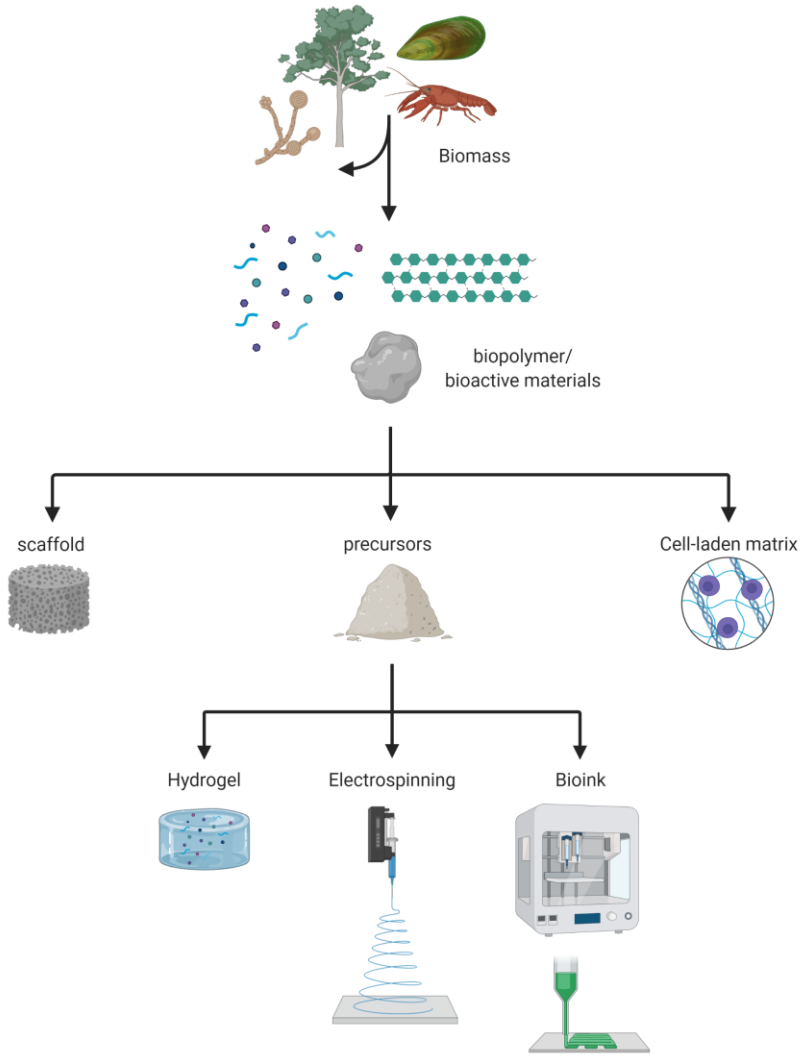
BioMatter *lab works at the interface of polymer science, physical chemistry, and biology. The overall focus of the lab is the fundamental understanding and development of biohybrid/bioinspired materials for biomedical applications with a specific emphasis on biomaterials engineering and tissue regeneration. Although significant advances in tissue engineering have been made in recent years, the continued lack of organs and tissue for transplantation calls for the development of innovative treatment alternatives. To achieve this, we are working on new approaches to modify natural polymers and new methods of manufacture, combining engineering, chemistry and biology to design biomaterials that control and direct the interaction with cells. While most of our target applications lie within biomedical engineering e.g., cell encapsulation, biomedical devices, and tissue engineering, we also apply our engineered hydrogels in food, nutraceutical delivery, agricultural, and environmental applications.*

http://biomatter.ulb.be/

Amin Shavandi (Head of the lab)

