University Politehnica of Bucharest – Romania
Reykjavik University - Iceland

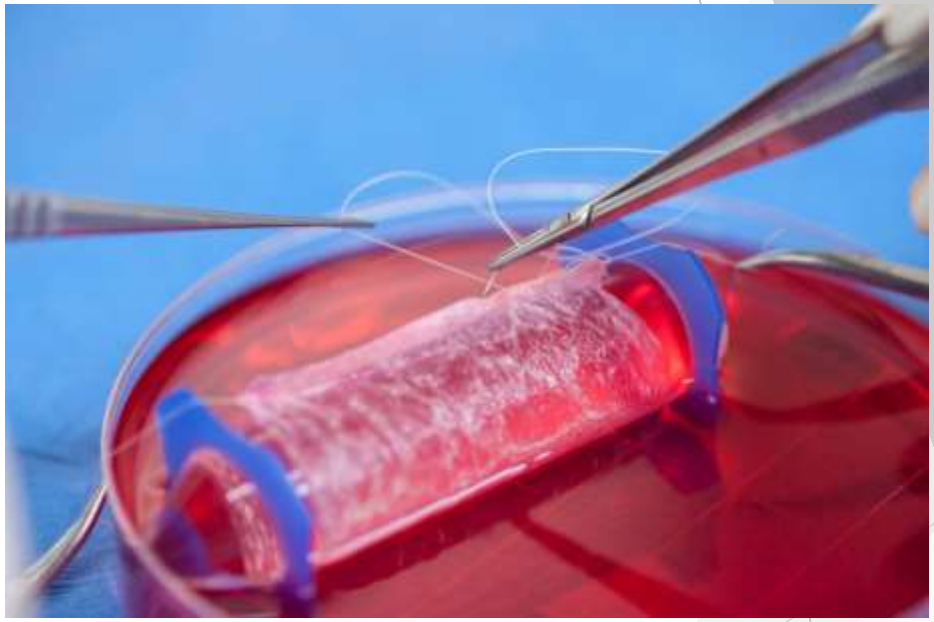
Faculty of Medical Engineering

Principles of Regenerative Medicine

Regenerative medicine

i. aims to replace tissue or organs that have been damaged by **disease**, **trauma**, or **congenital** issues, vs. the current clinical strategy that focuses primarily on treating the symptoms.

ii. interdisciplinary field aimed at creating biological replacements for injured tissues and dysfunctional organs.



Regenerative medicine - strategies

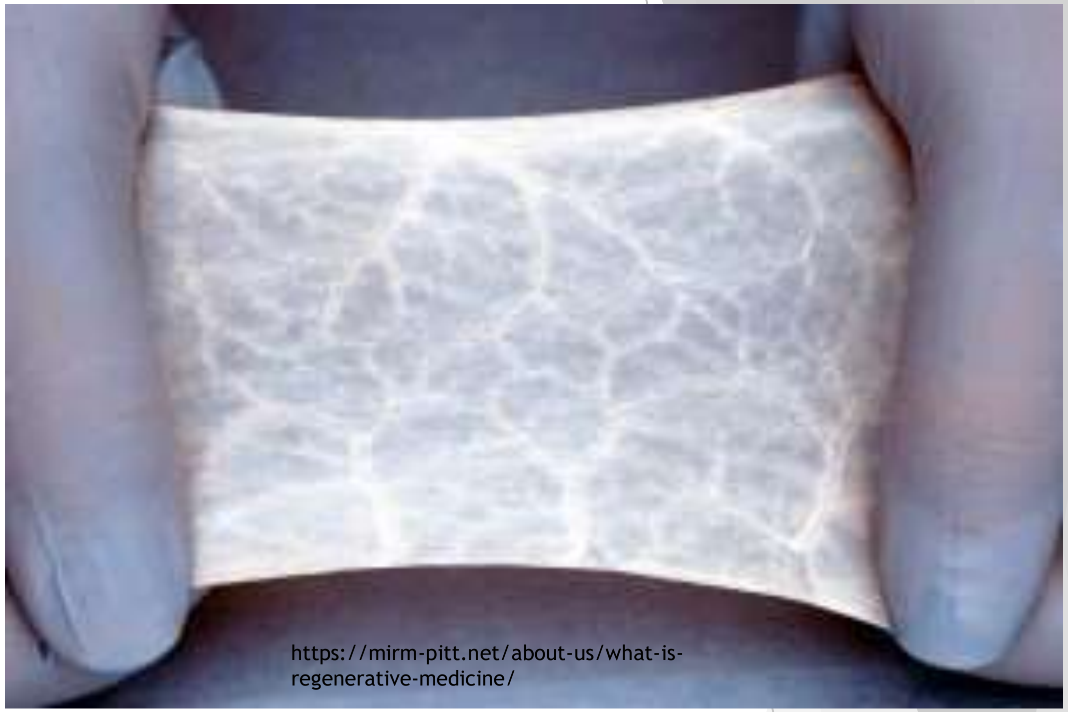
Regenerative medicine is a relatively new field that brings together experts in biology, chemistry, computer science, engineering, genetics, medicine, robotics to restore structure and function of damaged tissues and organs.

