Welcome to Israel!

It is with great pleasure that we welcome you to ICBBA 2018: the 3rd international conference on biological and biomimetic adhesives. Building on the success of the two previous conferences in Lisbon and Istanbul, this conference attempts to bring together leading scientists, clinicians, engineers, and delegates from industry at the forefront of bioadhesion science and technology.

We wish to thank all of our international and local speakers, our participants, sponsors and exhibitors and with you all an interesting, stimulating and enjoyable meeting.

Prof. Havazelet Bianco-Peled, Technion–Israel Institute of Technology, Israel
Prof. Alejandro Sosnik, Technion–Israel Institute of Technology, Israel

Conference Chairs

ICBBA 2018 ORGANIZING AND SCIENTIFIC COMMITTEE

- Prof. Havazelet Bianco-Peled, ICBBA Chair, Technion–Israel Institute of Technology, Israel
- Prof. Alejandro Sosnik, ICBBA Chair, Technion–Israel Institute of Technology, Israel
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- Prof. Aránzazu del Campo, INM-Leibniz Institute for New Materials, Germany
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- Prof. Seda Kizilel, Koç University, Turkey
- Dr. Romana Lopes Almeida Santos, University of Lisbon, Portugal
- Prof. Joao Mano, University of Aveiro, Portugal
- Dr. Anne Marie Power, National University of Ireland, Ireland
- Dr. Daniel Ruiz-Molina, Institute de Ciencia de Materials de Barcelona, Spain
- Prof. Ebru Toksoy Oner, Marmara University, Turkey
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- Mrs. Inbar Shclachet, Technion–Israel Institute of Technology, Israel
- Mrs. Yarden Shntenberg-Degani, Technion-Israel Institute of Technology, Israel
- Mrs. Yulia Shitrit, Technion-Israel Institute of Technology, Israel
- Mrs. Alexandra Bukchin, Technion-Israel Institute of Technology, Israel
<table>
<thead>
<tr>
<th>Time</th>
<th>Tuesday November 20, 2018</th>
<th>Wednesday November 21, 2018</th>
<th>Thursday November 22, 2018</th>
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<tr>
<td>8:30</td>
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<tr>
<td>9:00</td>
<td>Conference Registration</td>
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<td>9:30</td>
<td><strong>Bioadhesion: A session in Hebrew</strong> - open to the general public (Dekel Hall, 9:30-12:00)</td>
<td>Welcome &amp; Keynote session (Rimon Hall, 9:00-10:45)</td>
<td>Parallel Sessions (Dekel &amp; Shita Halls, 9:00-10:30)</td>
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<tr>
<td>10:00</td>
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<td>Parallel Sessions (Dekel &amp; Shita Halls, 9:00-10:30)</td>
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<td>10:30</td>
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<td>Coffee Break</td>
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<tr>
<td>11:00</td>
<td>Welcome &amp; Registration, COST MC members</td>
<td>Coffee Break</td>
<td>Poster Award Ceremony (Dekel Hall, 12:15-12:30)</td>
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<td>11:30</td>
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<td>Parallel sessions (Dekel &amp; Shita Halls, 11:15-13:00)</td>
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<td>Coffee Break</td>
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<tr>
<td>12:30</td>
<td>Welcome &amp; Registration, COST MC members</td>
<td>Lunch Break (Dining Room, 13:00-13:45)</td>
<td>Lunch Break (Dining Room, 13:00-14:00)</td>
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<td>Costa Action CA 15216: MC meeting (Dekel Hall, 14:00-16:00)</td>
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<td>Costa Action CA 15216: MC meeting (Dekel Hall, 14:00-16:00)</td>
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<td>15:00</td>
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<td>Parallel Sessions (Dekel &amp; Shita Halls, 15:00-16:30)</td>
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<td>15:30</td>
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<td>16:00</td>
<td>Costa Action CA 15216: MC meeting (Dekel Hall, 16:30-18:00)</td>
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<td>Coffee Break</td>
<td>Costa Action CA 15216: MC meeting (Dekel Hall, 17:00-18:00)</td>
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<td>18:00</td>
<td>Conference registration</td>
<td>Conference Dinner (18:30-23:00)</td>
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<tr>
<td>18:30</td>
<td>Welcome Reception (Dekel Hall, 18:30-20:00)</td>
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<tr>
<td>10:00 - 10:45</td>
<td><strong>Bioadhesion: A session in Hebrew - open to the general public (Dekel Hall)</strong> H. Bianco-Peled. <strong>Glue from the sea: Biomedical adhesives inspired by algal polymers</strong></td>
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<tr>
<td>11:00 - 12:00</td>
<td>Activities: Demonstrating the concept of bioadhesion</td>
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<tr>
<td>12:30 - 13:00</td>
<td>Conference registration (MC members)</td>
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<tr>
<td>13:00 - 14:00</td>
<td>Lunch (for MC members)</td>
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<td>14:30 - 16:00</td>
<td>COST Action CA 15216: MC meeting (Dekel Hall)</td>
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<td>16:00 - 16:30</td>
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<td>18:00 - 18:30</td>
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<tr>
<td>18:30 - 20:00</td>
<td>Welcome Reception</td>
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**November 21, 2018 (morning schedule)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>08:30 - 09:00</td>
<td>Registration</td>
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<tr>
<td>09:00 - 09:15</td>
<td>Opening</td>
</tr>
<tr>
<td>09:15 - 09:45</td>
<td>Marleen Kamperman, the Netherlands. <strong>Bioinspired ionic adhesives</strong></td>
</tr>
<tr>
<td>09:45 - 10:15</td>
<td>Terry W.J. Steele: <strong>Photo- and electro-activated carbene tissue adhesives</strong></td>
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<tr>
<td>10:15 - 10:45</td>
<td>Jonathan J. Wilker: <strong>Oysters: One animal, two glues</strong></td>
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<tr>
<td>10:45 - 11:15</td>
<td>Coffee break</td>
</tr>
<tr>
<td>11:15 - 11:35</td>
<td>Michael Varenberg, USA. <strong>Pulling angle and preliminary displacement in shear-induced attachment</strong></td>
</tr>
<tr>
<td>11:55 - 12:10</td>
<td>Silvia Marchesan, Italy. <strong>Nanomaterials derived from polydopamine for hydrogen peroxide production</strong></td>
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<tr>
<td>12:10 - 12:25</td>
<td>Chao Zhong, China. <strong>Engineering living cellular glues with synthetic biology</strong></td>
</tr>
<tr>
<td>12:25 - 12:40</td>
<td>Peter van Assenbergh, the Netherlands. <strong>Biomimetic adhesive micropillars with a hard core and a soft shell</strong></td>
</tr>
<tr>
<td>12:40 - 12:55</td>
<td>Miguel-Ángel Moreno-Villaécija, Spain. <strong>Novel approach for designing bioinspired catechol-based adhesives via thiol chemistry</strong></td>
</tr>
<tr>
<td>13:00 - 13:45</td>
<td>Lunch</td>
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<tr>
<td>Time</td>
<td>Session 3: Adhesives for healthcare applications I (Dekel Hall)</td>
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<tr>
<td>13:45 - 15:00</td>
<td><strong>Chair:</strong> João F. Mano</td>
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<tr>
<td>15:00 - 15:20</td>
<td>Meital Zilberman, Israel. <em>Composite gelatin-alginate hydrogels as bioadhesive materials</em></td>
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<tr>
<td>15:40 - 15:55</td>
<td>José Miguel Martín-Martínez, Spain. <em>Novel polyurethane pressure sensitive adhesives with controlled tack intended for medical patches</em></td>
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<tr>
<td>15:55 - 16:10</td>
<td>Ebru Toksoy Oner, Turkey. <em>Levan Based Bioadhesives for Biomedical Applications</em></td>
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<thead>
<tr>
<th>Time</th>
<th>Coffee break</th>
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<td>16:30 - 17:00</td>
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<tr>
<th>Time</th>
<th>Session 5: Adhesives for healthcare applications II (Dekel Hall)</th>
<th>Session 6: Natural adhesives I (Shita Hall)</th>
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<tbody>
<tr>
<td>17:00 - 17:20</td>
<td><strong>Chair:</strong> Boaz Mizrahi</td>
<td><strong>Chair:</strong> Anne Marie Power</td>
</tr>
<tr>
<td>17:00 - 17:20</td>
<td>João F. Mano, Portugal. <em>Bioinspired soft devices with fixation ability in biomedical applications</em></td>
<td>Romana Santos, Portugal. <em>Sea urchin reversible adhesives: a multidisciplinary journey towards biomimicry</em></td>
</tr>
<tr>
<td>17:20 - 17:40</td>
<td>Chenjie Xu, Singapore. <em>Improving the skin adhesion of microneedle patch through catechol-functionalization</em></td>
<td>David Labonte, UK. <em>Scaling of adhesion: shear forces and pad sliding reduce adhesion loss for large insects</em></td>
</tr>
<tr>
<td>17:40 - 17:55</td>
<td>Shaked Eliyahu, Israel. <em>Micoadhesive acrylated chitosan nanoparticles for drug delivery</em></td>
<td>Patrick Flammang, Belgium. <em>Involvement of sulfated biopolymers in adhesive secretions produced by marine invertebrates</em></td>
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<tr>
<td>18:30 - 23:00</td>
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<tr>
<td>18:30 - 23:00</td>
<td><strong>Conference Dinner</strong></td>
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### November 22, 2018

