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Electrospun polymeric membranes for tissue engineering and cell growth

Maria Helena Ambrosio Zanin

Palestra apresentada no INTERNATIONAL CONFERENCE ON MATERIALS SCIENCE AND ENGINEERING, 2024, Tokyo. ***Lecture....*** *28 slide.*

INSTITUTO DE PESQUISAS TECNOLÓGICAS

ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

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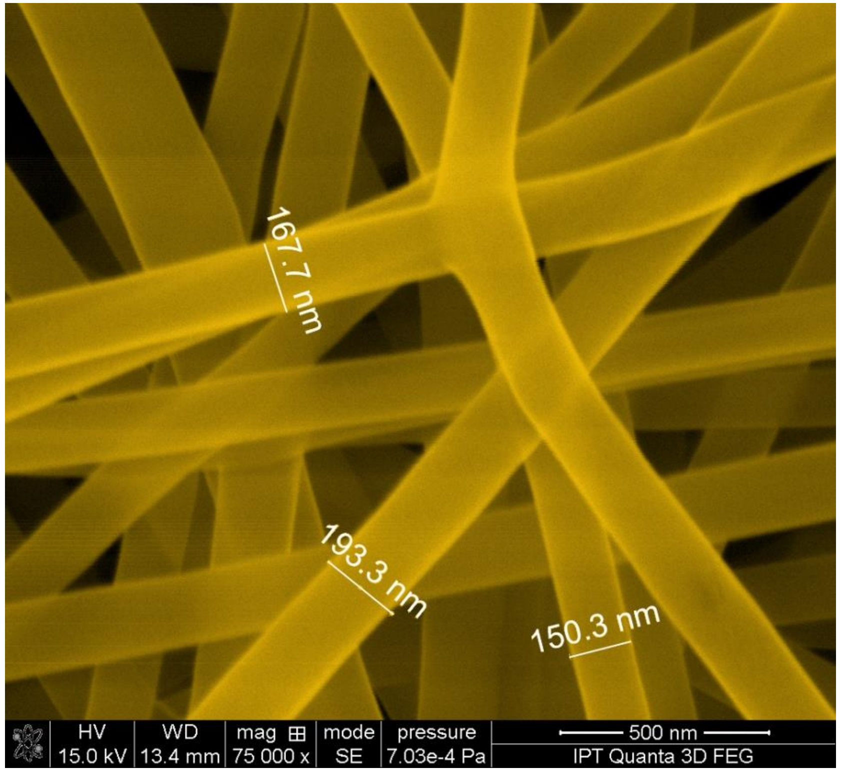
10th International Conference on
Materials Science & Engineering October 17-18, 2024 | Tokyo, Japan

SÃO PAULO GOVERNO DO ESTADO

ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

Outline

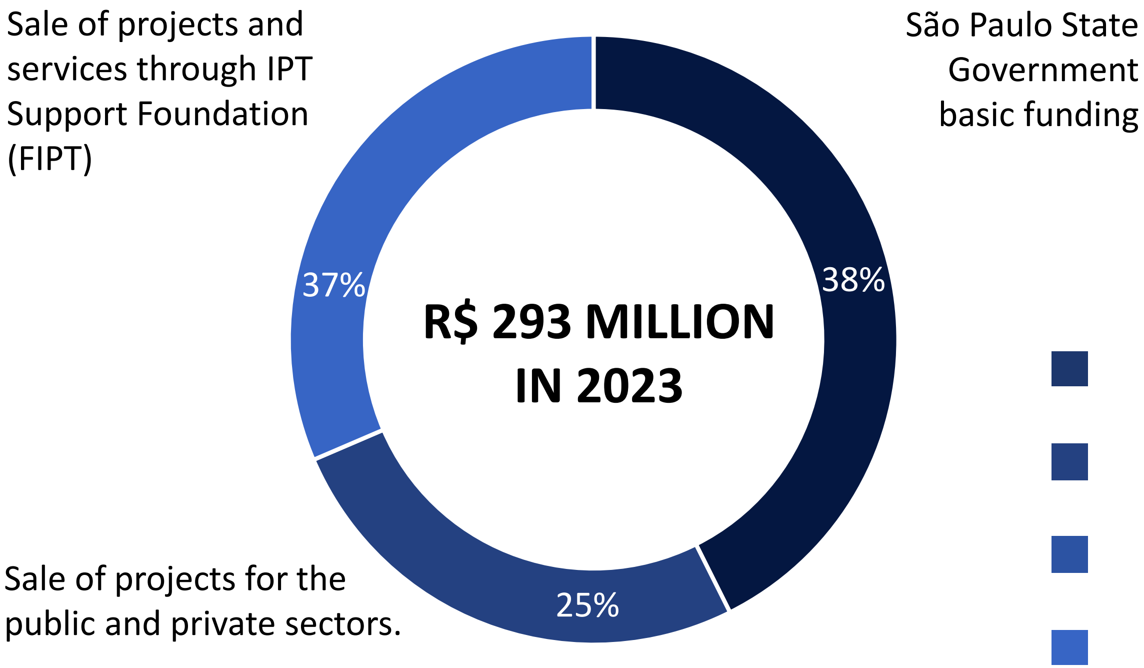
- ***Presentation of IPT***
- ***Tissue engineering***
- ***Electrospinning process***
- ***Polymers applied in scaffold development***
- ***Case studies of scaffold at IPT***
- ***Final considerations***



WHO ARE WE ?

IPT PROVIDES TECHNICAL SOLUTIONS FOR INDUSTRY, GOVERNMENTS AND SOCIETY, ENABLING THEM TO OVERCOME THE CHALLENGES OF OUR TIME

INCOMES



OUR NUMBERS (2022)

- 125 YEARS OF CONTRIBUTIONS TO SOCIETY
- > 1,000 EMPLOYEES AND PARTNERS
- 41% REVENUE IN INNOVATION PROJECTS
- > 1,830 CUSTOMERS SERVED
- SATISFIED CUSTOMERS NPS 84 (LEVEL OF EXCELLENCE)
- > 19,900 TECHNICAL DOCUMENTS ISSUED
- > 2,000 TESTING AND ANALYSIS PROCEDURES IN THE PORTFOLIO

BUSINESS UNITS

BIONANOMANUFACTURING
Processes, Chemistry, Biotech, Nanotech, Microfabrication

CITIES, INFRASTRUCTURE AND ENVIRONMENT
Territorial planning, Sustainability, Risks, Civil works

ENERGY
Generation, Infrastructure, Efficiency, Clean energy

BUILDING AND HOUSING
Confort, Performance, Safety, Materials, Sustainability

ADVANCED MATERIALS
Metallic, Polymeric, Composite, Cellulosic, Corrosion

DIGITAL TRANSFORMATION
IoT, Embedded Systems, Intelligent Transport Systems, AI, Analytics