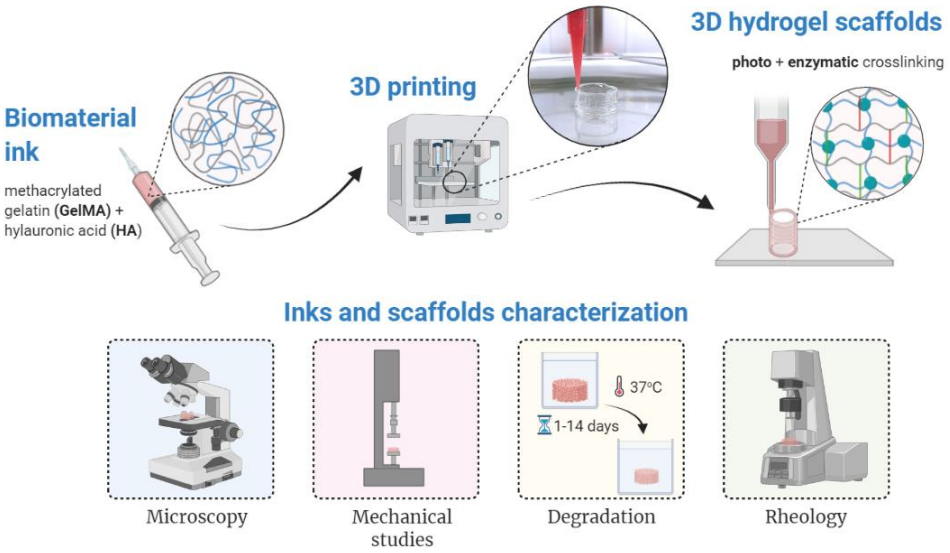
Master Thesis subjects 2022-2023 proposed by BioMatter *lab-BTL-3BIO*

Biomaterials engineering at the BioMatter lab



Investigation of new biomaterial inks for 3D-printing of vascular tissue scaffolds that can facilitate angiogenesis in artificial tissue models

3D tissue models are unquestionably valuable tools for deciphering the molecular basis of diseases, testing drugs, and developing tissue replacements. However, the lack of functioning vasculature system within a tissue model can remain a significant barrier for the practical application of such constructs, especially *in vivo*. Tissue or organ substitutes with any dimension exceeding 500 µm need to be vascularized to ensure cellular survival and blood vessel formation is essential for organ creation *in vitro*. Therefore, the project is guided by a hypothesis that the vascularization of the artificial tissue can be overcome by developing new 3D-printing strategies using methacrylated gelatin (GelMA) and hyaluronic acid (HA) biomaterial inks. Such GelMA-HA inks may help to create *ex vivo* blood vessels that could be easily integrated with model scaffolds. Briefly, the projects' tasks will cover, the formulation of biomaterial inks with different ratios of GelMA to HA, preceded by HA conjugation with Tyramine (HA-Tyr). Secondly, the optimization of a crosslinking method employing visible light photo-crosslinking and enzymatic crosslinking with horseradish peroxidase and H_2O_2 (HRP/H_2O_2). These steps will be validated by rheological measurements of biomaterial inks and crosslinked hydrogels to determine the most promising formulation for 3D printing. The last step will cover the fabrication of 3D hydrogel scaffolds (in the form of tubes) and their characterization concerning the targeted application (mechanical properties, degradation rate). Hopefully, the resulting hydrogels may become a promising matrix material for the fabrication of vessel-like structures essential for the creation of artificial tissues with clinically relevant dimensions.



Abstract of the Master thesis project' created in Biorender.com

Related literature:

- L. Xu, M. Varkey, A. Jorgensen, J. Ju, Q. Jin, J.H. Park, Y. Fu, G. Zhang, D. Ke, W. Zhao, R. Hou, A. Atala, *Bioprinting small diameter blood vessel constructs with an endothelial and smooth muscle cell bilayer in a single step,* Biofabrication. 12 (2020). https://doi.org/10.1088/1758-5090/aba2b6.
- Sharifi, S., Sharifi, H., Akbari, A. et al. *Systematic optimization of visible light-induced crosslinking conditions of gelatin methacryloyl (GelMA).* Sci Rep 11, 23276 (2021). https://doi.org/10.1038/s41598-021-02830-x
- Xiaohang Qu, Ling Yan, Shuang Liu, Yunfei Tan, Jing Xiao, Yuan Cao, Ke Chen, Wenqian Xiao, Bo Li & Xiaoling Liao, *Preparation of silk fibroin/hyaluronic acid hydrogels with enhanced mechanical performance by a combination of physical and enzymatic crosslinking,* Journal of Biomaterials Science, Polymer Edition, 32:12, 1635-1653, (2021) https://doi.org/10.1080/09205063.2021.1932070