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<thead>
<tr>
<th>Time</th>
<th>Session 7: Adhesives for healthcare applications III (Dekel Hall)</th>
<th>Session 8: Natural adhesives II (Shita Hall)</th>
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<tbody>
<tr>
<td>08:30 - 09:00</td>
<td>Registration</td>
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<tr>
<td>09:00 - 09:20</td>
<td>Tomer Fuchs, Israel. <strong>Sealantis, Bio-Mimetic tissue adhesives – A journey from the academic lab to the operating room.</strong></td>
<td>Thomas Endlein, Germany. <strong>The use of friction pads by tree frogs for climbing curved surfaces.</strong></td>
</tr>
<tr>
<td>09:20 - 09:40</td>
<td>Klemen Bohinc, Slovenia. <strong>Nanoparticle's Charge Properties</strong></td>
<td>Dong Soo Hwang, Korea. <strong>Cation – π interaction mediated mussel underwater adhesion.</strong></td>
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<tr>
<td>09:40 - 09:55</td>
<td>Yulia Shitrit, Israel. <strong>Acrylated Chitosan for mucoadhesive drug delivery systems</strong></td>
<td>Eleftheria Athanassiadou, Greece. <strong>The challenges of bio-adhesives in the wood panel industry.</strong></td>
</tr>
<tr>
<td>09:55 - 10:10</td>
<td>Germán Febas, Spain. <strong>New bioadhesive based on allyl isothiocyanate by Chemical Vapor Deposition (CVD)</strong></td>
<td>Naoe Hosoda, Japan. <strong>The influence of surface free energy of the substrate on traction force by the seven-spotted ladybird beetles.</strong></td>
</tr>
<tr>
<td>10:10 - 10:25</td>
<td>Andreia Almeida, Portugal. <strong>Mucoadhesive camptothecin polymeric micelles as nanodelivery systems for oral chemotherapy to treat colorectal cancer</strong></td>
<td>Thomas Ederth, Sweden. <strong>Chemical imaging of adhesive interfaces of marine fouling organisms.</strong></td>
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<tr>
<td>10:30 - 11:00</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>11:00 - 11:20</td>
<td>Meital Reches, Israel. <strong>Peptide self-assembly into functional coatings</strong></td>
<td>Peter Ladurner, Austria. <strong>Biological adhesion of flatworms.</strong></td>
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<tr>
<td>11:20 - 11:40</td>
<td>Moshe Herzberg, Israel. <strong>Relations between biofilm viscoelasticity and membrane biofouling: A case study of cellulose in the extracellular polymeric matrix</strong></td>
<td>Nicholas Aldred, UK. <strong>Probing the permanent adhesion of barnacle cypris larvae.</strong></td>
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<tr>
<td>11:55 - 12:10</td>
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<td>Sylvia Nürnberger, Austria. <strong>Tick attachment cement – first characterization of a potential tissue glue.</strong></td>
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<td>12:10 - 12:30</td>
<td><strong>Poster award ceremony</strong></td>
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<td>12:30 - 13:30</td>
<td><strong>Lunch</strong></td>
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<td>13:30 - 17:00</td>
<td><strong>Tour in Caesarea National Park, an ancient town on the coast of the Mediterranean, 30 minutes’ drive from Haifa</strong></td>
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</table>
P1  **Daniele Liprandi, Italy**
A 3D numerical model for membrane delamination

P2  **Michal Zurovec, Czech Republic**
The expansion of genes encoding silk adhesives in the greater wax moth, Galleria mellonella

P3  **Ana S. Viana, Portugal**
Electropolymerization of biomimetic polydopamine films for biosensing applications

P4  **Ana S. Viana, Portugal**
Characterization of the temporary adhesive of the sea urchin Paracentrotus lividus by Atomic Force Microscopy

P5  **Shaked Eliyahu, Israel**
Mucoadhesive Acrylated Chitosan Nanoparticles for Drug Delivery

P6  **Denise Beconcini, Italy**
Evaluation of mucoadhesive polymeric nanoparticles as a delivery system for cherry extracts polyphenols

P7  **Yarden Shтенб erg, Israel**
Mucoadhesive alginate pastes with embedded liposomes for local oral drug delivery

P8  **Arita Dubnika, Latvia**
Development of lipid based liposomes for adhesive patches

P9  **Gabriel Furtos, Romania**
Adhesion of self-adhesive resin cements

P10  **Yulia Shitrit, Israel**
Acrylated Chitosan for mucoadhesive drug delivery systems

P11  **Avia Leader, Israel**
Probing bacteria-surface interactions via organelle adhesion.