METROLOGICAL AND REGULATORY TECHNOLOGIES
Mechanics, Electrical, Flow Measurement, Aerodynamics, Chemistry

BIONANOMANUFACTURING CENTER

INDUSTRIAL BIOTECHNOLOGY
BIOPROCESS DEVELOPMENT AND SCALE-UP
GENETIC ENGINEERING
TECHNICAL AND ECONOMICAL FEASIBILITY OF PROCESSES
WASTE UTILIZATION
MICROBIOLOGY

40 PEOPLE
9 PhDs
9 MScs
15 GRADUATES
7 TECHNICIANS

MICROMANUFACTURING
MICROFLUIDIC DEVICES
SENSORS, ACTUATORS AND EMBEDDED SYSTEMS
MICROFABRICATION
MINIATURIZATION OF DEVICES, SYSTEMS, AND PROCESSES

9 PEOPLE
3 PhDs
2 MScs
4 GRADUATES

CHEMICAL PROCESSES AND PARTICLE TECHNOLOGIES
CHEMICAL TECHNOLOGY
NANOTECHNOLOGY
ENCAPSULATION AND CONTROLLED RELEASE SYSTEMS
INDUSTRIAL CRYSTALLIZATION
FUNCTIONAL MATERIALS

34 PEOPLE
7 PhDs
5 MScs
17 GRADUATES
5 TECHNICIANS

CHEMISTRY AND MANUFACTURES
ANALYTICAL DEVELOPMENT
TECHNICAL TEXTILES
PPEs – PERSONAL PROTECTIVE EQUIPMENT
FOOTWEAR
OPINIONS FOR TAX CLASSIFICATION AND LEGAL ISSUES

38 PEOPLE
07 MScs
20 GRADUATES
11 TECHNICIANS

QUICK DATA

- 7, 000 SQUARE METERS OF LABORATORIES
- 35 % OF MASTERS AND PHDS
- 60% OF THE REVENUE FROM INNOVATION PROJECTS
- BENCH TO PILOT SCALE PROJECTS
- MULTIDISCIPLINARY TEAM
- EMBRAPII'S UNITS: MATERIALS AND BIOTECHNOLOGY
- ISO 17025 AND ISO 9001 ACCREDITATION

Open Experience IPT

O IPT opens it campus to the largest open innovation action in hardtech in Brazil, connecting distinct sotckholders of this ecosystem.

Cornerstone of the CITI Project – São Paulo State International Technology and Innovation Center.

Mode 1

Innovation hub

Become part of in a unique and transformative ecosystem that brings together companies and starups that undertake together in the creation of technologies that drive new businesses.

Mode 2

Innovation center

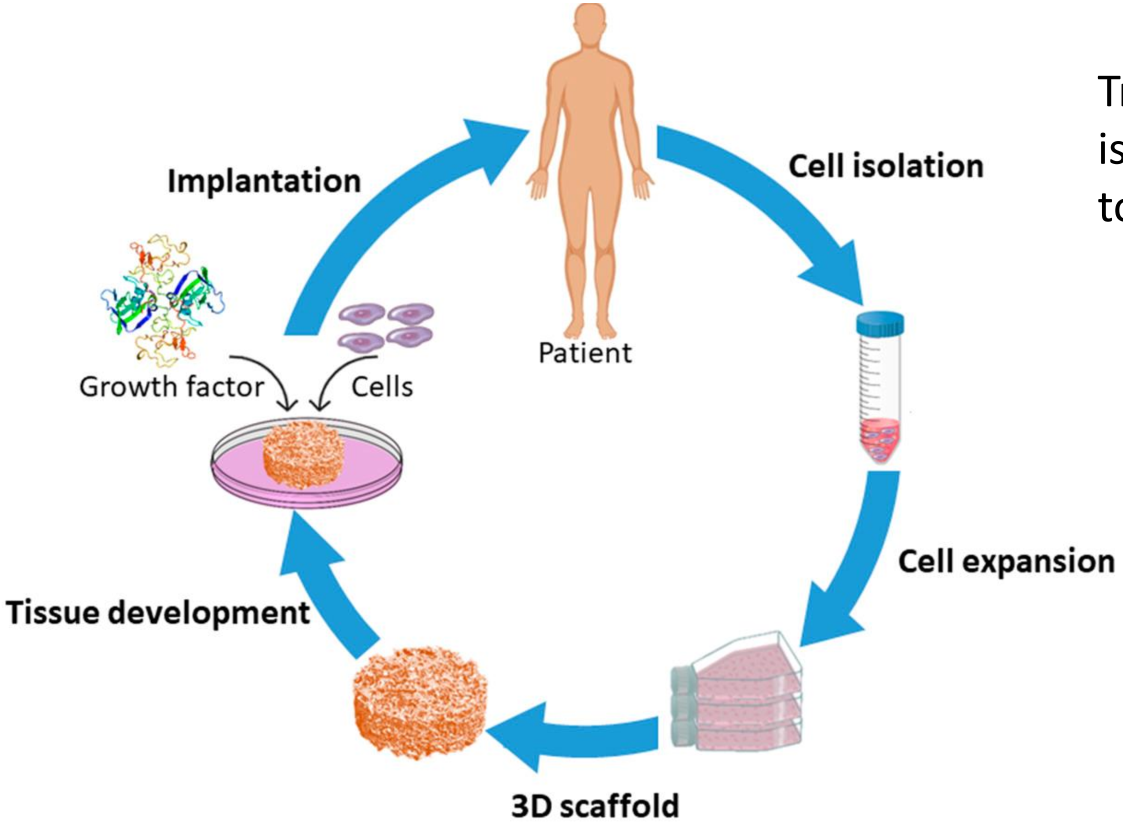
Install your company´s Technology Center within the IPT campus and leverage your development capacity.

