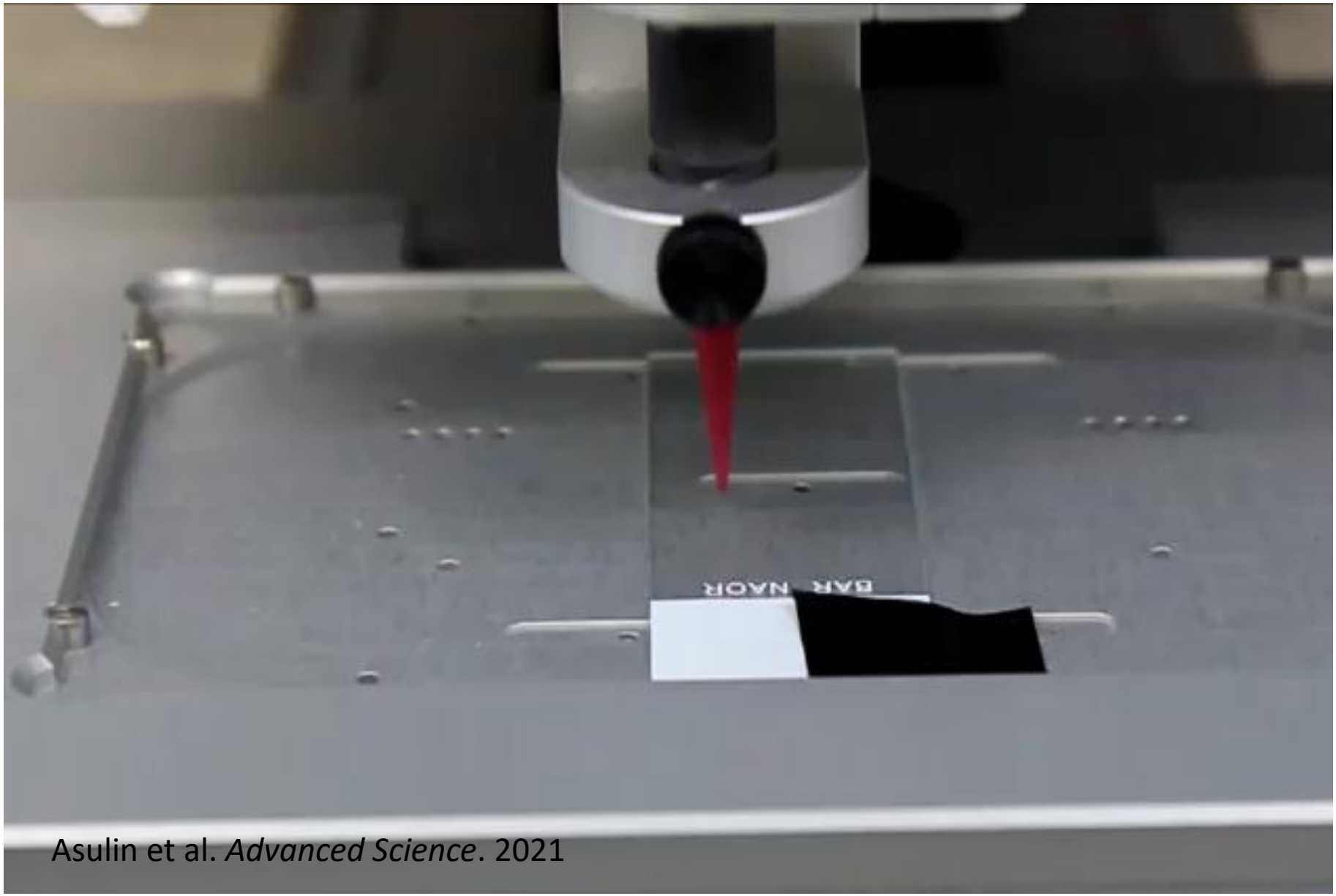


e Topography

- Complex organ topographies
- Adaption of device to