- **tissue engineering**
- **cellular therapies**
- **medical devices**
- **artificial organs**

Regenerative medicine strategies

- tissue engineering
- cellular therapies
- medical devices
- artificial organs

Biocompatible scaffolds are implanted in the body at the site where new tissue is damaged and new healthy tissue has to be formed. If the scaffold posses certain geometric shape and is able to attract cells the outcome is new tissue in the shape desired (new functional engineered tissue).



Regenerative medicine strategies

- tissue engineering
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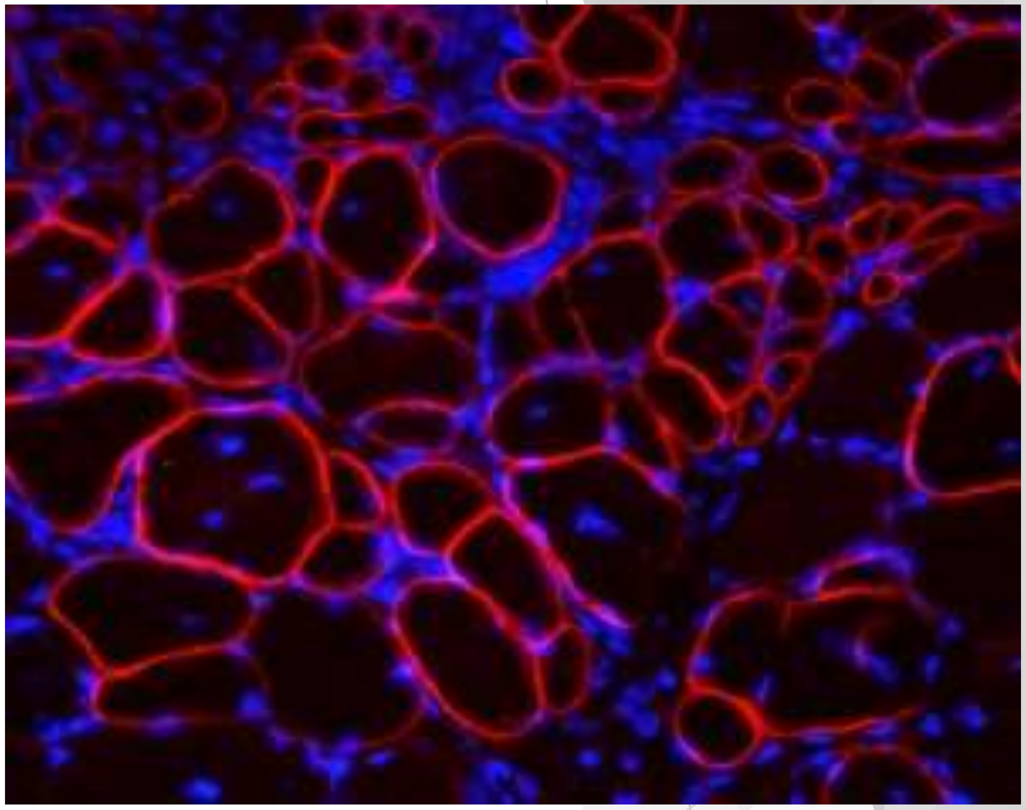
Billions of adult stem cells are used by the body for repairing itself. Several studies indicated that if adult stem cells are harvested and implanted at the place of diseased or damaged tissue, restoration of the tissue takes place under the right / certain conditions. The cells can come from blood, fat, bone marrow, dental pulp, skeletal muscle or cord blood (sources of adult stem cells). Currently the ability to prepare harvested stem cells to be injected into patients to repair diseased or damaged tissue it is one of the main challange.