TISSUE ENGINEERING

Interdisciplinary field that applies engineering, biology and life sciences principles to developing biological substitutes that can maintain, restore, or improve the function of organs and tissues

TISSUE ENGINEERING

Seeding of cells in combination with growth factors on a three-dimensional (3D) matrix, referred to as “a scaffold”, which acts as a temporary framework on which cells can adhere, grow and differentiate in vitro before implantation *in vivo*



Schematic of the scaffold-based tissue engineering approach

Transplantation of cells isolated from a healthy part to an injured tissue

Injection of factors that initiate/induce tissue regeneration like growth factors, differentiation factors, polysaccharides, and peptides to a targeted site

Asadian *et al*. 2020

TISSUE ENGINEERING

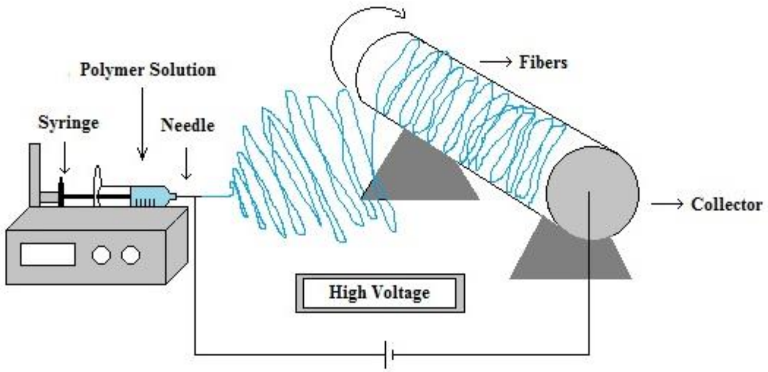
Requirements that have been identified as crucial to the scaffold

Asadian *et al*. 2020

- It needs to be bio-compatible to integrate well with the host body without eliciting any mutagenic, carcinogenic, or cytotoxic behavior which can cause a major inflammatory response.
- The scaffold must possess the mechanical properties necessary to temporarily offer structural support until new tissue has formed.
- The scaffold must possess surface properties that allow attachment, migration, proliferation, and differentiation of cells.
- The scaffold must be biodegradable in a way that additional surgery is not required for implant removal. Ideally, the degradation rate should match the rate of new tissue formation.
- The porosity of the engineered scaffold and the scaffold's surface-volume ratio should be high to enable cell attachment, to provide in-growth sites for cells to adhere and proliferate, and to facilitate nutrient exchange upon *in vitro* or *in vivo* culture.
- The scaffold should simulate the native extracellular matrix (ECM) both in structure as well as in biological function. The ECM is known to have a fibrillar structure: collagen, the most abundant ECM protein in the human body, is made of continuous fibers with diameters that vary in the ranges of 50 to 500 nm.

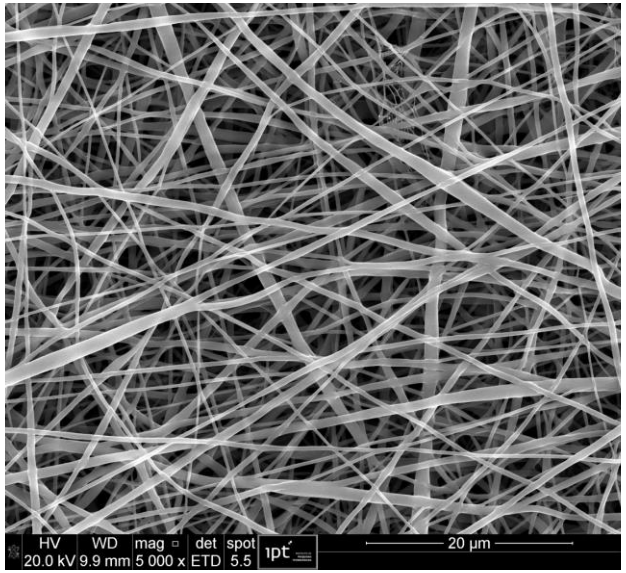
SCAFFOLD BASED ON NANOFIBER

Nanofiber Scaffolds: Flexible and porous obtained by the Electrospinning process



Schematic of electrospinning monoaxial process

- ✓ High surface area and porosity
- ✓ Substrate for cells until a new extracellular matrix is regenerated in the area
- ✓ Biodegradable
- ✓ Biocompatible



PCL:Gelatin nanofiber composite

(ZHANG et al 2007)

ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

Biomaterials relies on four main classes of materials:

i. Polymers,

ii. Ceramics,

iii. Metals

iv. Composites (blends and combinations of the aforementioned materials).

Biomaterials : natural or synthetic sources

ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

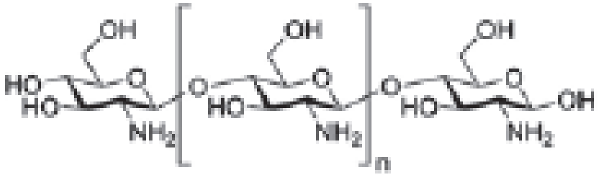
Materials	Degradation period	Hidrophobicity
Polycaprolactone (PCL)	> 20 months	Hydrophobic
Poly L-lactic acid (PLLA)	20 ≈ 60 months	Hydrophobic
Polydioxanone (PDO)	6 months	Hydrophilic
Polyglycolic acid (PGA)	1 ≈ 4 months	Hydrophilic
Poly (lactic-co-glycolic acid) (PLGA)	2 months	Depend of PLA and PGA compositions. Increase of PLA => less hydrophilicity

ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

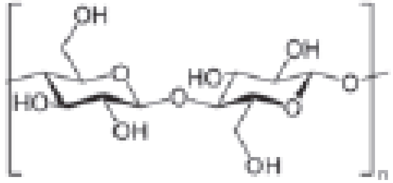
Natural and Chemically modified natural materials	
Cellulose and its derivatives and lignin	Drug release etc.
Chitosan	Antimicrobial Medical application
Proteins (e.g. collagen and fibrinogen, grow factor)	Medical application such as drug delivery and tissue engineering
Gelatin	Tissue engineering
Collagen	Tissue engineering

ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

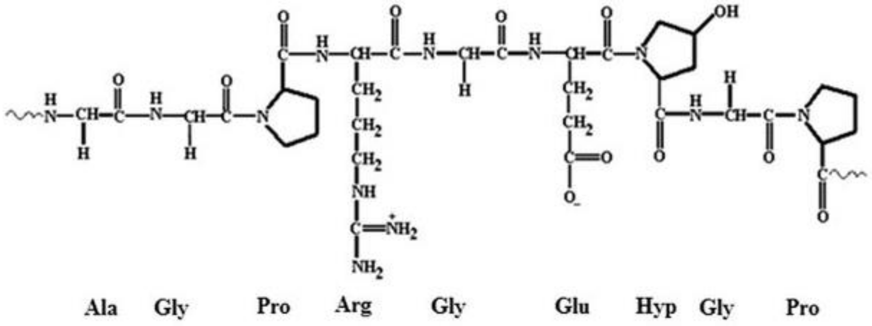
Natural Polymeric



Chitosan

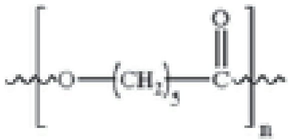


Hyaluronic acid



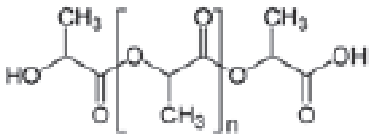
Gelatin

Synthetic Polymeric

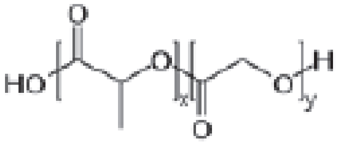


PCL

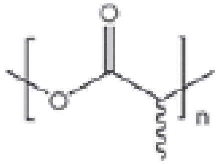
PGA



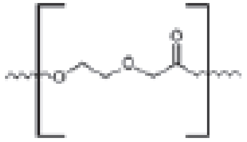
PLA



PLGA

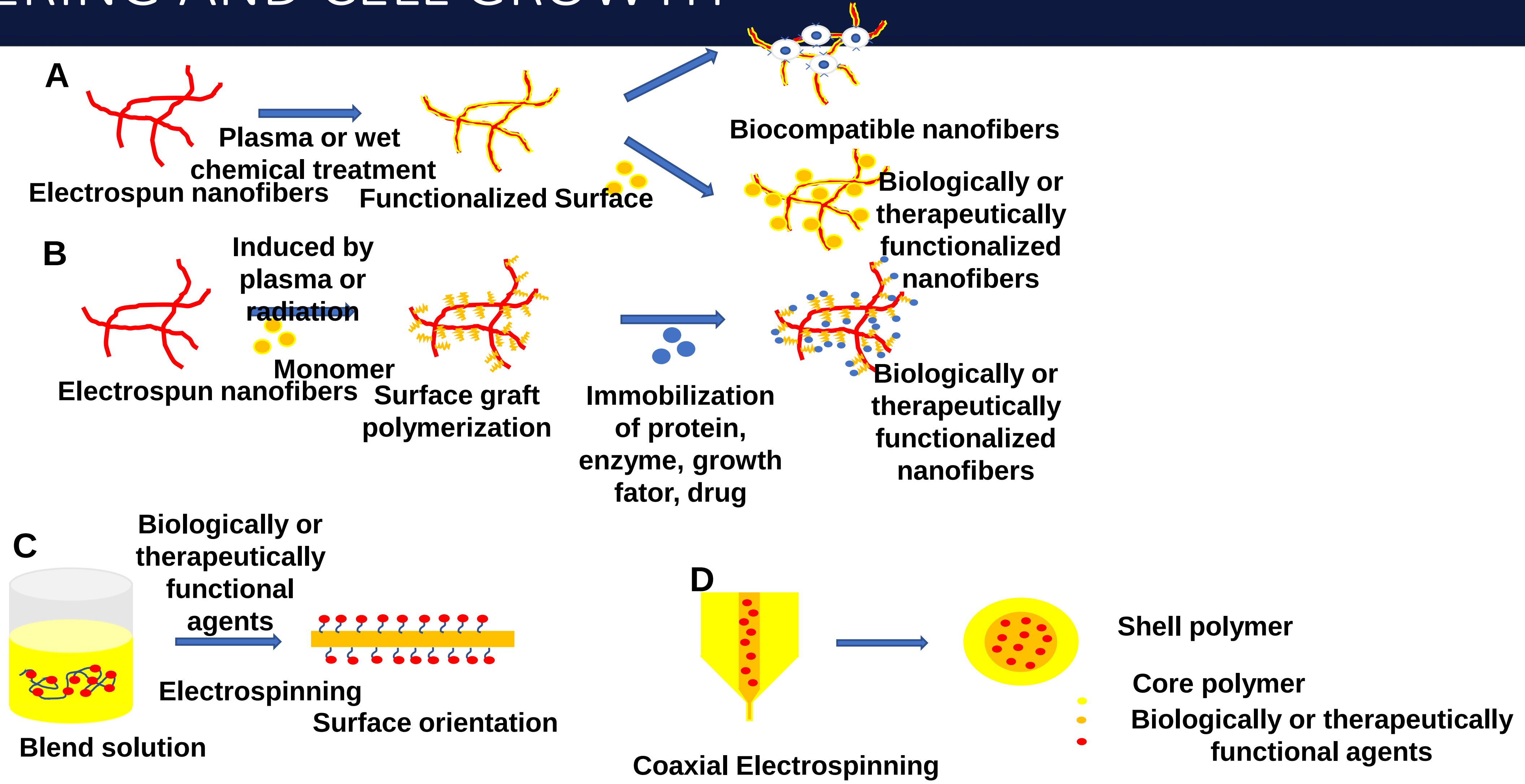


PLLA



PDO

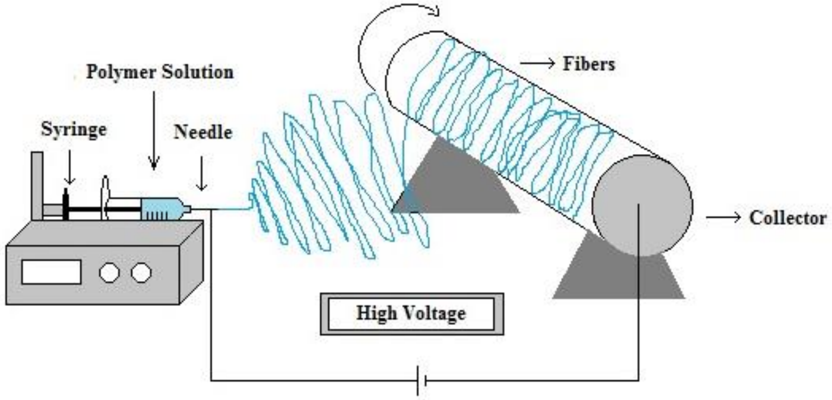
ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH



SET UP OF ELECTROSPINNING PROCESS TO PRODUCE POLYMERIC MEMBRANES

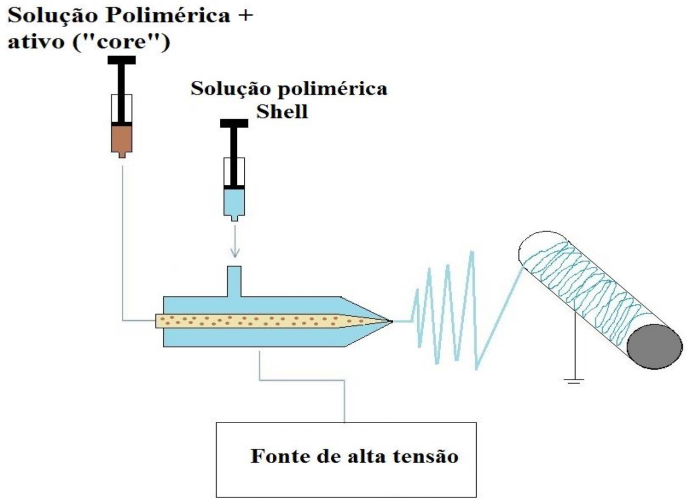
- **Simple nozzle or monoaxial electrospinning**

Systems that employs only one capillary containing the polymer solution to be electrospun in the presence of high voltage.