P12  **Fan Zeng, Austria**
Bioadhesion in the Ascidian Ciona intestinalis specially the adhesive secreting collocytes

P13  **Marie Bonneel, Belgium**
Adhesion of sea cucumber Cuvierian tubules: Identification and characterization of adhesive proteins
P14 **Morgane Algrain, Belgium**
Localization and characterization of Asterias rubens adhesive proteins

P15 **Birgit Lengerer, Belgium**
Evolution of temporary adhesive proteins in sea stars

P16 **Maura Tilbury, Ireland**
Recombinant expression of barnacle cement proteins

P17 **Tsuf Croitoru-Sadger, Israel**
3D Printing of Complementary Pre-Polymers for Oral Delivery

P18 **Sivan Nir, Israel**
Understanding and tailoring peptide self-assembly for the formation of surface-modified antimicrobial particles

P19 **Todorka Vladkova, Bulgaria**
Reduced biofilm formation on strong hydrophobic coatings

P20 **Todorka Vladkova, Bulgaria**
Strong antibacterial effect of Ag/Cu doped TiO2 thin films on E. coli

P21 **Dagmar Voigt, Germany**
Gripping ease in southern green stink bugs

P22 **Maria Helena Macedo, Portugal**
New three-dimensional intestinal tissue engineering model as multifunctional platform for drug and nanoparticle absorption studies

P23 **Janek von Byern, Austria**
Biomechanical properties of fishing lines of the glowworm Arachnocampa luminosa (Diptera; Keroplatidae)

P24 **W. Jon. P. Barnes, Scotland**
Relative roles of adhesion and gripping in climbing tree frogs

P25 **Donghui Li, USA**
A library of novel photoswitchable adhesives for medical tape applications

P26 **Elad Arad, Israel**
Functionalized Titanium Dioxide Nanoparticles for Targeting and Disrupting Amyloid fibrils

P27 **Inbar Schlachet, Israel**
Mixed mucoadhesive amphiphilic nanoparticles for the treatment of pediatric tumors of the Central Nervous System by intranasal administration

P28 **Chen Moshe Halamish, Israel**
Novel PVA-based nano carries for mucosal drug delivery
Bioinspired Ionic Adhesives

Marleen Kamperman

1Polymer Science, Zernike Institute for Advanced Materials, University of Groningen, Groningen, the Netherlands
2Physical Chemistry and Soft Matter, Wageningen University & Research, Wageningen, the Netherlands

Email: marleen.kamperman@wur.nl, web site: http://www.pcc.wur.nl

Biology provides numerous stimulating illustrations of successful design strategies. As biology evolved to complex designs, synthetic mimics are evolving towards new levels of complexity achieving larger combinations of properties within one material. In my group we utilize biologically inspired strategies to develop polymeric materials for next generation adhesives and functional materials.

In this talk I will present recent developments in mimicking the adhesive secretions of marine animals such as P. californica and M. edulis by creating fully synthetic polymeric systems. Characteristic of the proteins found in the adhesive plaque of mussels and sandcastle worms is a high proportion of cationic, anionic and catecholic residues (hydroxylated tyrosine, DOPA). DOPA is involved in a versatile combination of functions: covalent crosslinking, complexation to mineral substrates, and bonding to hydrophobic (fouled) surfaces. The anionic and cationic residues are often said to be involved in a secondary interaction that aids cohesion, namely complex coacervation. This is an attractive phase separation of mixtures of polyanions and polycations that results in a highly polyelectrolyte-rich phase in equilibrium with almost pure solvent. Complex coacervates have very low surface tensions and are water insoluble, which makes them highly desirable for underwater adhesives. Additionally, they are mechanically well-suited for adhesion due to their high storage and loss moduli that provide, respectively, bonding strength and dissipation of energy. We aim to reproduce the working mechanism of mussels and sandcastle worms by developing a new class of underwater adhesives based on complex coacervates reinforced with physical interactions.

Keywords: Bio-inspiration, adhesives, complex coacervation, polymer chemistry, wet adhesion
Photo- and Electro-activated Carbene Tissue Adhesives

Terry Steele

Materials Science & Engineering, Nanyang Technological University, Singapore, Singapore,
wjsteele@ntu.edu.sg, web site: http://www.labsteele.com

Instant curing adhesives typically fall within two categories, being activated by either heat or chemical means. These curing strategies limit applications to specific substrates and can only be activated under limited certain conditions. A significant need exists for adhesives that allow for manipulation and subsequent adhesive activation in wet or low temperature surfaces. Herein, we present the development of an instant curing adhesive through photo- or low voltage activation. The photocuring and electrocuring bioadhesives are synthesized by grafting carbene precursors on dendrimers to form viscous liquids. The adhesives are activated at low UV intensities (1-50 mW, cm²) or voltages (<10V with material properties evaluated in real-time using photo- or electro-rheology. Polymer crosslinking is immediately terminated when stimulus is discontinued. Crosslinking initiation and propagation are observed to be stimulus and time dependent, enabling tuning of both elasticity and adhesive strength. Adhesion bond strengths on a variety of substrates will be presented.
Oysters: One Animal, Two Glues

Andreś M. Tibabuzo Perdomo, Erik M. Alberts, Stephen D. Taylor, Debra M. Sherman, Chia-Ping Huang, and Jonathan J. Wilker

1 Department of Chemistry, Purdue University, West Lafayette, Indiana 47907-2084, United States
2 Life Science Microscopy Facility, Purdue University, West Lafayette, Indiana 47907, United States

Email: wilker@purdue.edu, web site: http://chem.purdue.edu/wilker/

Oysters are one of the most dominant species when it comes to ensuring the health of coastal ecosystems. By cementing together, these shellfish create extensive reef structures that can be meters deep and kilometers long. Such structures absorb storm surge energy, provide a place for other organisms to live, hold dirt in place, and the many bivalves filter large volumes of water. Our group is trying to understand the nature of how oysters stick themselves together. We have found that the adult adhesive is predominantly inorganic, being ~85% inorganic calcium carbonate. Such a composition is rather unusual for adhesives, which tend to be nearly all organic. Structural studies are revealing how organic versus inorganic components of the system are arranged for the needed function. Furthermore, we are following the animals as they age with regard to surface bonding. When oysters are larvae, they have a pre-made adhesive gel ready to eject upon finding a suitable location for settlement. This material is a hydrated mix of proteins and polysaccharides. As soon as metamorphosis takes place and the animals become juveniles, they produce an adhesive that differs dramatically from what is formed by larvae. A surface contacting organic adhesive is deposited. Above this glue forms inorganic columns that are part of the shell. The animals are then bonded in place for life. In learning how oysters create adhesives we are hoping to both understand the generation of biological materials as well as reveal design cues for future synthetic systems.

Figure 1. An oyster ~48 hours after settlement, starting to produce the juvenile stage adhesive.