target surface

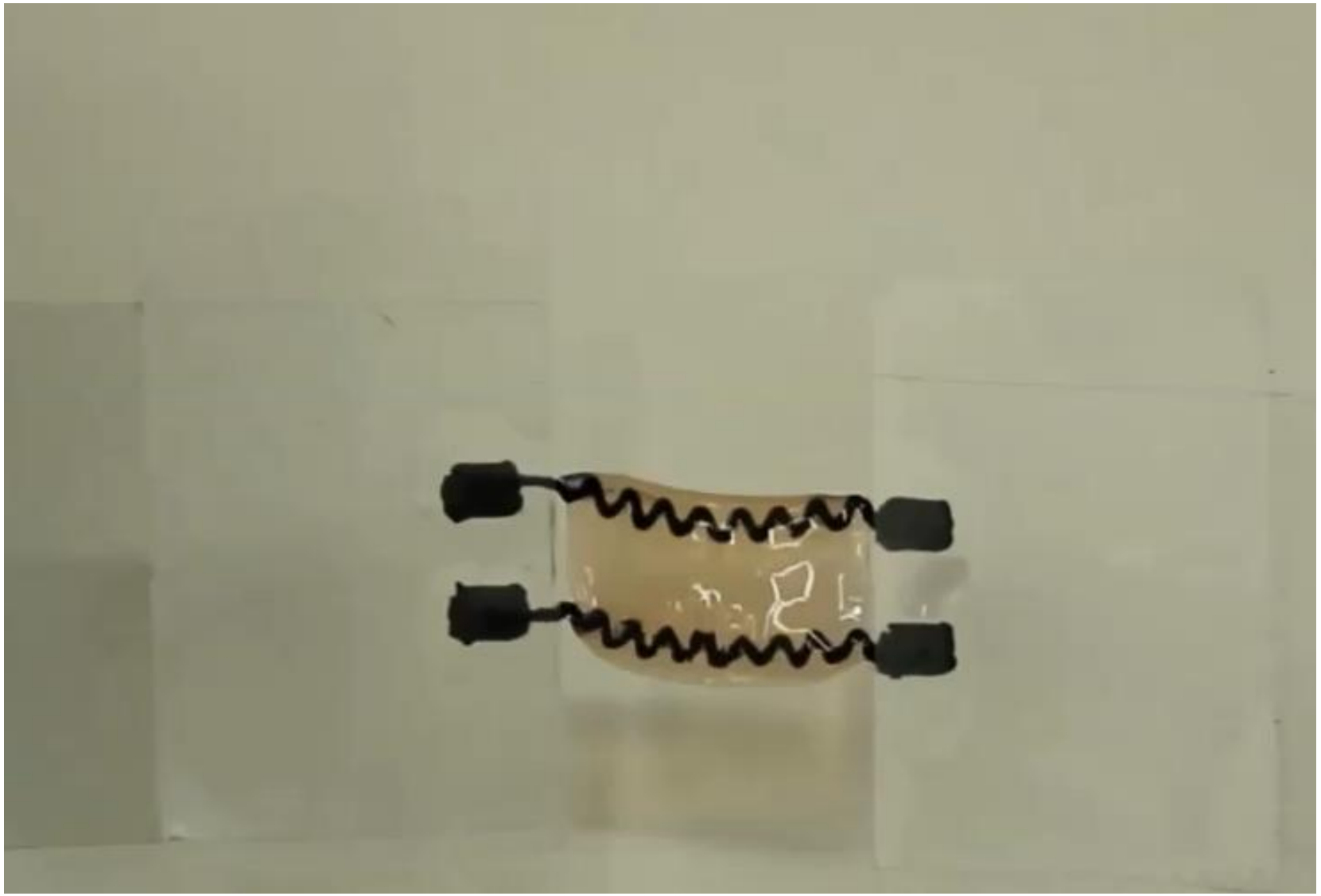
Feiner and Dvir. *Nature Reviews Materials*. 2018