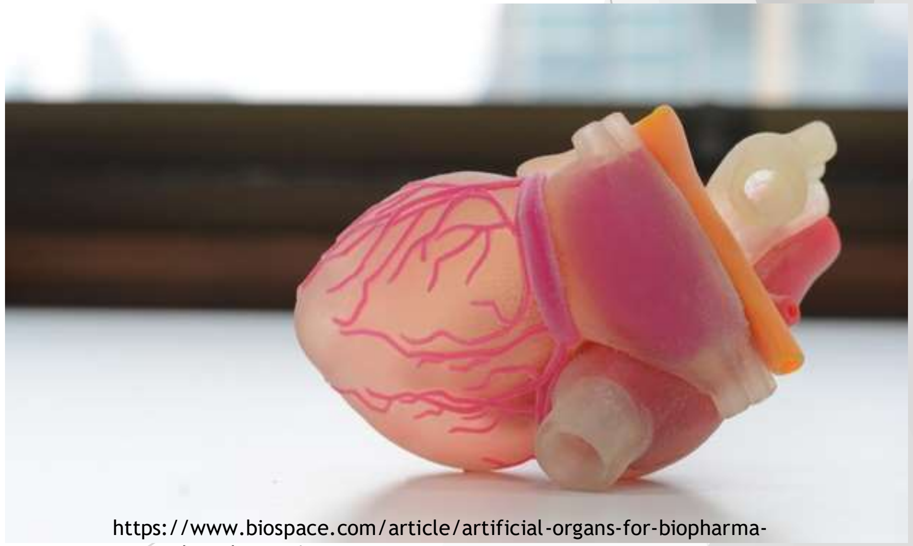
https://mirm-pitt.net/about-us/what-is-regenerative-medicine/

Regenerative medicine strategies

- tissue engineering
- cellular therapies
- medical devices
- artificial organs

The principal clinical strategy in organ fail is to transplant an organ from a donor. The availability of donor organs, and the requirement that the donor take immunosuppression drugs—which have side effects are the main challenges. In several instances where the time to find a appropriate donor organ requires an interim strategy to support the function of the failing organ until a transplantable organ is available. Technologies in various stages of maturity are currently available. (e.g. ventricular assist devices as a bridge to a heart transplant).

https://mirm-pitt.net/about-us/what-is-regenerative-medicine/



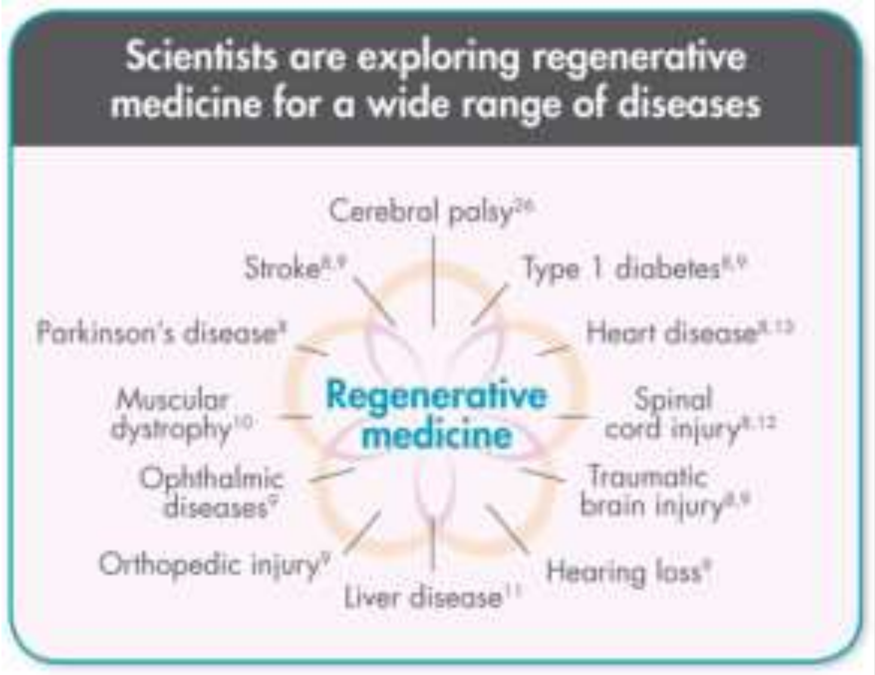
https://www.biospace.com/article/artificial-organs-for-biopharma-research-and-more/

Regenerative medicine challenges

Clinical translation is limited to thin, small, and/or acellular structures.

What products of tissue engineering have you encountered?

What products of tissue engineering will be produced in the future?



Regenerative medicine therapies

Since tissue engineering and regenerative medicine emerged as an industry about two decades ago, a number of therapies have received Food and Drug Administration (FDA) clearance or approval and are commercially available.