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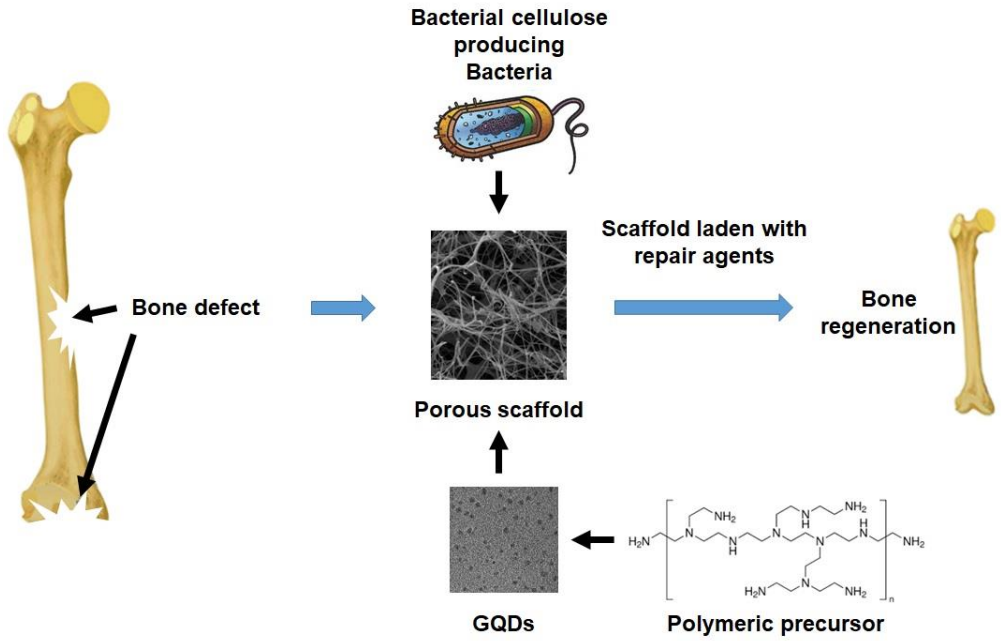
Graphene-based engineered living materials for bone tissue engineering

A bone scaffold is a three-dimensional structure that not only helps with bone regeneration but also can provide a method of delivery for therapeutic molecules to the site of action. Therefore, the capability of bone scaffolds in fulfilling these responsibilities will be essential in bone repair. Three-dimensional graphene-based hydrogels hold great potential for the design of future tunable scaffolds for bone tissue engineering. The main advantage of these porous nanostructures is their controllable surface characteristics and structural properties that can be engineered through the synthesis process. On the other hand, engineered living materials (ELMs) are a new class of smart materials that are produced via a microorganism, such as bacteria. In this project, these two concepts (graphene-based hydrogels and ELMs) will be combined to design and fabricate new scaffolds applicable in bone tissue engineering. The main area that will be covered in this project is the synthesis of porous ELMs using bacteria with graphene quantum dots (GQDs) as the precursor. First, GQDs, as one of the youngest members of the graphene-based materials family, will be synthesized from precursors such as polyethylenimine. Then, synthesized GQDs will be converted into a porous three-dimensional scaffold using a bacterial cellulose polymeric nanofiber network produced via bacteria. It is expected that the final GQDs-based porous ELMs can be tuned to be laden with particles and nanoparticles applicable in bone tissue engineering.



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Pomace-based biorefineries for co-producing bioelectricity and polyphenolic compounds

The global transition to the circular economy has been identified as a core strategy capable of circumventing imminent climate catastrophe. The execution of the circular economy paradigm requires the development of integrated biorefineries that incorporate technical, economic, and environmental performance considerations. To this regard biorefinery approaches that explore alternative pomace valorization strategies to produce polyphenolic compounds and bioelectricity will be comparatively assessed. In the study, the candidate will compare the performances of Phase II biorefineries that facilitate polyphenol and bioelectricity production via established green extraction methods of ethanol extraction and sub-critical water extraction and a Phase I biorefinery that emphasizes bioelectricity production (**Figure A**). The project will therefore require model development as a basis for simulating the alternative valorization strategies while employing ASPEN Plus to undertake relevant mass balance, energy balance, phase equilibria and thermodynamic calculations. Classic Chemical Engineering plant design and economic assessment methods will be employed in the calculation of the Net present values (NPVs) of the different biorefineries and the associated environmental burdens of the pathways subsequently assessed using the Potential Environmental Impacts (PEI) metric. By employing Multi-Criteria Decision Analysis, the candidate is expected to develop a concise decision support algorithm that will aid policymakers in the exploration of large-scale pomace valorization strategies in Belgium, for the benefit of all Belgians.