Printing electronic cardiac patches



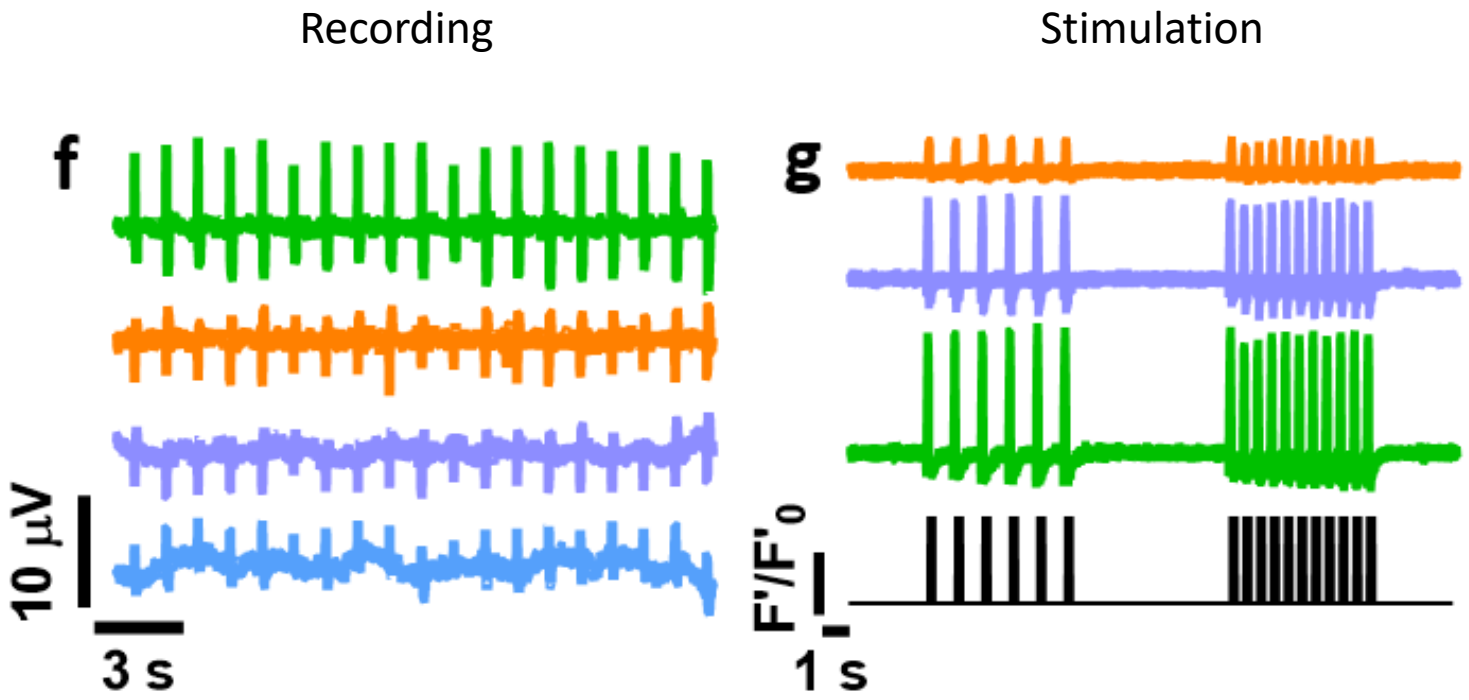
Asulin et al. *Advanced Science*. 2021

Asulin et al. *Advanced Science*. 2021



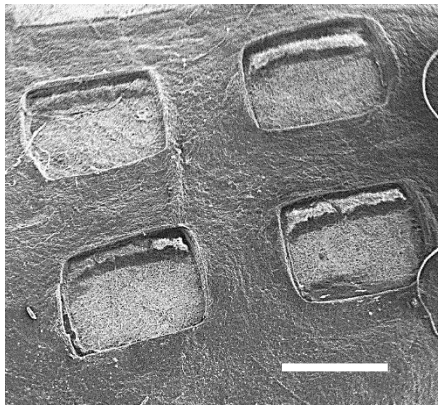
Asulin et al. *Advanced Science*. 2021

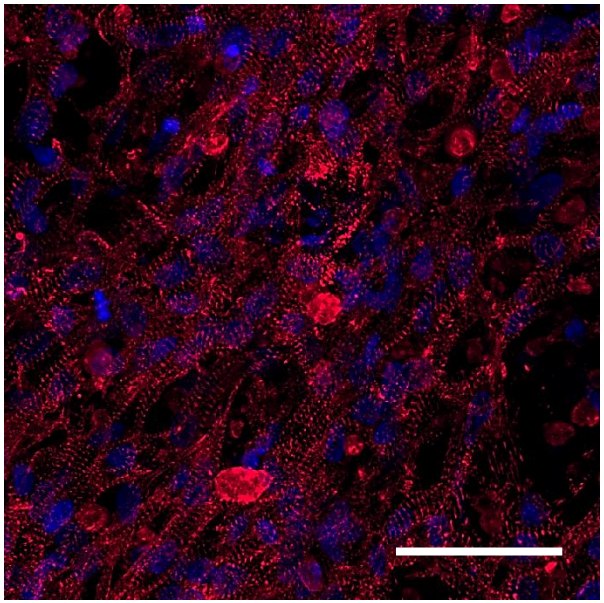
Printed electrode function