Category	Name	Biological agent	Approved use
Biologics	laViv	Autologous fibroblasts	Improving nasolabial fold appearance
	Carticel	Autologous chondrocytes	Cartilage defects from acute or repetitive trauma
	Apligraf, GINTUIT	Allogeneic cultured keratinocytes and fibroblasts in bovine collagen	Topical mucogingival conditions, leg and diabetic foot ulcers
	Cord blood	Hematopoietic stem and progenitor cells	Hematopoietic and immunological reconstitution after myeloablative treatment
Cell-based medical devices	Dermagraft	Allogenic fibroblasts	Diabetic foot ulcer
	Celution	Cell extraction	Transfer of autologous adipose stem cells
Biopharmaceuticals	GEM 125	PDGF-BB, tricalcium phosphate	Periodontal defects
	Regranex	PDGF-BB	Lower extremity diabetic ulcers
	Infuse, Infuse bone graft, Inductos	BMP-2	Tibia fracture and nonunion, and lower spine fusion
	Osteogenic protein-1	BMP-7	Tibia nonunion

PDGF - platelet derived growth factor

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4664309/

Regenerative medicine therapies

Injection of stem cells or progenitor cells

Induction of regeneration (biologically active molecules alone / or as a secretion by infused cells (immunomodulation therapy)

Transplantation of *in vitro* grown organs and tissues (tissue engineering)

Regenerative medicine strategies

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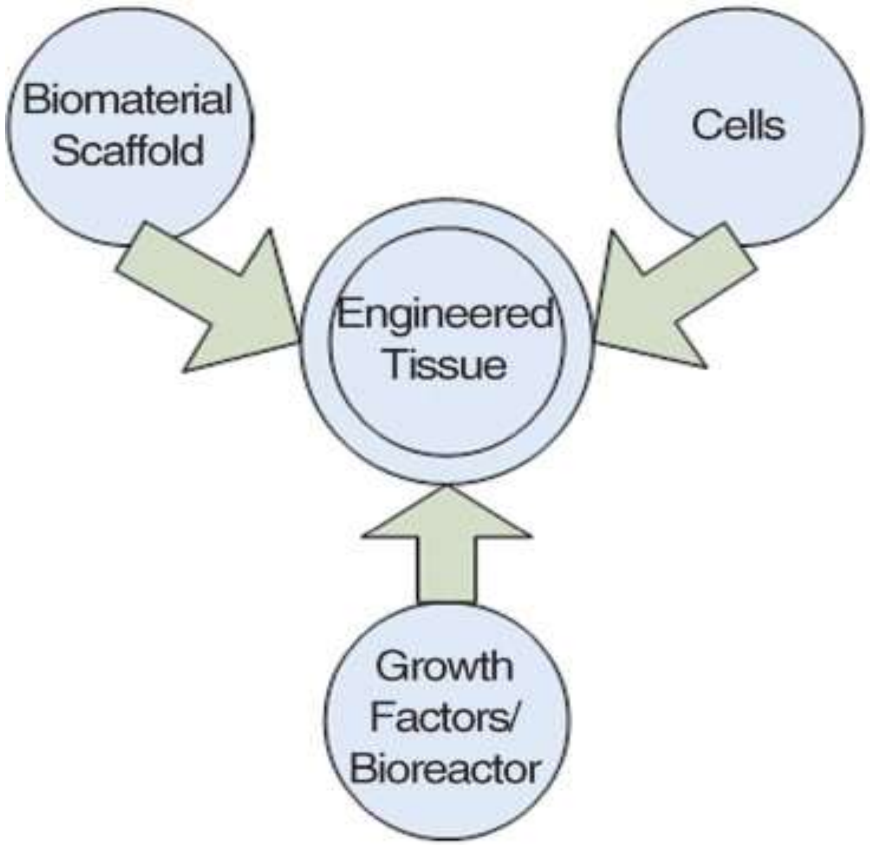
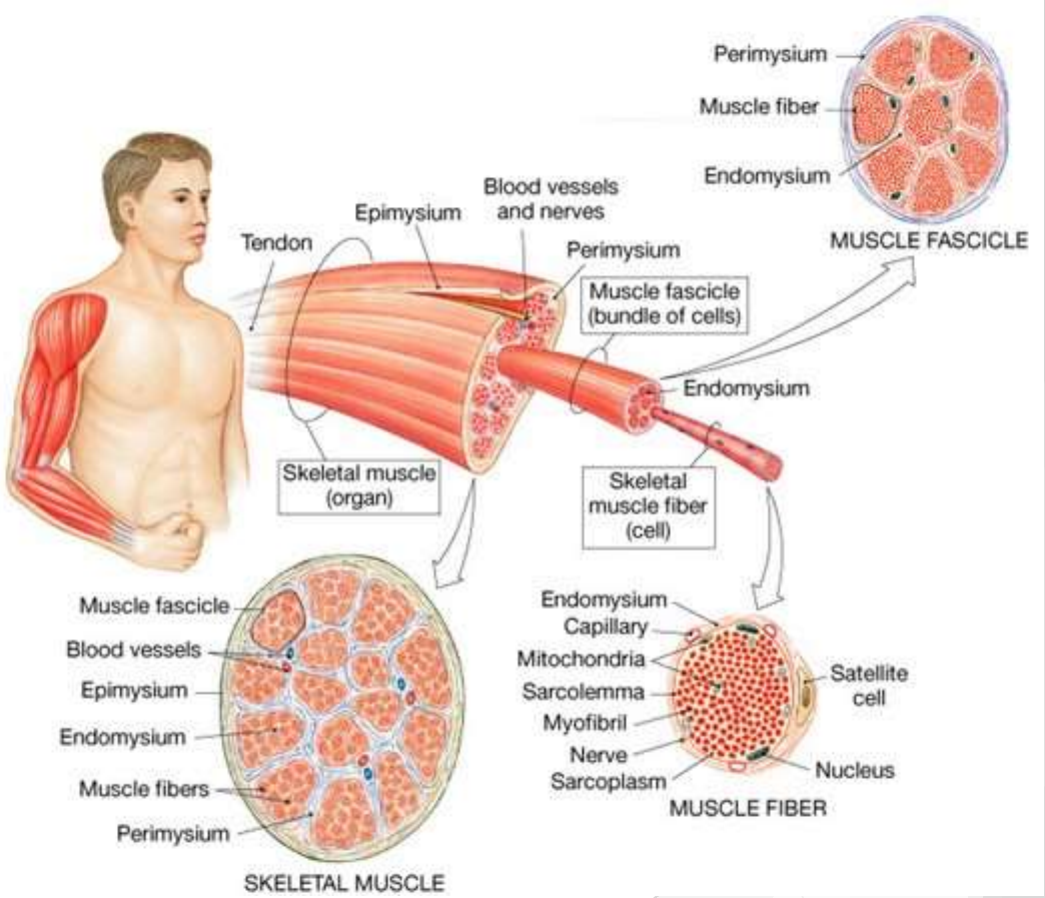