To date, a handful of different gecko-like adhesives inspired by spatula-shaped attachment hairs have been suggested based on wedge and flap geometry of contact elements. However, while these surface designs have been shown to have directionality in adhesion, high friction, long lifetime and the ability to work in vacuum, an experimental verification of the very basic concept of the pulling angle effect has not yet been reported. To close this gap, here we use wall-shaped adhesive microstructures of three different flap heights to systematically study the effect of pulling angle on the normal and tangential components of the pull-off force tested at different preliminary tangential displacements. In accord with the prediction of the Kendall model for the normal component of peeling force, there is an optimal normal force that is required to detach the wall-shaped adhesive microstructure. The optimum is obtained at about half the distance needed to initiate sliding and at pulling angles that range within 60–90°, which suggests that the wall-shaped microstructure can tolerate relatively large inaccuracies in the loading direction. The increase of the attachment force with increasing flap height is found to correlate with the flap thickness, which decreased with increasing flap height.
Polymerization of Catechols with Ammonia/ammino based linkers: A Successful Approach for Polydopamine-like Coatings

Javier Saiz-Poseu, Josep Sédó, Beatriz García, Felix Busque, Daniel Ruiz-Molina

Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and The Barcelona Institute of Science and Technology, Campus UAB, Bellaterra, 08193 Barcelona, Spain; Departament de Química, Universitat Autònoma de Barcelona, Campus UAB, 08193 Bellaterra, Spain

Keywords: catechol, polydopamine, nanoparticles, nanocapsules, coating, multifunctional

Inspired by the pioneering work of Messersmith et al., one of the most widespread methodologies used over the last years for control of the surface properties has been the melanin-like oxidative polymerization of dopamine into a polydopamine (PDA) primer coating, followed by its functionalization with appropriate functional groups. In PDA, catechols and quinones are assumed to play complementary roles: on the one hand, o-dihydroxyl groups in nonoxidized catechol moieties presumably confer adhesion to substrates; on the other hand, residual, highly electrophilic o-quinones act as reactive points for the covalent attachment of functional side chains. Though, despite its versatility and simplicity, PDA modification relies on the existence of a sufficient amount of reactive groups in the primer coating, which cannot be accurately controlled and, because of PDA insolubility, restricted to in situ polymerization methodologies.

Recently, we have reported the development of an alternative, simpler approach to fabricate catechol-based material. In this novel strategy, a single monomer bearing both a catechol ring and at least one desired functional side chain (i.e., designed to carry a maximum amount of functional groups) is first synthesized and then polymerized by means of a simple and inexpensive procedure consisting of treatment with ammonia in aerobic conditions. Compared to PDA, the main differences would be, first, the nitrogen source -which is endogenous in the case of catecholamines and external in our case (ammonia)- and, more importantly, the fact that this novel approach does not rely on uncontrolled residual reactivity in order to introduce a specific functionality in the coating because it is already built in the catecholic monomer. Following this approach we have fabricated different families of coatings and nanoparticleless of applicability as biosurfaces, drug delivery carriers and/or water treatment.

Fig. 1: Schematic example of a hydrophobic coating obtained with our approach

Nanomaterials derived from polydopamine for hydrogen peroxide production

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Bioinspired-adhesives have attracted great interest in nanotechnology. In particular, polydopamine can be formed under mild conditions. The resulting bio-adhesive can be used to easily create an N-doped nanoscale-thick organic coating on a number of nanostructures. A variety of nanocarbons (i.e., graphene oxide, nanotubes, nanohorns, nanocones) have been coated in this manner. Indeed, the first choice for a template fell on nanocarbons, since their composites have proven to be really attractive systems for wide applications, ranging from medicine and tissue regeneration, to energy and catalysis.

Subsequent graphitization of the polydopamine-coated nanocarbons yielded nanostructured metal-free organic catalysts for the sustainable electrochemical production of hydrogen peroxide, which is a commodity product of wide use, and also a convenient low-cost sanitizer for economically disadvantaged societies. In particular, carbon nanohorns proved to possess the ideal porosity for the selective production of hydrogen peroxide with excellent performance at all pH values investigated (pH 1-13), good stability, and excellent reproducibility. Current work is focusing on other nanostructured templates, similarly coated with the bioadhesive-polydopamine, and subsequently graphitized, in the quest to develop further bio-adhesive derived nanomaterials for green applications in water.

Fig1. Mussel-derived polydopamine is a precursor of nanomaterials for hydrogen peroxide green production.

Many marine organisms harness diverse protein molecules as underwater adhesives to achieve strong and robust interfacial adhesion under turbulent environments. In addition to the unique molecular features of their specific glue compositions, natural underwater glues also owe their outstanding performance to the dynamic processing details ranging from protein expression, delivery to assembly and curing, which are spatiotemporally and dynamically coordinated by cells.

Taking cues from nature, we describe living cellular glues that recapitulate dynamic features of natural adhesives by leveraging engineered bacterial biofilms. Using synthetic biology tools, we implemented inducible transcriptional and translational control over the expression of adhesive proteins and associated functional enzyme. We demonstrated that adhesive proteins could be extracellularly secreted and assembled into adhesive fibrous networks around cells, displaying strong adhesion in wet conditions. Programmable light-sensing bacterial could sense light and respond to produce adhesive fibers with spatiotemporal control. As such, the living cellular glues could capture spherical particles to repair cracks on demand. In summary, we have developed an engineering platform that readily facilitates the further development of smart living glues with previously unattainable dynamic spatial-temporal, self-healing, and evolvable properties.

Biomimetic adhesive micropillars with a hard core and a soft shell

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Structured adhesive systems in nature, such as gecko and tree frog toe pads, have attracted great interest over the last decades. In those systems, an important contributor to adhesion is contact area maximization and intimate contact formation resulted by flexible setae and a toe pad with low effective elastic modulus in geckos [1,2] and tree frogs [1,3] respectively. In addition to a “soft” exterior, “hard” units in the form of tendons and fibers have been identified in both geckos and tree frogs, presumably functioning as internal force-transmitting structures that preserve the contact established by the soft external structures. [4–7] Despite recent advances, mimicking multi-component adhesives remains challenging. [8,9]

Here, we present a facile two-step process for fabricating biomimetic adhesive micropillars consisting of two components with different degrees of deformability. First, PDMS micropillars (~3 MPa) were prepared to act as the hard core, followed by spin-coating a soft layer of PDMS (~1 MPa) to act as a shell. The shell thickness \( t \) (Fig. 1) was controlled by the speed and duration of spin-coating. Fabricated adhesive microstructures were characterized with SEM, WL-interferometry and optical microscopy.

The shell thickness of the fabricated microstructures varied in a range of 0.2–3 μm, with an accuracy below 0.1 μm. The “hard” core is suggested to inhibit collapsing of pillars, resulting in a reusable adhesive. [10] Adhesion and friction on glass of fabricated structured adhesives will be next measured with a custom-made setup.

Fig. 1. SEM images of a cross-section of a microstructure with a hard PDMS core and a soft PDMS shell of thickness \( t \). The scalebars are 20 μm (left) and 5 μm (right).

Novel Approach for designing Bioinspired Catechol-based Adhesives Via Thiol Chemistry

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During last decade the development of novel bioinspired materials based on the byssus proteins of mussels has attracted the interest on many fields due to its intrinsic property of underwater adhesion. In that way, several catechol derivatives have been investigated to obtain polymeric materials with similar features and some of them have already shown outstanding underwater adhesive properties.[1] Nevertheless, those presenting higher adhesion have been focused basically on industrial applications because of its poor applicability on biological substrates.