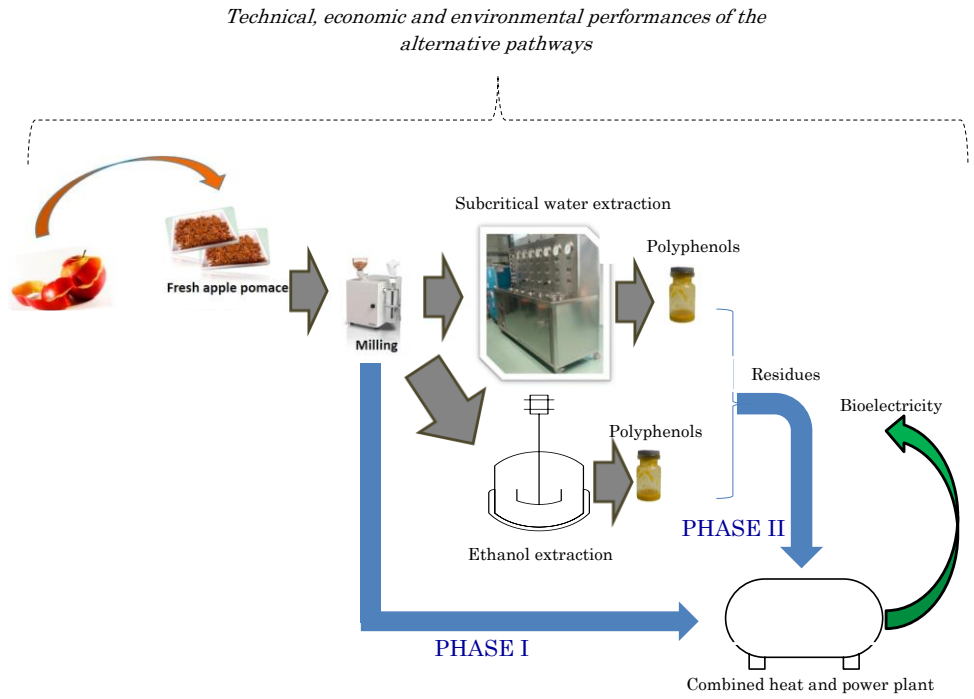

Figure A: Pomace valorization for polyphenol and bioelectricity production

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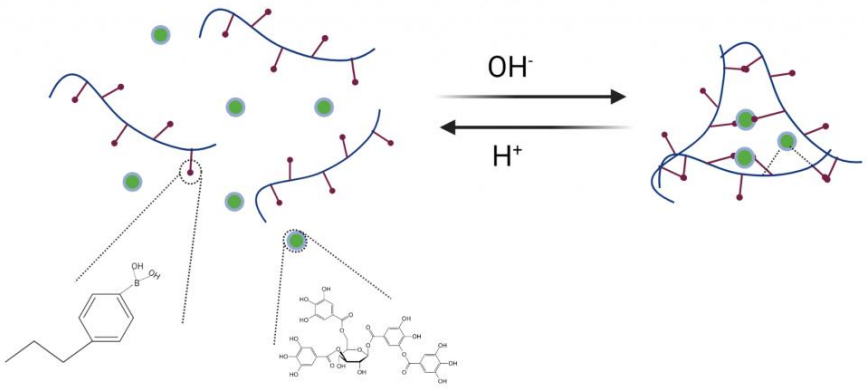
Boronic acid alginate hydrogel reinforced by tannic acid for tissue adhesive applications