Tissue Complex Organization

Tissue development *in vitro*

Understand of tissue organization in our body

Understand the tissue function of our body



https://www.slideserve.com/creda/chapter-10-muscular-tissue

From macroscopic to molecular level
7-10 levels of structural organization

Cellular Microenvironment

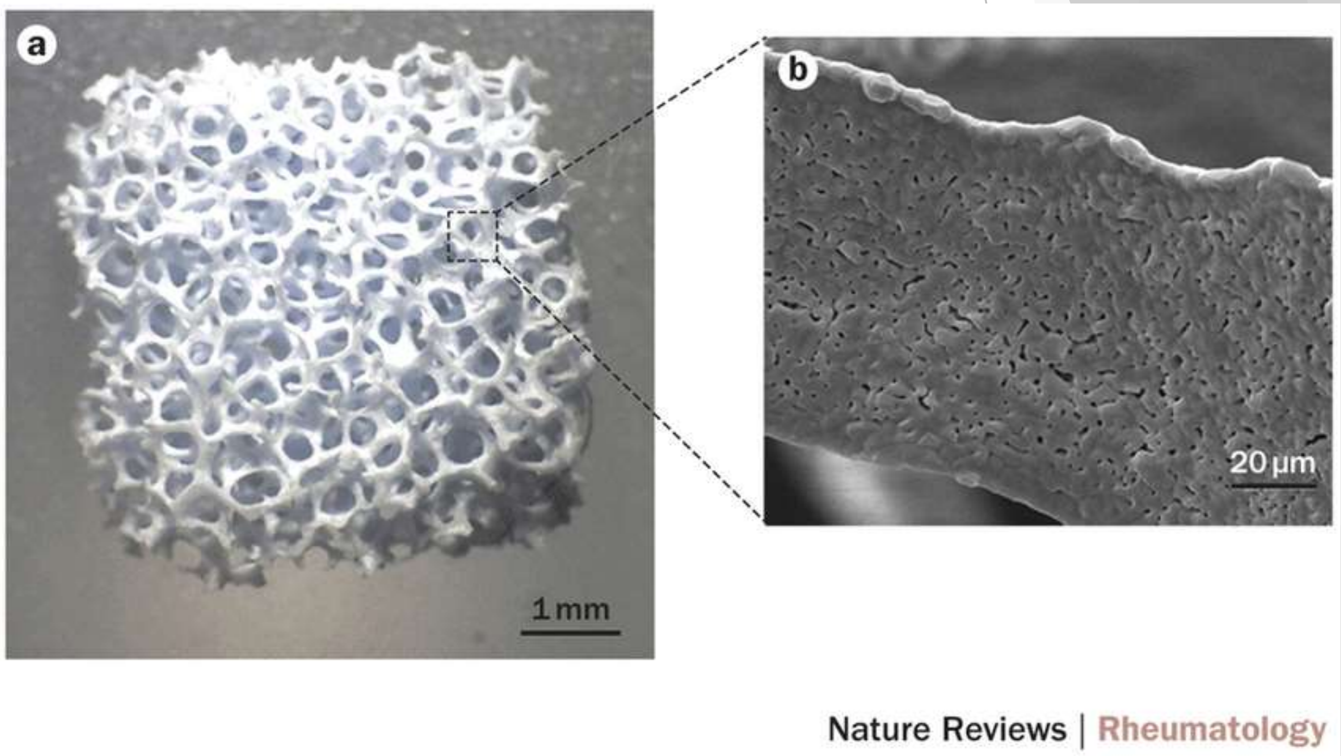
Cells are entirely responsible for synthesizing tissue constituents and assembly to subunit