While the area of bioadhesives is an appealing field of application, only few catechol containing polymers have been used on biological substrates with high adhesion and biocompatibility,[2] being required here more research. In this work, we present an alternative and novel reaction pathway, using a novel catechol containing molecule. A polysulfide backbone is obtained by oxidative reaction in presence of iodine,[3] but preserving the catechol from its oxidation. This new way for synthesizing catechol containing polymers, as well as the use of these novel kind of compounds, provide us captivating alternatives to get promising bioadhesives.

Quartz crystal microbalance with dissipation monitoring (QCM-D) is a powerful tool for studying adsorption and adhesion of molecules, polymers and nanoparticles by monitoring the change in frequency and dissipation of resonant oscillations of a solid substrate. However, its use for analyzing deposition and adhesion of microparticles and living cells on surfaces from solutions and, in particular, quantifying the contact mechanics, has been hampered by the difficulties of interpreting the response and loading regimes [1, 2]. Here we present a new full quantitative model of a QCM-D response, presented as an equivalent mechanical circuit using electroacoustic analogy (Fig 1). As an essential feature, we propose to model the interaction of the particle with surrounding fluid as a freely oscillating sphere, which is a valid approximation for micron-sized and larger particles. This largely reduces the number of fitting parameters and help isolate those pertinent to the contact mechanics. We applied the model to examining deposition of different microparticles as well as GFP-tagged *Pseudomonas fluorescens* bacteria on a number of substrates using QCM-D combined with real-time microscopy. The parameter space was increased by varying type and size of particles, surface chemistries and mechanics of the substrate, and ionic strength of solution. In this way, we could observe and quantify the wide spectrum of possible responses and transition from inertial to elastic loading, including rarely observed resonant regimes. Ultimately, we found that the model offers a reasonable quantitative description of the observed response and its frequency dependence for different abiotic particles and substrates as well as for bacteria and enables to extract physical characteristics of the contact in mixed and resonant regimes. This model can be a useful tool for interpreting and quantifying QCM data on deposition and adhesion of particles and living cells to surfaces, including time-dependent adhesion phenomena.

**Fig1.** Experimental setup (left) and the proposed model for particle-QCM-D interaction (right)

Bioinspired Wax-based passive anti-biofouling surfaces preventing biofilm formation

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Biofilm formation enables bacteria to grow under unfavorable conditions, provides them with protection, and increases their resistance to antimicrobial agents. Once a biofilm has formed, it is difficult, and in some systems, impossible to treat. Strategies based on the release of biocidal agents have shown only transient efficiency. Herein, we will present a novel bioinspired passive approach to the prevention of surface biofilm attachment by exploiting superhydrophobic surfaces formed via the self-assembly of paraffin or fluorinated wax crystals. Our surfaces show exceptional ability to inhibit biofilm formation of both Grampositive Bacillus cereus and Gram-negative Pseudomonas aeruginosa over a 7 day period (up to 99.9% inhibition) [1]. We will first discuss the formation of these surfaces and the crystal growth mechanisms [2-3] and then show the anti-microbial properties.

Figure 1 depicts the wax crystals on a surface.

![Figure 1: Paraffine wax crystals on a surface.](image)

Animals like beetles or geckos display complex structural features in the way the contact is subdivided in a hierarchical, tree-like manner, and the interplay between contact size and hierarchical organization in the detachment-sliding process is an issue that remains to be adequately addressed. Here, we study the influence of hierarchical fibrillar architectures on the load distribution at the interface between the contact elements and the substrate, and the corresponding detachment and sliding behaviour.

We first present an analytical model to derive the load distribution in a fibrillar system, including hierarchical splitting of contacts, i.e. a “hierarchical shear-lag” model. Our study suggests that hierarchical architectures counterbalance high load concentrations resulting from contact unit size reduction and that contact splitting generates multiple detachment fronts, so that hierarchical organization helps to avoid non-uniform load distributions that are detrimental to adhesive performance. We show that these results can be summarized in a generalized adhesion scaling scheme for hierarchical structures, proving the beneficial effect of multiple hierarchical levels. Additionally, we introduce a hierarchical formulation of the spring-block model based on the classical Amontons-Coulomb force with statistical dispersion on microscopic friction coefficients. We thus show that it is possible to tune the friction properties of a hierarchical surface and provide some insight on the mechanisms involved at different length scales.

Our models can thus be used to predict the adhesive and frictional performance of hierarchical structures such as those found in biological structures.
Numerical simulation of sliding inception in biomimetic wall-shaped adhesive microstructure

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The problem of quick and easy reversible attachment is of great importance in different fields of technology. Known solutions to the problem of reversible attachment are associated with considerable technical expenditure, special geometry, chemical compatibility or physical properties of mating surfaces and formation of residues. On the other hand, in the process of evolution, nature has developed effective attachment systems that make it possible for many animals to attach and climb on surfaces irrespective of their orientation, geometry and chemical composition. Inspired by these systems, here we develop and study a shear-activated dry adhesive.

To resist sliding, a device based on a structure of soft wall-shaped projections is proposed, in which friction forces are decoupled from normal forces such as load or adhesion.

Using commercial FEM package ANSYS, we have created a model to study the interactions of the proposed structure against a flat surface. A bilinear traction vs. separation law is proposed to approximate the adhesive attraction in the contact interface. To describe friction, which is independent of the normal pressure between the wall-shaped projections and the counter surface, the Tresca friction law was used.

We have found that upon application of tangential load, the wall-shaped projection deforms in a manner that increases the contact area, and that the static friction varies accordingly.

We have compared the numerical results with our previous experimental work and have found good agreement for the higher range of the applied normal forces.
Interfacial Adhesion – from single molecule to densely packed film

Zhenyu J. Zhang¹, Evangelos Llamas¹, Mark Geoghegan² (Times New Roman, size 11, underline present author)

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Macromolecules, be it natural or synthetic polymers, could adopt various conformations at an interface, depending on the chemical nature of the polymer, number of repeat units, interaction between polymer and surface, and the characteristics of the surrounding medium. This would consequently determine the interfacial adhesion. In this talk, I will discuss the results acquired from two representative systems, single molecules and surface grafted polymer brush, using a series of interfacial characterization techniques such as atomic force microscopy (AFM), quartz crystal microbalance (QCM), and ellipsometry.

Single molecule mechanics: individual molecules could be immobilized to the end of an AFM tip, allowing us to probe single molecule mechanics quantitatively¹⁻³. The resultant force curves could reveal which types of conformation such molecule would prefer to adopt, and how that changes in response to surrounding medium and the surface in contact. More importantly, the adhesion between such molecule and the surface can be quantified directly, which has been proven as an invaluable tool for designing interfacial adhesive.

Polymer brush: when numerous polymeric chains, with one end immobilized on a solid substrate, are packed densely enough, they form a unique layer called polymer brush. Such layer can be used as coating to manipulate surface adhesion. I will discuss a system, surface grafted poly(2-(methacryloyloxy)ethylphosphorylcholine) (PMPC) that is predominantly used in biomedical applications. PMPC brush was found to change interfacial structure, as shown in figure 1, when being exposed to different types of alcohol, and consequently alter the interfacial adhesion and friction⁴⁻⁶.