- **Coaxial electrospinning or coaxial electrospray**

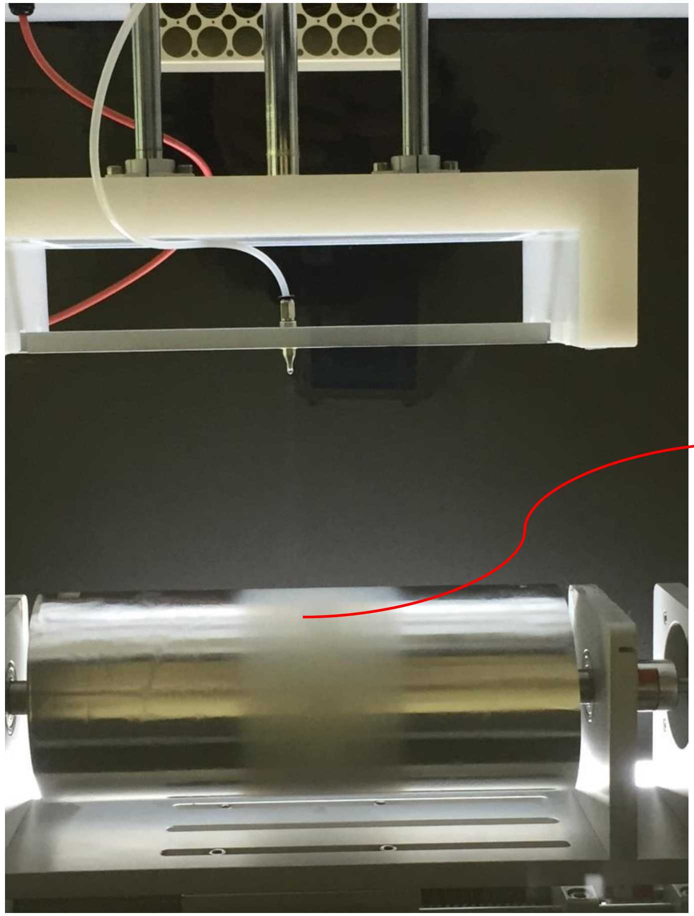
Basically, in coaxial electrospinning, two capillaries /needles are arranged coaxially to dispense two different solutions, for example, polymer solution and substance to be encapsulated, concurrently with a controlled flow in the presence of high voltage.