- Different cell types
- Cell-cell communications
- Local chemical environment
- Local geometry

I. EMPTY SCAFFOLDS
II. CELLULARIZED SCAFFOLDS

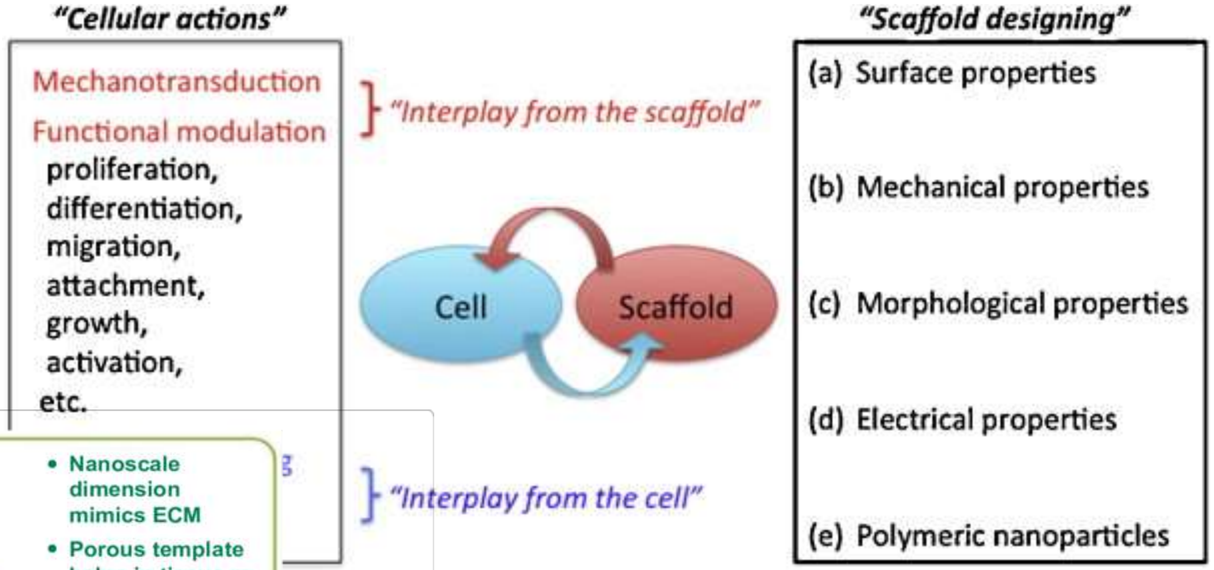
EMPTY SCAFFOLDS

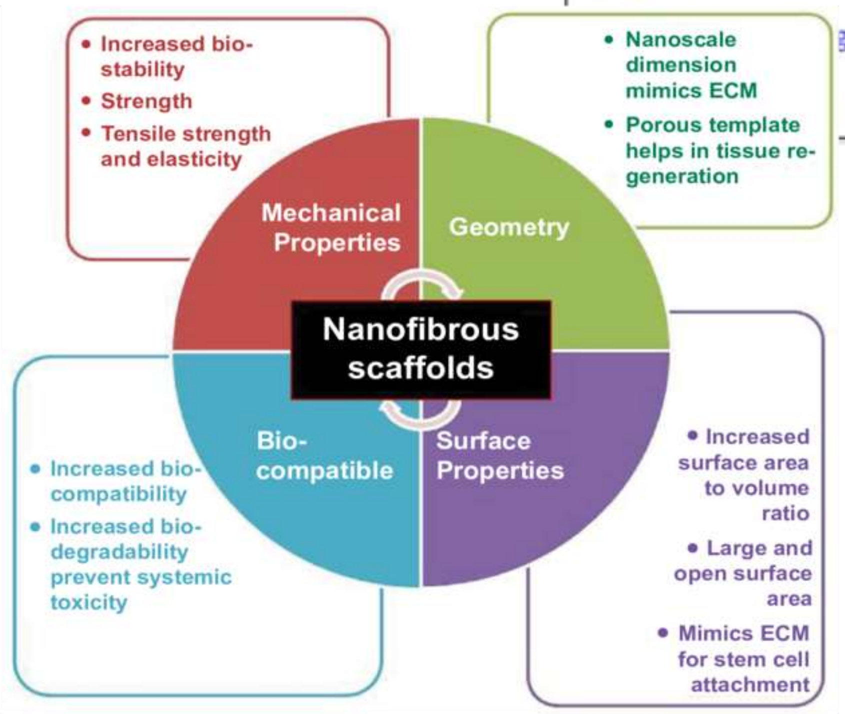
1. POLYMER SCAFFOLDS
2. CERAMIC SCAFFOLDS
3. COMPOSITE SCAFFOLDS
4. *IN VITRO* OBTAINED SCAFFOLDS
5. ECM SCAFFOLDS
6. DECELLULARIZED ORGANS SCAFFOLDS