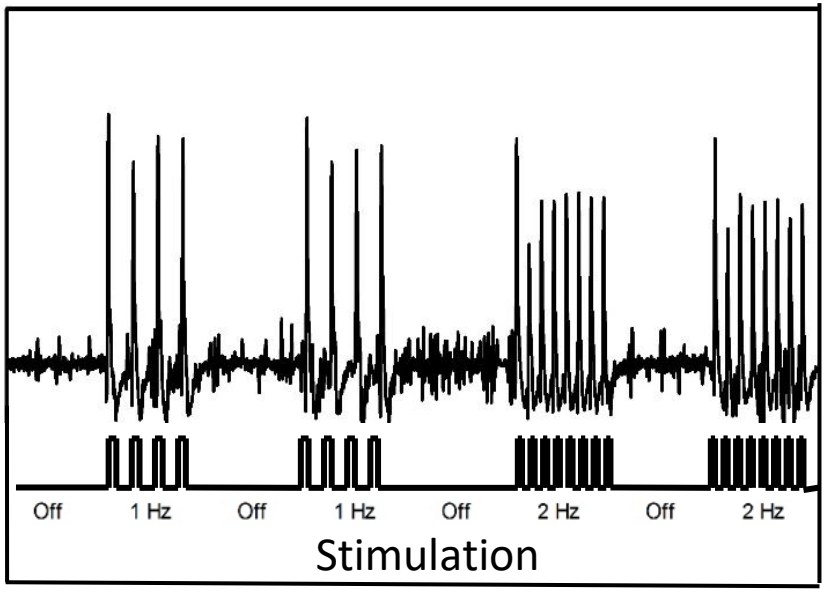


Asulin et al. *Advanced Science*. 2021

Degradable electronics

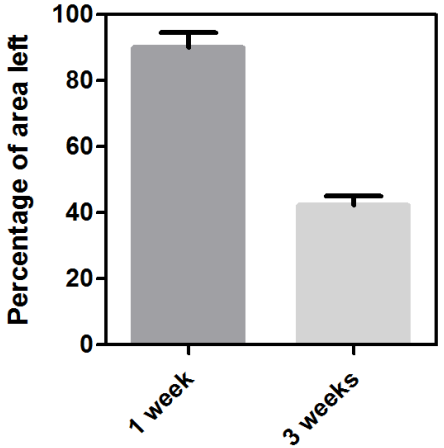


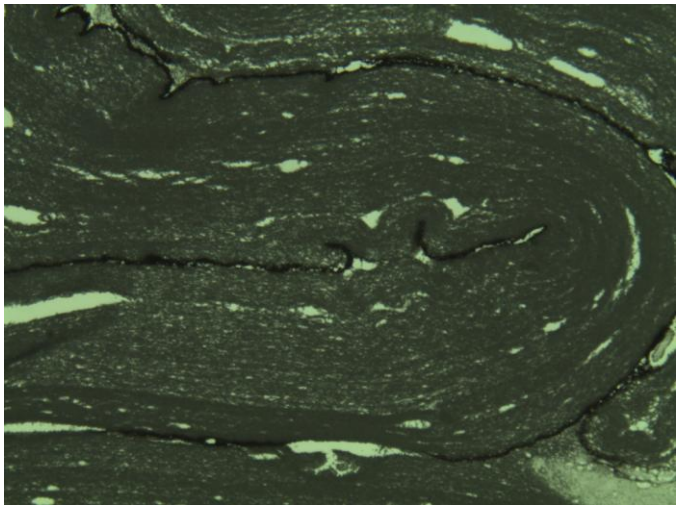


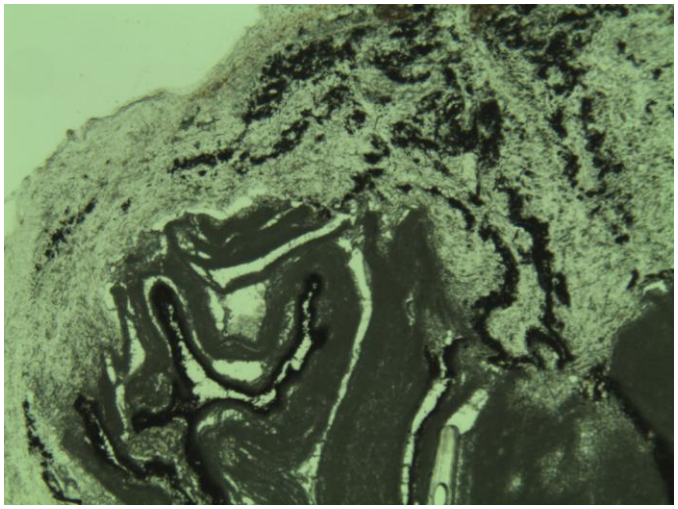


Feiner, Fleischer et al. *Journal of Controlled Release*. 2018

In vivo degradation