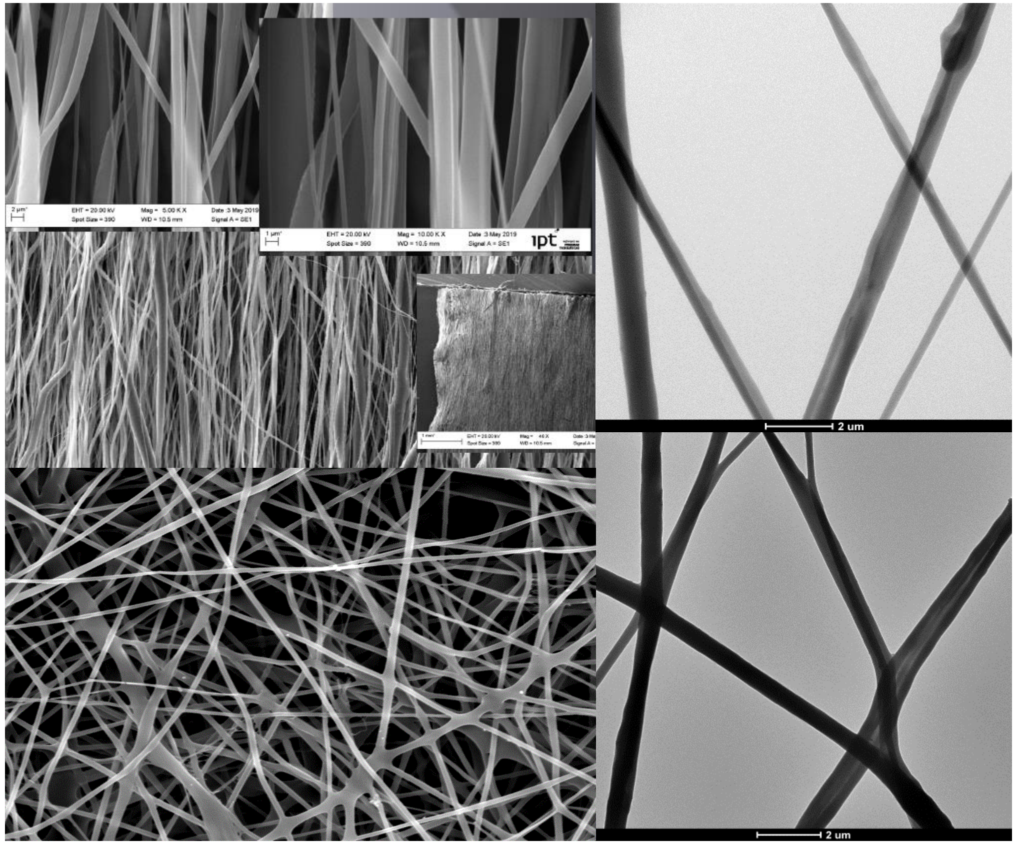


ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

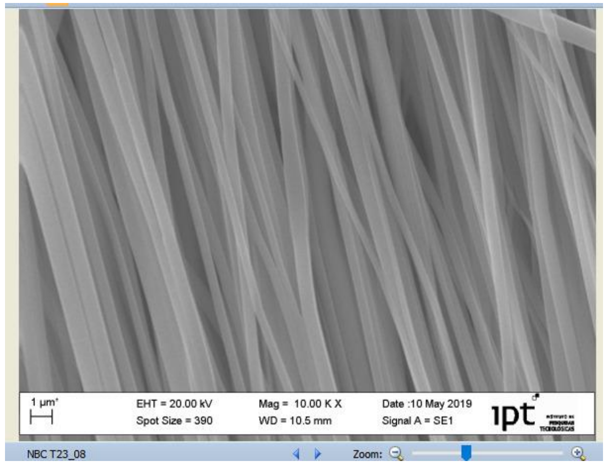
Nanospinner 24-XP

DIFFERENT MORPHOLOGIES OF NANOFIBERS DEVELOPED BY ELECTROSPINNING AT IPT

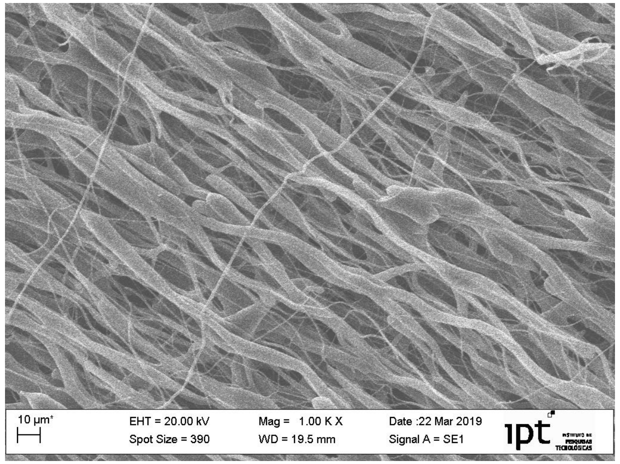




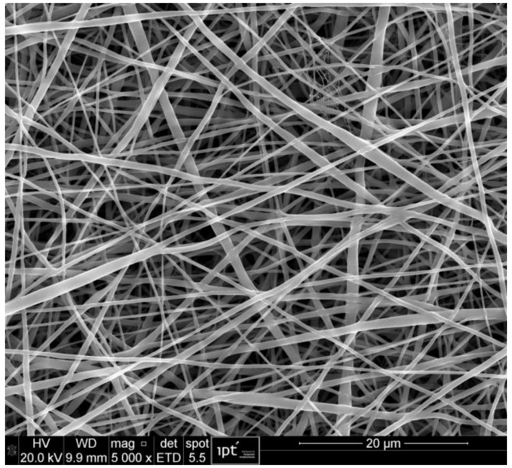
ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH



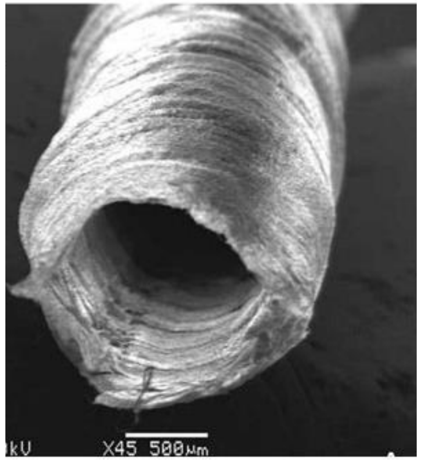
PLGA



PCL



PCL:Gelatin

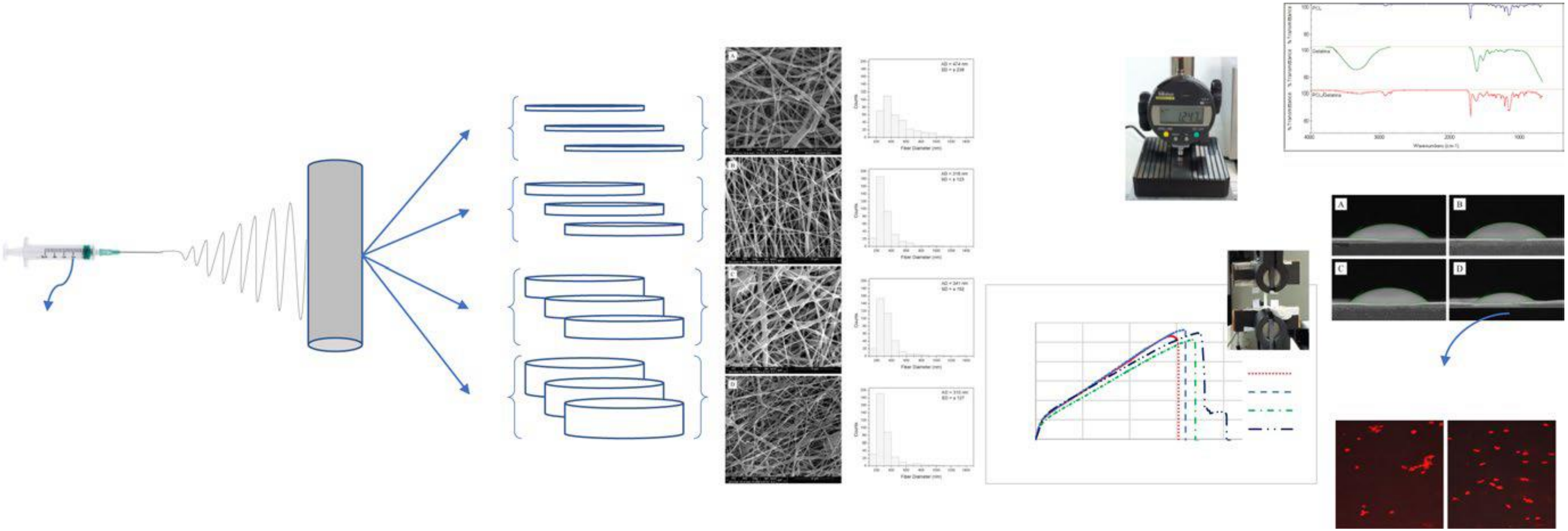


Conduit wall PCL/PLGA

(Asadian et al.2020)

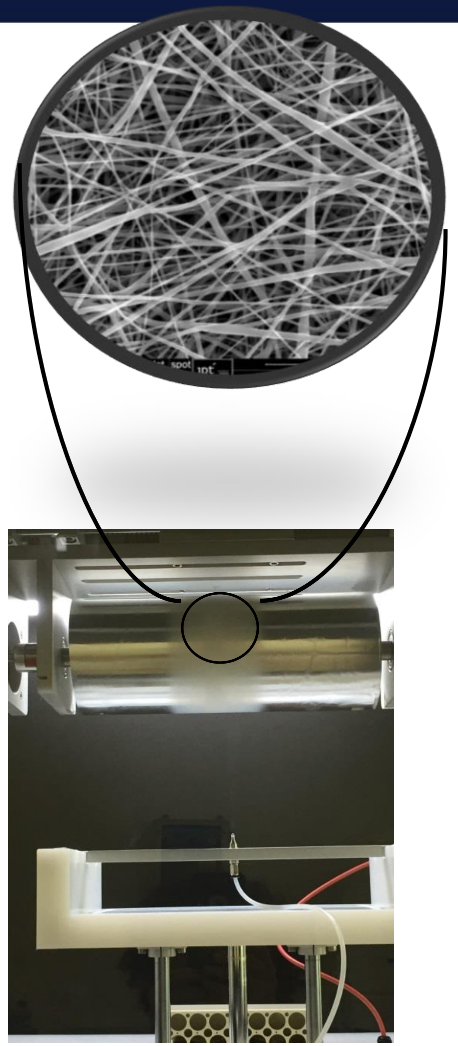
CASE STUDIES OF THE SCAFFOLD AT IPT BASED ON THE THEME “DEVELOPING AND UNDERSTANDING MATERIALS FOR USE IN INNOVATIVE ENGINEERING APPLICATIONS”