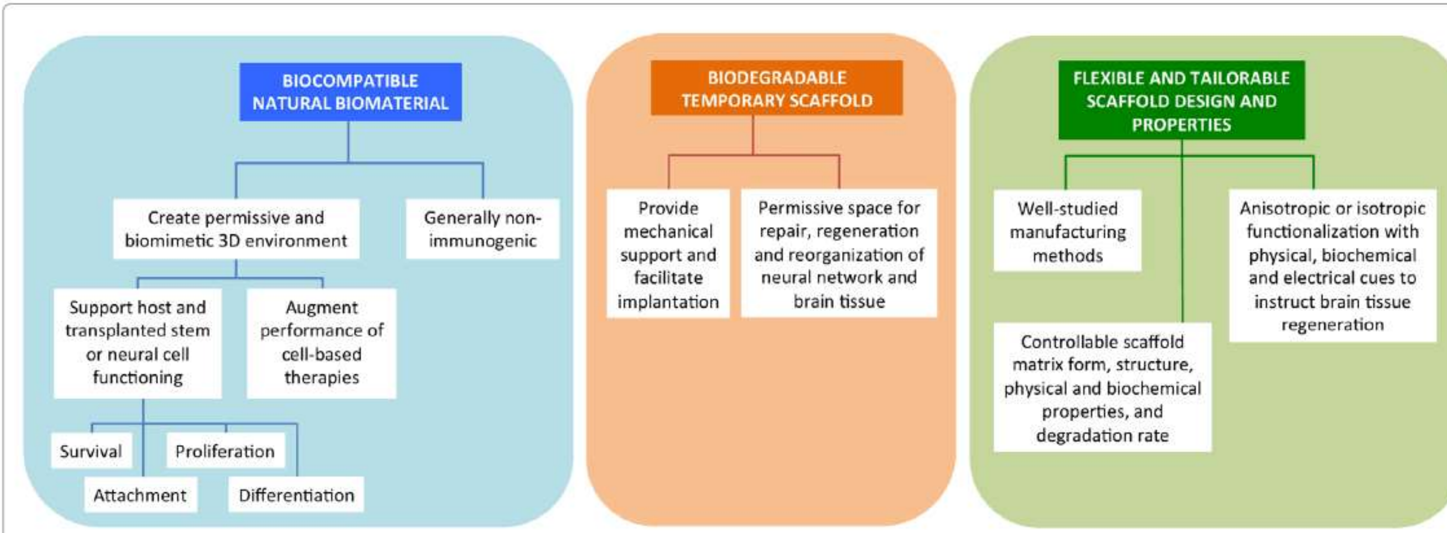


https://www.nature.com/articles/nrrheum.2015.27

SCAFFOLDS GENERAL FEATURES

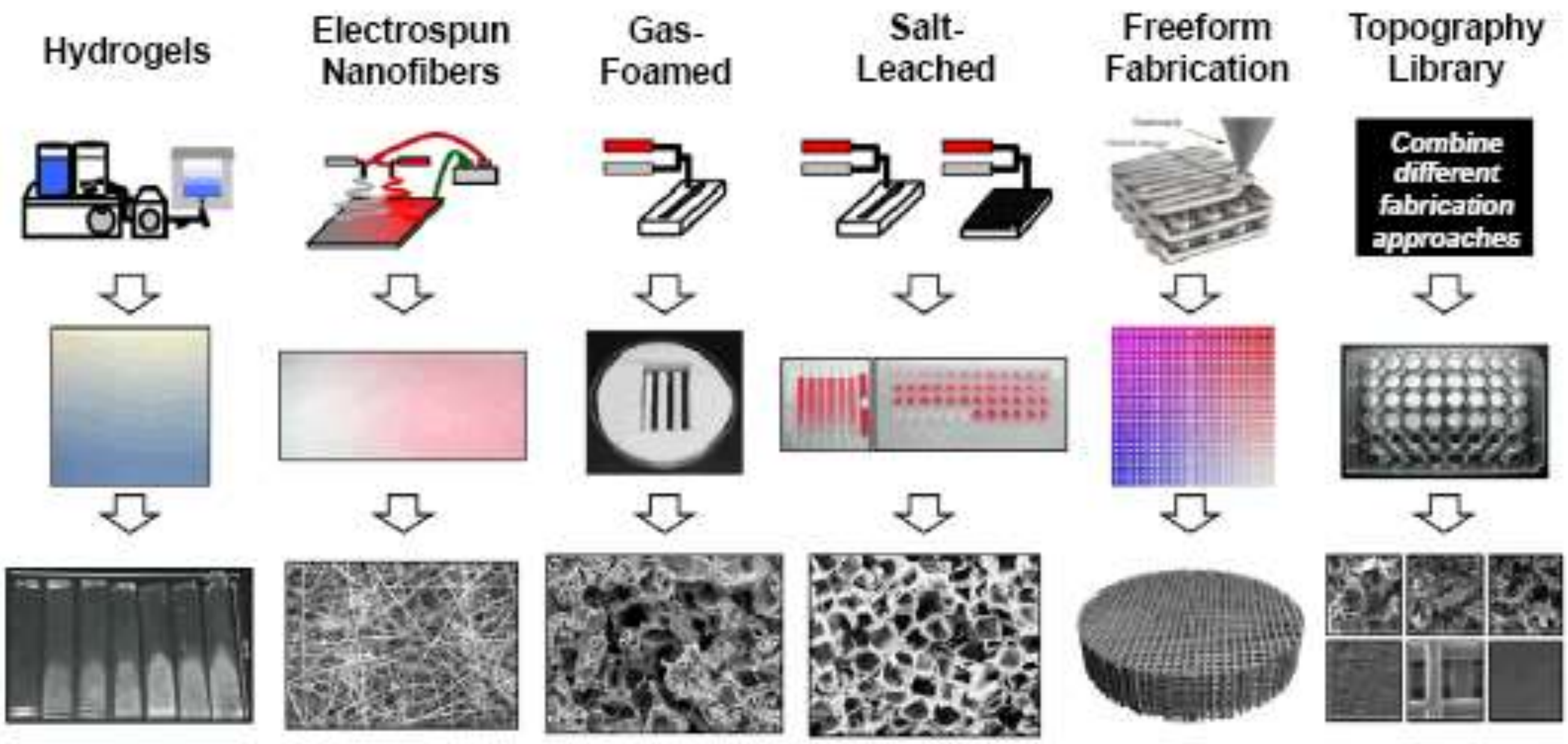






https://onlinelibrary.wiley.com/doi/full/10.1002/adfm.202010609

SCAFFOLDS FABRICATION METHODS



Different scaffold fabrication methods

https://www.nist.gov/mml/bbd/biomaterials/scaffold-fabrication-airbrushed-scaffolds-combinatorial-methods

The financial support provided by Education, Scholarships, Apprenticeships and Youth Entrepreneurship Programme in Romania, financed by the EEA Grants 2014-2021, Cooperation Projects in Higher Education Area, project Mixed Reality e-learning platform dedicated to Medical Engineering (REALME), contract RO-EDUCATION-0177 / 21-COP-0017, is kindly acknowledged.

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