The development of bioadhesives has emerged as one of the critical research fields in tissue sealants, wound dressings, and hemostatic agents. Alginate-based bio adhesives are being increasingly used due to alginate's unique properties, including biocompatibility and availability to chemical modification for optimizing adhesive properties. Mussels-imitated cis-diol-based alginate-boronic acid hydrogels have demonstrated good adhesiveness and pH-responsive self-healing properties. However, high pH (>7) requirements in gel formation and its low hemostatic activity might limit its biomedical applications. Thus, we are looking for innovative approaches to strengthen the physiochemical and biological activity of alginate boronic acid-based hydrogels. Tannic acid is a natural polyphenol with high hemostatic activity containing a high density of pyrogallic acid or catechol groups which make it an excellent candidate for the formation of boronate ester bonds with boronic acid. Furthermore, TA can form multiple hydrogen bonds with carboxyl and hydroxyl groups of the alginate which contributes to an advancement in the toughness and self-healing properties of the hydrogel. Hence, this project aims to design an adhesive hydrogel with high hemostatic activity through reinforcing interaction between cis-diols that are embedded in alginate and boronic acid and also dynamic covalent boronate ester bonds between tannic acid and boronic acid.



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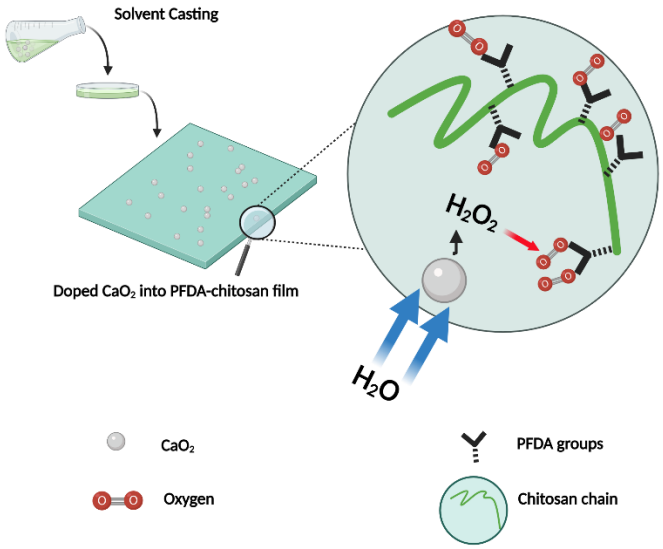
Oxygen generating wound dressing for diabetic wounds

Delayed diabetic wound healing is a multi-factorial problem, and for successful healing outcomes, multifaceted treatment is required. Therefore, there is an unmet clinical need to develop novel therapeutic approaches for diabetic foot ulceration. Hypoxia has been characterized as one of the major causes of the delayed healing process. Consequently, various technologies have been developed for topical oxygen therapies, including delivering pure oxygen under ambient or pressurized conditions, on-site oxygen release via oxygen carriers such as perfluorocarbons (PFCs), or chemical decomposition oxygen-releasing molecules such as peroxides. However, oxygen dosing is a critical factor, and controlled oxygen delivery remains the major challenge. To address the limitations of the currently available oxygen-generating biomaterials for wound healing, we are going to develop PFDA chitosan-based films doped with calcium peroxide (CaO_2) as an oxygen generating wound dressing (Fig). We hypothesize that the CaO_2 doped chitosan generates oxygen from the reaction of CaO_2 and water. PDFA groups on the chitosan chain act as an oxygen buffering shell where the excess of fast oxygen release will be trapped and released in a sustained manner. For carried out this, it is required **A**) To conjugate 40-45% PFDA groups on chitosan chain (replacing primary amino groups of chitosan with PFDA groups, **B)** To doped different content CaO_2 into PFDA-chitosan films, **C)** To study oxygen releasing rate from the chitosan films, and **D)** To evaluate the physicochemical properties of the developed materials.

Also, you can read the following articles for further details about the topic. [1-2]

1. Cele, Z. E.; Somboro, A. M.; Amoako, D. G.; Ndlandla, L. F.; Balogun, M. O., Fluorinated quaternary chitosan derivatives: Synthesis, characterization, antibacterial activity, and killing kinetics. *ACS omega* **2020,** *5* (46), 29657-29666.
2. Shiekh, P. A.; Singh, A.; Kumar, A., Oxygen-releasing antioxidant cryogel scaffolds with sustained oxygen delivery for tissue engineering applications. *ACS applied materials & interfaces* **2018,** *10* (22), 18458-18469.