Fig1. Friction-load relationship acquired on PMPC brush in three different types of alcohol, alongside schematic diagrams showing how interfacial molecular configuration changes.

1. Z. Zhang et al., Nanotechnology 19, 035505 (2008).
The Influence of the Conditions for Polyelectrolyte Multilayer Build-up on Bacterial Adhesion Capacity

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It is well known that bacterial adhesion can be controlled by tailoring various material surface properties, such as surface charge, on which we concentrate in our study. [1] We correlated the conditions at which the polyelectrolyte multilayers are formed (polypelectrolyte concentration, salt concentration), the number of polyelectrolyte layers, and the type of the terminating layer with corresponding bacterial adhesion. Additionally, we also investigated the adhesion of bacteria on protein-terminated polyelectrolyte multilayers. In our study we prepared poly(allylamine hydrochloride)/sodium poly(4-styrenesulfonate) (PAH/PSS) polyelectrolyte multilayers [2] on silica surface. These synthetic polyelectrolytes have been widely used in the process of polyelectrolyte multilayer formation, and we also used them extensively in our investigations of polyelectrolyte complexes. [3]

Surface roughness and hydrophobicity of obtained polyelectrolyte multilayers were determined by atomic force microscopy and tensiometry. The surface charge was examined by the zeta potential measurements of silica particles covered with polyelectrolyte multilayers, whereby ionic strength and polyelectrolyte concentrations significantly influenced the build-up process. For adhesion experiments, we used the bacteria Pseudomonas aeruginosa and Escherichia Coli. The extent of adhered bacteria on the surface was determined by scanning electron microscopy. The results showed that the extent of adhered bacteria mostly depends on the type of terminating polyelectrolyte layer, since relatively low differences in surface roughness and hydrophobicity were obtained. [1] In the case of polyelectrolyte multilayers terminating with a positively charged layer, bacterial adhesion was more pronounced than in the case when the polyelectrolyte layer was negatively charged.

Fig. 1. Schematic presentation of bacterial adhesion on PAH/PSS polyelectrolyte multilayers terminating with PSS (6 layers) and PAH (5 layers).

Interest in soft and hard tissue adhesives as alternatives for conventional wound closing and bone fixation applications has increased in recent decades as a result of possible advantages such as better comfort and lower cost. Bioadhesives is a research topic of very high challenge because they must be able to be spread on wound surfaces, which are wet with tissue fluids or blood, provide adhesion, facilitate healing and maintain biocompatibility.

Novel tissue adhesives based on the natural polymers gelatin and alginate, and crosslinked by carbodiimide, were recently developed and studied by us. The combination of these three materials resulted in high strength, high biocompatibility and additional desired properties for various specific applications. Unique bioadhesives were achieved when loaded the basic formulations with functional additives, such as hemostatic agents (1), drug molecules (2) and bioactive ceramics (3). Addition of the hemostatic agent kaolin improved the adhesion, sealing ability and overall function in a hemorrhagic environment. Delivering an antibiotic drug locally using our bioadhesive decreased the risk of infections and increase the therapeutic effect of bioadhesive. Our functional bioadhesives will be described in terms of formulation-structure-property effects as well as in-vivo results.

Bioadhesives based on natural polymers which also include functional fillers (hemostatic agents, drugs and ceramic fillers) are novel. They actually behave as composite bioadhesives, and thus present a new concept of adhesive biomaterials. The understanding of the relationships between formulation parameters, structure and the resulting relevant in-vitro properties and in-vivo functioning, are of great scientific and medical relevance. They are expected to provide new solutions to the basic needs in various medical fields.

Figure 1: Environmental SEM micrographs showing the structure of the composite bioadhesives loaded with: (a) The hemostatic agent kaolin, (b) the analgesic drug bupivacaine, (c) hydroxyapatite.

Many bio-adhesive materials adhere weakly to tissue due to their high water content and weak structural integrity. Others provide desirable adhesive strength but suffer from toxicity, rigid structure and lack of elasticity after administration. Central challenges in this field are the understanding of the complex structures of tissue adhesives and to develop practical synthetic routes that overcome their main shortcomings. In this presentation I will discuss new strategies for designing bio-adhesive materials based on neat (without water or other solvents) liquid polymers that solidify after administration while allowing interactions with the tissue. Bio-adhesives based on these structures could be an attractive alternative to sutures and staples since they can be applied more quickly causes less pain and may require less equipment while maintaining the desired adhesion strength.
Novel polyurethane pressure sensitive adhesives with controlled tack intended for medical patches

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Pressure sensitive adhesives (PSAs) are commonly used in the manufacture of medical patches and bandages. Several polymers are used for manufacturing PSAs such as synthetic rubbers, acrylics, silicones, polyesters and polyurethanes, and they are commonly applied in solution. Because of environmental regulations, organic solvents must be removed from PSA formulations. On the other hand, the pressure sensitive adhesion property is not typical of the polyurethanes because of their low tack and low peel adhesive strength. Previous patent [1] proposed the addition of tackifiers to polyurethanes or the compounding with other polymers for obtaining PSAs. In a different approach, Nakamura et al. [2] have added crosslinking agents for obtaining polyurethane PSAs. In this study, different approach for preparing 100% solids polyurethane PSAs consisting in the design of the segmented structure of the polyurethane, i.e., the control of the degree of phase separation of the hard and soft segments is proposed.

Solid thermoplastic polyurethanes (PUs) with pressure sensitive adhesion property were synthetized by reacting 4,4’-diphenylmethane diisocyanate (MDI) with 1,4-butanediol and mixtures of polypropylene glycols (PPGs) of different molecular weights (1000 and 2000 Da). Good tack at 10-37 ºC was obtained in PUs prepared with PPG2000+PPG1000 mixtures containing 50 wt% or more PPG2000 (Figure 1). The pressure sensitive adhesion properties of the PUs were related to their minor content of bonded urethane groups and more important degree of phase separation. Furthermore, these PUs followed Dahlquist’s criterion, they showed low glass transition temperatures, high tack, and low 180º peel strength. Therefore, the PUs had good potential as pressure sensitive adhesives.

Fig 1. Variation of the tack of PUs as a function of the temperature.

Levan is a fructose homopolysaccharide which gained attention recently for its unusual combination of properties distinguishing it from other natural biodegradable polysaccharides like chitosan, cellulose or starch [1]. Levan has been found in habitats as diverse as salterns and thermal waters to tropical plants and sugar factories. In biological systems, levan is a multifunctional molecule associated with various roles such as serving as a storage compound for energy during periods of starvation, enabling adhesion of the producer organism in a favorable environment as well as being involved in biotic and abiotic stress resistance and signaling [2]. With its exceptionally high adhesive strength, very low intrinsic viscosity, stabilization of biological membranes and excellent biocompatibility, this natural adhesive meets the technical requirements not fulfilled by other biodegradable polymers.

Among the strongest bioadhesives, film-forming levan is garnering interest for its role in some simple solutions to difficult problems. One of these is illustrated by using levan and its chemical derivatives in laser-based techniques to construct levan films for healing wounds and burned tissue. Another is the development of bioresorbable electronic implants. This talk on levan based bioadhesives will present the mechanisms by which it forms bonds as well as the state of the art of its various practical and biomedical applications like electrospun or Layer-by-layer deposited thin films, hydrogels or drug delivery systems.