CASES STUDIES AT IPT - SCAFFOLDING

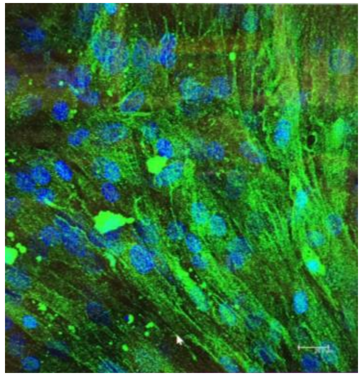


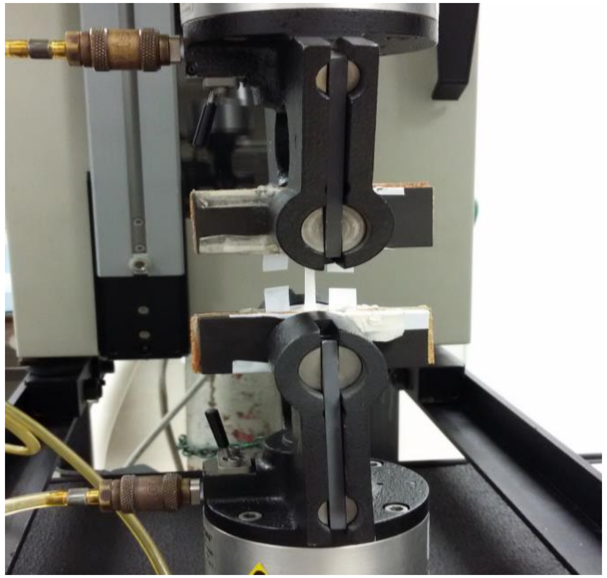
Kimura· VT; Zanin MHA; Wang, SH. Influence of thickness on the properties of electrospun PCL/gelatin nanofiber scaffolds. Polymer Bulletin. 2024.