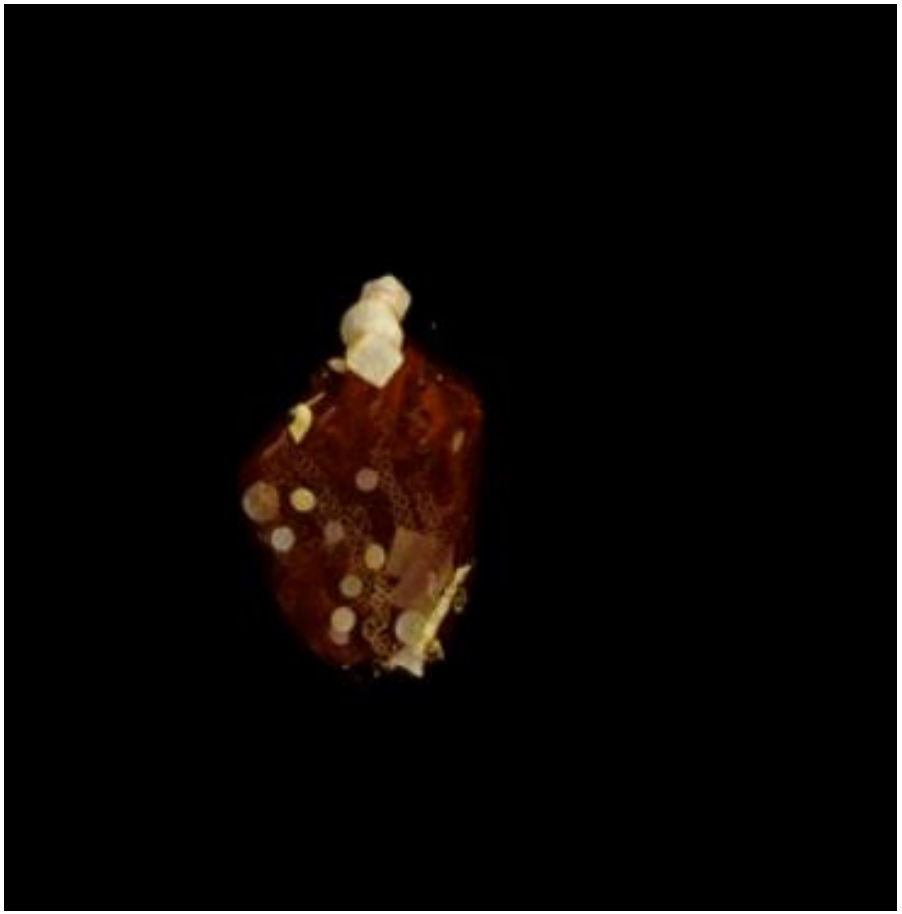


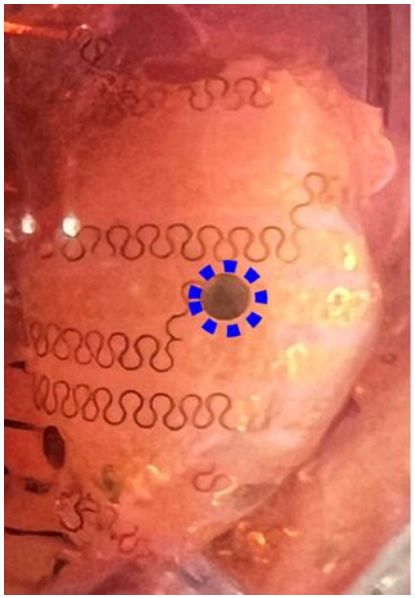


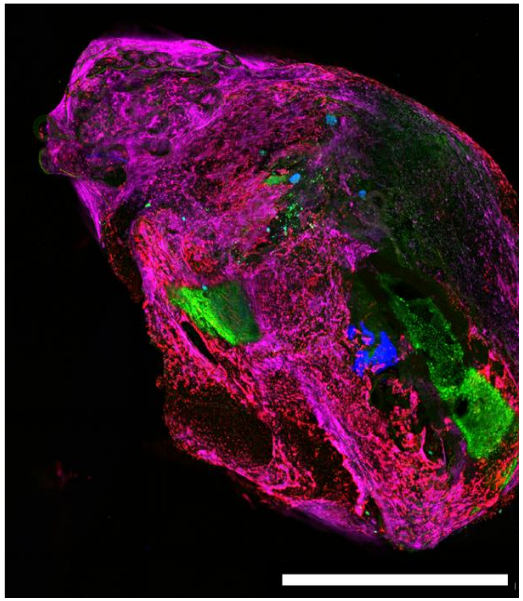


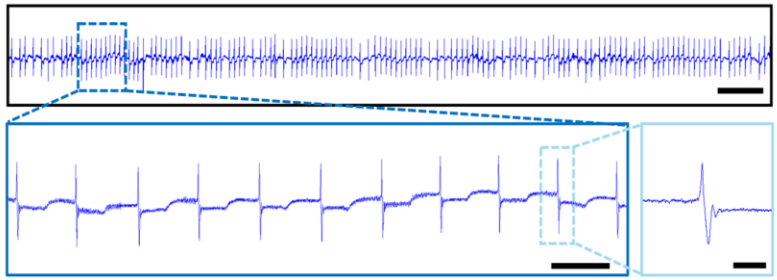
Feiner, Fleischer et al. *Journal of Controlled Release*. 2018

Engineering a whole bionic heart



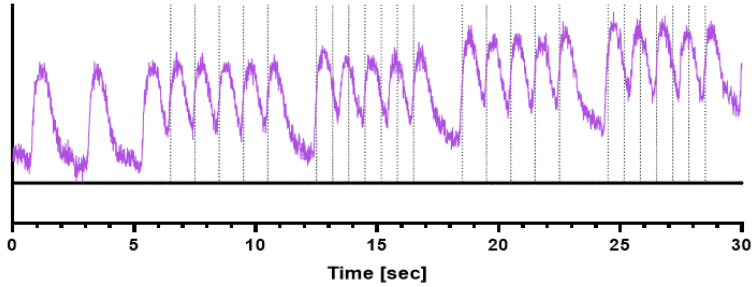






Recording

Stimulation



Oved et al. In Preparation

Acknowledgment

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Yosi Shacham (TAU)
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Itai Benhar (TAU)
Rachela Povotzer (BIU)
Yoram Etzion (BGU)

Ministry of Science

ISF

Sagol Family

THE SAGOL NETWORK