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Biomimetic nanoparticles for enhanced FcRn-mediated delivery across mucosal barriers

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Oral administration remains a challenge for delivering of pharmaceuticals through biological barriers [1, 2]. Functionalization of nanoparticles (NPs) is a strategy to bind specifically to the surface receptors and so to surpass biological obstacles and improve the bioavailability of drugs [3]. The neonatal Fc receptor (FcRn) is a cellular receptor that binds and rescues albumin and IgG antibodies from intracellular degradation, extending their half-life [4]. FcRn binds both its ligands in a strict pH dependent manner, mediating the transport of its ligands across polarized epithelial cells [5]. Herein, we aimed to explore whether polymeric nanoparticles (NPs) conjugated with engineered human albumin (HSA) variants for enhanced FcRn binding could be an attractive strategy for delivery of encapsulated drugs across mucosal barriers. For this purpose, NPs were designed using double emulsion/evaporation technology where engineered human albumin was site-specifically conjugated to the polymers. The physical-chemical properties of the NPs were characterized by dynamic light scattering and electron microscopy. Insulin encapsulation efficiency was monitored by HPLC and albumin conjugation efficacy by 2-way anti-HSA and FcRn-binding ELISAs. Both protein secondary structure was studied using FTIR. Also, recycling and permeability studies were evaluated with Human endothelial cell-based recycling assay (HERA) and in vitro transcytosis assays, respectively.

NPs with approximately 150 nm, presented an insulin encapsulation efficiency over 80% and albumin on the surface after conjugation. The encapsulation and conjugation processes do not seem to interfere with protein secondary structure. Also, with FcRn binding ELISA at pH 5.5, FcRn-binding properties of HSA are retained post conjugation. NPs-HAS variants bind with expected (comparing with naked HSA) binding hierarchy to hFcRn in ELISA: NPs-KAHQ < NPs-WT < NPs-KP < NPs-TNNEKP. Plus, results from HERA suggest that NPs with conjugated albumin are recycled in an FcRn-dependent manner, being NPs-KP and NPs-TNNEKP recycled more efficiently than NPs-KAHQ. The same pattern is observed in permeability studies. Next, we will explore the use of the NPs using the state-of-the-art humanFcRn transgenic mouse model. In short, the FcRn-targeted approach may pave the way for more efficient delivery of NP-encapsulated drugs.

This paper will describe the adhesive proteins in stalked barnacles, which are less understood than acorn barnacle models. The absence of standard techniques to culture the lifecycle in stalked barnacles, along with the complex metamorphosis in the barnacle lifecycle makes working with this group a challenge. And as it is still unclear what overlaps exist between adult and larval glues, manipulation of the larval phase in order to understand adult adhesion is currently not possible. However, because stalked barnacles are fouling organisms, pursuing this line of research is a potentially useful contribution to anti-fouling development as well as being interesting from a biotechnology perspective.

In the present study the discovery of adhesive genes is described in adult *Lepas anatifera*. Homologues could be found for all the known adhesive proteins found in acorn barnacles, apart from the 20K protein. The Settlement Inducing Protein Complex (SIPC), which has an adhesive function in larvae, was also described in *L. anatifera*. While a high degree of similarity was seen in the SIPC across acorn and stalked barnacles groups, indicating that this is highly conserved in barnacle taxa, this was not the case in adhesive proteins. The extent to which this is an adaptation to preferred habitats and settlement substrates is not clear at this point. Meanwhile a low sequence similarity across taxa in adhesive proteins, along with few discernible ‘motifs’, makes it difficult to determine the mechanism(s) at play during adhesion in these organisms. However, recombinant expression of individual proteins may be the best hope for beginning to address this question.

The cp19k protein of the goose barnacle *Pollicipes pollicipes* was recombinantly expressed in *E. coli* to study bioadhesion in this stalked barnacle species. The behaviour of this protein was examined by Surface Plasmon Resonance on a variety of Self Assembled Monolayers with surfaces chemistries of different charge and hydrophobicity. The process of examining individual proteins in this manner is an alternative approach to a long tradition of examining the properties of complexes of barnacle proteins working together e.g. the mixture of proteins found in larval temporary adhesive footprints and permanent larval adhesives.

Engineered silk proteins as adhesives: the role of phase separations

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We have used protein design and engineering with the general aim of creating structural materials and adhesives. Studying the behavior of modified variants of silk proteins, we noted that a 3-block architecture leads to protein assembly with interesting adhesive function. In the 3-block system, a central block of Araneus diadematus ADF3 spidroin protein was flanked by cellulose binding modules (CBMs) in both termini [1]. The protein undergoes phase separation giving highly concentrated droplets (i.e. coacervates) that have a low viscosity and a very low interfacial energy. The coacervates infiltrated networks of cellulose fibers very efficiently and led to a high-toughness adhesive behavior. We conclude that protein architecture affects strongly the phase behavior of protein and in accordance with previous investigations the initial coacervation of proteins played a critical role for the functionality of the proteins as adhesives.

Fig1. Structuring of silk-inspired 3-block proteins within coacervates affect their adhesive and cohesive properties. Image of a semi-dried sample being pulled apart. Image width 20 micrometer.

The expansion of genes encoding silk adhesives in the greater wax moth, *Galleria mellonella*

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Lepidopteran silk represents a heterogeneous family of structural proteins produced by altered larval labial glands called silk glands. Information on the molecular structure of silk proteins is limited to a handful of species. We found that *G. mellonella* silk has a higher proportion of soluble proteins than that of *B. mori* or *A. yamamai*. In order to detect all major components in the silk of *G. mellonella*, we used silk gland transcriptome sequencing and identified 27 candidate cDNAs encoding putative secretory proteins that may represent novel silk components. Eight of these candidates were confirmed by proteomic analysis or by N-terminal Edman sequencing. The association of several other candidates with silk was supported by sequence similarity with known silk proteins and northern blotting. Our results show that *G. mellonella* adhesive sericins form the largest subfamily among silk proteins. The pattern of branching in a sericin phylogenetic tree is in agreement with the birth-and-death model of evolution. We also found that *G. mellonella* silk glands produce seroins, mucins, protease inhibitors, imaginal disc growth factor and several abundant but unknown low molecular weight proteins. Profound changes in the number of soluble silk components and their remarkable divergence reflects fast adaptation of these insects to different environments.

![Scanning microscopy of the outer side of G. mellonella cocoon, scale 10 um](image)

**Fig1.** Scanning microscopy of the outer side of *G. mellonella* cocoon, scale 10 um


Zurovec M., Kludkiewicz B., Kucerová L., Sehnal F. (submitted) The expansion of genes encoding soluble silk components in the greater wax moth, *Galleria mellonella*. *Biomacromolecules*
Glycosylated Biofilm Proteins as Bioadhesives: An Engineered Protein Glycosylation System

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Glycosylation is a common posttranslational modification in eukaryotes where glycan molecules are attached to certain motifs in proteins. Glycosylation has crucial roles in different cellular processes in eukaryotes such as folding, stability and cell-to-cell adhesion; and highly adhesive proteins such as seashell glue or some mussel adhesive proteins are discovered to be heavily glycosylated. In recent years protein glycosylation is also found in Campylobacter jejuni and some pathogenic bacteria. Even though the role of glycosylation in bacteria is not completely unraveled, studies suggest that C. jejuni glycosylation is of significant importance for gut colonization via epithelial cell adhesion.