CASES STUDIES AT IPT - SCAFFOLDING

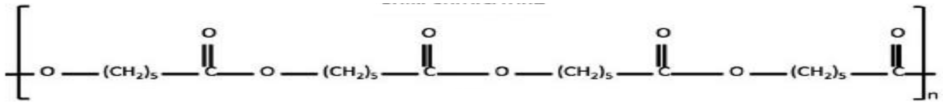


Stem Cell

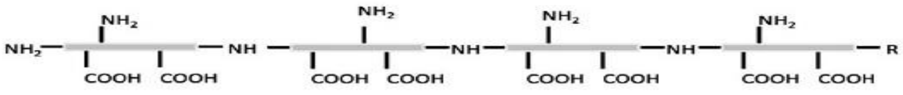




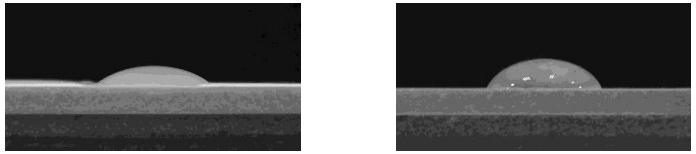
Mechanical tensile strength



PCL



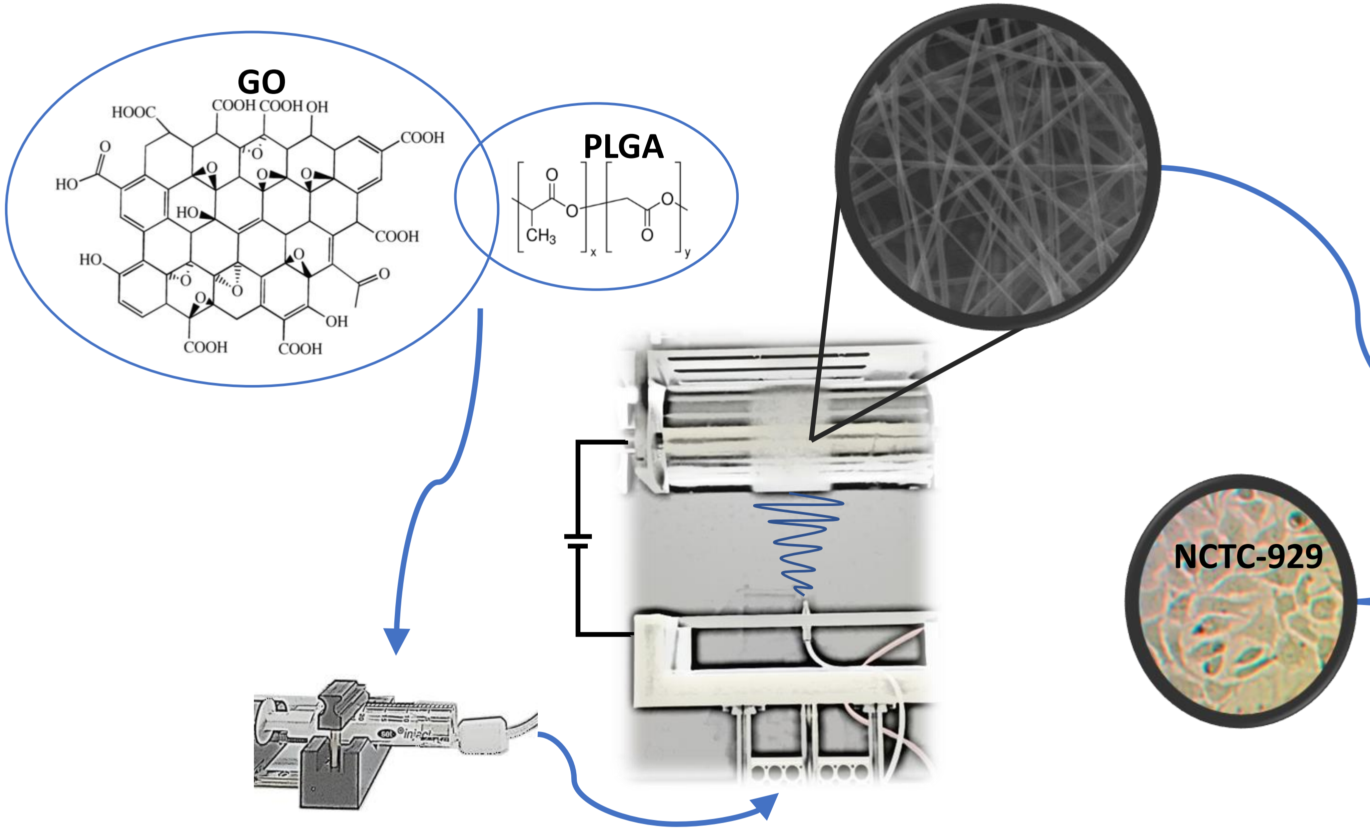
Gelatin

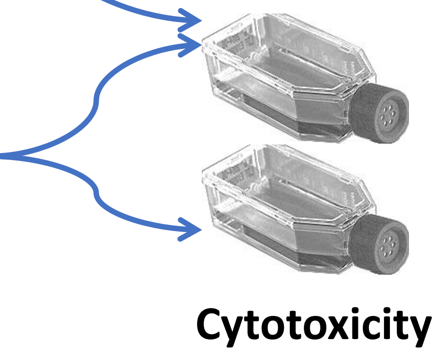


Wettability

CASES STUDIES AT IPT - SCAFFOLDING

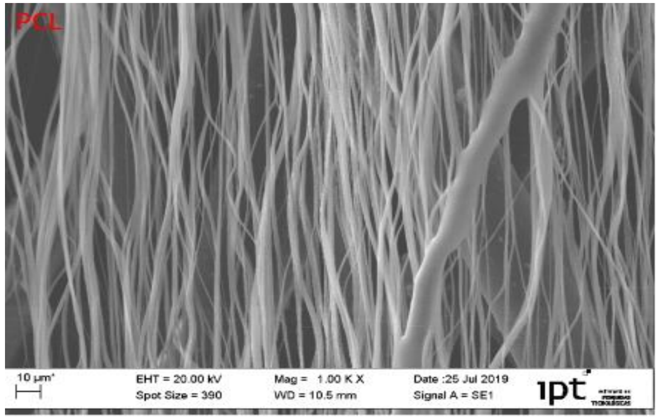
ZANIN, M. H. A.; KIMURA, V. T. ; SANT'ANNA, D. A. . Fabrication of Graphene oxide-PLGA hybrid nanofiber for tissue engineering application'. In: 27th Assembly of Advanced Materials Congress, 2019, Stockholm. Abstracts.... Stockholm: IAAM, 2019. p. 186-187.

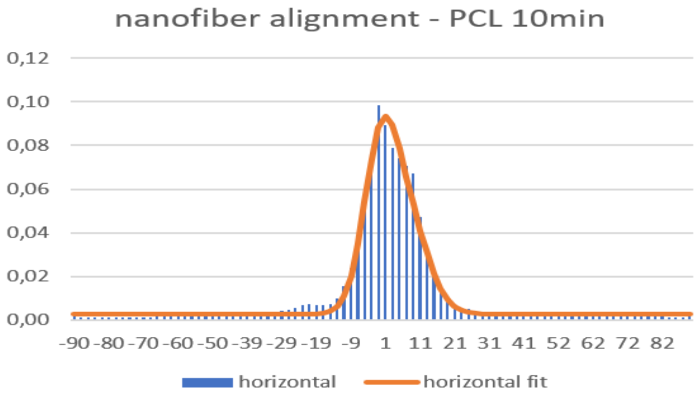


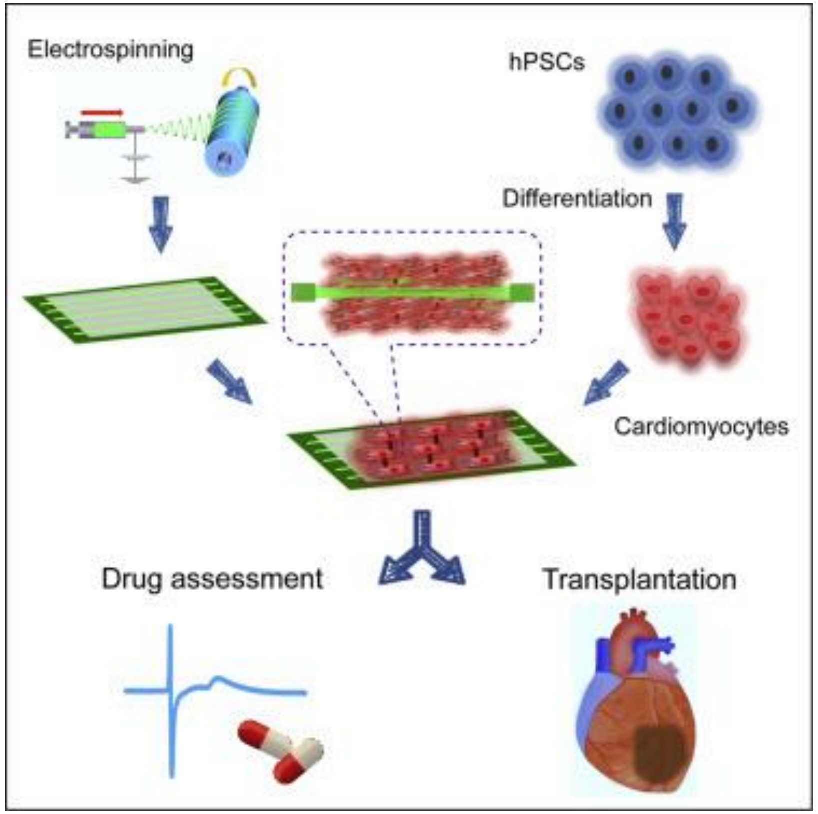


CASES STUDIES AT IPT - SCAFFOLDING

Alligned nanofiber scaffold **for cardiomyocytes based on induced pluripotent stem cells**







FINAL CONSIDERATIONS ON SCAFFOLD CONSTRUTION USING ELESCTROSPINNING TECNOLOGY

- ✓ Vascularization of the constructed tissues.
- ✓ The precise insertion of different cell types into porous 2D or 3D scaffolds.
- ✓ The type of construction material, which can interfere with cell differentiation when adhering stem cells.
- ✓ Biodegradability of materials/polymers.
- ✓ Material degradation time compatible with the regeneration time of the target tissue.

ELECTROSPUN POLYMERIC MEMBRANES FOR TISSUE ENGINEERING AND CELL GROWTH

✓ The choice of polymer and solvent in the electrospinning process is decisive for the end application, considering that the polymer can be electrospun and the residual solvent is not a contaminant for the end product.

✓Although this technology is simple, the adjustment of the process needs to be considered for each polymer used and a rigorous study of the process variables must be carried out.

✓Stability of the functionalization/binding of the molecule on the scaffold in biological fluid and/or sterilization.

✓Electrospinning nanofibers can mimic the structure of the natural extracellular matrix, making them promise for the application in tissue engineering, as the scaffold as example.

Thank you!

- Dra. Maria Helena Ambrosio Zanin

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