Abstract of the Master thesis project' created in Biorender.com

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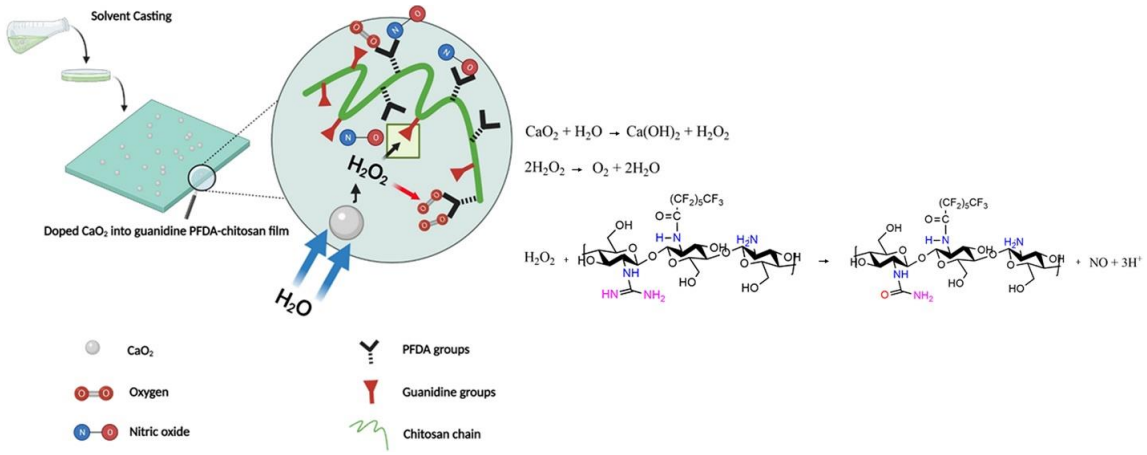
Smart O_2 and NO generating core-shell nanofibrous wound dressing

Granulation tissue formation in the hypoxic wound is significantly slower, while the infection rate is tenfold higher than the normoxic wounds. Increasing infectability of the hypoxic wound could be (at least in part) attributed to the impaired activity of leukocytes at low oxygen pressure. biomaterial scaffolds incorporated with gas generating chemicals such peroxides for generating oxygen or conjugated with gas generating groups such S-Nitrosothoil, N-Diazeniumdiolate, and zeolite for nitric oxide producing have been developed for local and controlled delivery of oxygen and nitric oxide to the tissues. In this project a gas capturing and nitric oxide generating groups will be conjugated on a biopolymer chain and will be doped with CaO_2 as hydrogen peroxide and oxygen generating agent as smart wound dressing materials (Fig). We hypothesize the reaction of peroxides with water generates hydrogen peroxide, which can subsequently degrade into oxygen and water which can react with guanidine groups of chitosan to generate nitric oxide. Moreover, the generated gases will be dissolved by PFDA groups conjugated on the chitosan chain and released at a slower rate. For this aim, it is required **A)** To conjugate 40-45% PFDA groups on the chitosan chain (replacing primary amino groups of chitosan with PFDA groups, **B)** To replace remaining amino groups of the PFDA chitosan with guanidine groups, **C)** To doped different content CaO_2 into guanidine PFDA-chitosan films, **D)** To study oxygen and nitric oxide-releasing rate from the chitosan films, and **D)** To evaluate the physicochemical properties of the developed materials. [1-4]

1. Cele, Z. E.; Somboro, A. M.; Amoako, D. G.; Ndlandla, L. F.; Balogun, M. O., Fluorinated quaternary chitosan derivatives: Synthesis, characterization, antibacterial activity, and killing kinetics. *ACS omega* **2020,** *5* (46), 29657-29666.
2. Shiekh, P. A.; Singh, A.; Kumar, A., Oxygen-releasing antioxidant cryogel scaffolds with sustained oxygen delivery for tissue engineering applications. *ACS applied materials & interfaces* **2018,** *10* (22), 18458-18469.
3. Zhang, X.; Fan, J.; Lee, C.-S.; Kim, S.; Chen, C.; Lee, M., Supramolecular hydrogels based on nanoclay and guanidine-rich chitosan: injectable and moldable osteoinductive carriers. *ACS applied materials & interfaces* **2020,** *12* (14), 16088-16096.
4. Nagase, S.; Takemura, K.; Ueda, A.; Hirayama, A.; Aoyagi, K.; Kondoh, M.; Koyama, A., A novel nonenzymatic pathway for the generation of nitric oxide by the reaction of hydrogen peroxide and D-or L-arginine. *Biochemical and biophysical research communications* **1997,** *233* (1), 150-153.



Abstract of the Master thesis project' created in Biorender.com

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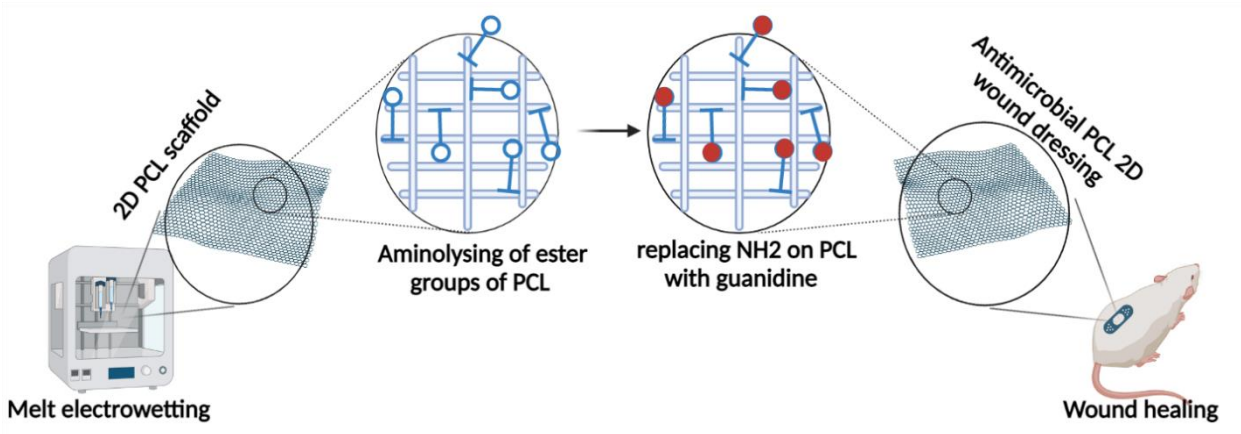
Antimicrobial polycaprolactone 2D wound dressing by melt electrowetting method

Most of the available wound dressings are ineffective and suffer from limitations such as poor antimicrobial activity, inability to provide suitable moisture to the wound, and poor mechanical performance. Inappropriate wound dressings can result in a delayed wound healing process. Nano-size range scaffolds have triggered great attention because of their high capability to deliver bioactive agents, high surface area, improved mechanical properties, mimic the extracellular matrix (ECM), and high porosity. Polycaprolactone (PCL), a bioresorbable and biocompatible, synthetic polymer with Food and Drug Administration approval for use in the human body, has been selected as scaffold material due to its mechanical stability, flexibility, and superior melt processing properties. To increase PCL's biological functionality bioactive and expand their application, this project aims to conjugate antimicrobial agent on the PCL surface. We hypothesize that by aminolysing of ester groups of PCL, it would replace primary amino groups with guanidine groups that are potent antibacterial agents. To achieve this goal, it is required **A)** To develop a 2D scaffold by electro writing method based on PCL, **B)** To aminolyze the surface of the scaffolds by immerging it in isopropyl alcohol solutions of ETDA, EDEA, and HMD (10 wt/vol%) under stirring to ensure that the whole scaffold will be aminolyzed, **C)** To replace primary amino groups on PCL surface with guanidine groups, **D)** To study physicochemical properties of antimicrobial PCL scaffolds.
See the following articles for further details about the topic. [1-3]

1. Toledo, A.; Ramalho, B.; Picciani, P.; Baptista, L.; Martinez, A.; Dias, M., Effect of three different amines on the surface properties of electrospun polycaprolactone mats. *International Journal of Polymeric Materials and Polymeric Biomaterials* **2021,** *70* (17), 1258-1270.
2. Zhao, Y.-T.; Zhang, J.; Gao, Y.; Liu, X.-F.; Liu, J.-J.; Wang, X.-X.; Xiang, H.-F.; Long, Y.-Z., Self-powered portable melt electrospinning for in situ wound dressing. *Journal of nanobiotechnology* **2020,** *18* (1), 1-10.
3. Piyasin, P.; Yensano, R.; Pinitsoontorn, S., Size-controllable melt-electrospun polycaprolactone (PCL) fibers with a sodium chloride additive. *Polymers* **2019,** *11* (11), 1768.



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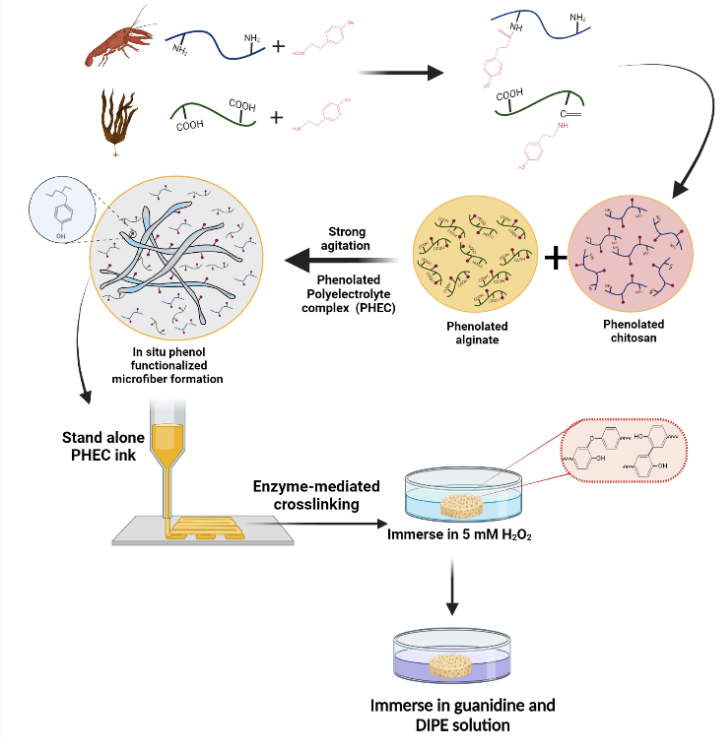
Antibacterial printable marine-based hydrogels

The design of 3D printable bio-based hydrogels with enhanced mechanical properties and minimal chemical modification can open new opportunities in the field of biomedical applications. A facile and safe approach is proposed to prepare mechanically reinforced chitosan-based hydrogels via a phenolated polyelectrolyte complex (PHEC) and enzyme-mediated crosslinking. PHEC will be formed between phenolated chitosan and alginate, leading to the formation of in situ phenol-functionalized microfibers. By replacing amino groups by phenol groups, the antibacterial activity of chitosan will be decreased, which has a critical role in tissue engineering. Therefore, to compensate the antibacterial activity of the chitosan and increasing antibacterial activity of the system, the guanidine groups will be conjugated on remaining amino groups of chitosan. To achieve this goal, it is required **A)** To conjugate phenol groups on chitosan and alginate, **B)** To synthesize a printable hydrogel based on phenolated chitosan and alginate by enzymatic crosslinking, **C)** To achieve a 3D hydrogel by 3D printing device, **D)** To conjugate guanidine groups on remaining amino groups of chitosan on 3D hydrogel surface by immersing the gel into guanidine solution, and **E)** To characterize physicochemical properties of 3D gels.

Please read the following articles for further details about the topic.[1-2]

1. Jafari, H.; Delporte, C.; Bernaerts, K. V.; Alimoradi, H.; Nie, L.; Podstawczyk, D. A.; Tam, K. C.; Shavandi, A., Synergistically complexation of phenol functionalized polymer induced in-situ microfiber formation for 3D printing of marine-based hydrogel. *Green Chemistry* **2022**.
2. Zhang, X.; Fan, J.; Lee, C.-S.; Kim, S.; Chen, C.; Lee, M., Supramolecular hydrogels based on nanoclay and guanidine-rich chitosan: injectable and moldable osteoinductive carriers. *ACS applied materials & interfaces* **2020,** *12* (14), 16088-16096.



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