Biofilm is a community of microorganisms sticked together by an extracellular matrix to provide protection from external factors. Biofilm is an adhesive structure that consists of bacterial cells, proteins, saccharides, nucleic acids and so on. Several microorganisms such as Escherichia coli produces highly ordered functional amyloid fibers in bacterial biofilms named curli, that contribute to adaptation to the environment. Bacterial amyloid proteins facilitate resistance against proteolysis, pH and extreme temperatures. Engineered curli proteins are depicted to be promising tools as bionanomaterials for many functional applications such as protein fiber networks, nanoparticle biotemplates and substrate adhesion. Considering that bacteria use curli as tools to adhere onto several surfaces/other cells, there are opportunities for using them as bioadhesive agents for designed applications.

In this work, it is hypothesized that glycosylation of biofilm proteins may enhance their adhesiveness and enable their use as bioadhesives or cell adhesion scaffolds. To this end, E. coli BL21 (DE3) cells are modified to contain C. jejuni protein glycosylation pathway (pgl). Functionality of the pathway is determined by detecting the glycan groups of alkaline phosphatase enzyme functionalized with DQNAT glycosylation motif (ALP-DQNAT), using soybean agglutinin (SBA) lectin blot. Secondly, biofilm proteins of E. coli CsgA and CsgB, Bacillus subtilis TapA and TasA, Pseudomonas aeruginosa FapB, FapC and Vibrio cholerae RbmA, RbmC and Bap1 are genetically modified to include DQNAT glycosylation motif and modified proteins are expressed in E. coli BL21 (DE3) pgl cells. Successful glycosylation of biofilm proteins is shown using SBA lectin blot. As the following step, glycosylated and non-glycosylated biofilm proteins will be purified and the change in their adhesive properties are observed using atomic force microscopy (AFM). Additonally, using QCM-D their adhesion characteristics are studied. Finally, cell adhesion assay on coated surfaces with different mammalian cell lines are being performed to test effect of glycosylation of biofilm protein on cell adhesion.
Production and characterization of recombinant sea star adhesive proteins

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Biological adhesives often offer impressive performance in their natural context and, therewith, the potential to inspire novel adhesives for an increasing variety of applications in medicine or in material sciences. Sea stars represent an interesting model for the study of marine adhesion. Indeed, they can attach strongly but temporarily to a variety of substrata using a multitude of small appendages, the tube feet. After the tube foot has become detached, the adhesive material, which appears as a fibrous meshwork-reinforced hydrogel, remains firmly bound to the substratum as a footprint [1].

Recently, transcriptome analysis and proteome analysis were combined to obtain sequences for all footprint-specific proteins [2]. Among these 35 proteins, 20 share similarities with known proteins but 15 others, within the most abundant in the secreted adhesive, remain unidentified. One of the adhesive proteins, the sea star footprint protein-1 (Sfp1) was characterized [3]. It is a major structural protein involved in footprint cohesion and possibly in adhesive interactions with the tube foot surface. This large protein is translated from a single mRNA and then cleaved into four subunits displaying specific protein-, carbohydrate- and metal-binding domains (Fig. 1).

Figure 1. The four subunits and the main structural domains of Sfp1 [4]. Green, calcium-binding EGF-like domain; yellow, galactose binding lectin domain; red, discoidin domain; blue, von Willebrand Factor; purple, C8 domain. The framed parts correspond to produced recombinant proteins.

Based on the amino acid sequence of Sfp1, two recombinant proteins were designed and produced in the bacterium Escherichia coli: one corresponding to the C-terminal part of Sfp1β (green frame in Fig. 1) and one corresponding to Sfp1δ (black frame in Fig. 1). Proteins were solubilized from inclusion bodies, purified and refolded. Native PAGE and size exclusion chromatography showed that the two proteins form oligomers quickly during refolding. The secondary structure of the two proteins was characterized by Fourier transform infrared (FTIR) and circular dichroism (CD) spectroscopy. Both proteins appear to contain a combination of α-helices and β-sheets. Finally, the nanomorphology and nanomechanical properties of protein films were investigated by atomic force microscopy.

Bioinspired soft devices with fixation ability in biomedical applications

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Polymers have been widely used to develop implantable devices in a variety of biomedical applications, including in advanced therapies, such as tissue engineering and regenerative medicine, or in controlled drug delivery. From the different sources of polymeric biomaterials, polysaccharides have been proposed to produce matrices able to interact favourably with cells. Due to their hydrophilic nature and richness in chemically active groups, such macromolecules can be used to produce a variety of structures fabricated using aqueous-based or other environmental-favourable procedures. Adhesive and fixation ability are important characteristics in such systems for many situations where it is necessary their physical integration with the surrounding tissues. Examples will be shown on the use of mussel inspired adhesive polymers obtained through the modification of polysaccharides with catechol groups. We have used such materials to fabricate free-standing films, using the layer-by-layer technology, that could be used as biocompatible patches for tissue regeneration applications. The ability of the catechol groups to coordinate with iron ions also enabled the development of high-toughness and self-healing hydrogels. Such materials could be used as injectable supports for cells in tissue engineering.
Improving the skin adhesion of microneedle patch through catechol-functionalization

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Microneedles (MNs) are arrays of miniaturized needles down to the micrometer scale. They have been prevalently adopted in biomedical applications due to their pain-free, risk-free, and easy-to-use properties [1, 2]. Currently, MNs are fixed on skins during administration with the assistance of extra adhesives, such as bandages, scotch tapes, or 3M adhesives. The adhesive backings cannot be easily removed and easily cause uncomfortable skin symptoms, such as skin redness and mild erythema, which greatly impedes the application of MNs.

Inspired by the mussel adhesion chemistry [3], we develop a self-adhesive MN patch which can attach on the skin by itself after inserted into skin (Figure 1). Hyaluronic acid (HA) was firstly modified with methacrylate group and then modified with catechol group. The self-adhesive MN patch was fabricated using template method. The CA-MeHA was made as the shell of MNs, which provides the adhesive property. Then MeHA was applied to make the inner matrix of MNs, in which the drugs can be loaded inside for various applications. Then UV was applied to crosslink the MNs. The self-adhesive MNs showed higher adhesive property than pure MeHA MNs when inserted into porcine skins ex vivo. Furthermore, the MNs was applied into mice skin, showing and firm attachment on mice skin during the movement of mice. After removed from skin, there is no redness and mild erythema observed on skin.

Figure 1. The schematic illustration of the possible mechanism of self-adhesive MN patch attaching on skin.

Reference
The aim of this study was to investigate the effect of acrylate modification on the mucoadhesion of chitosan at the nanoscale. Nanoparticles were fabricated from acrylated chitosan (ACS) via ionic gelation with tripolyphosphate and were characterized in terms of size, zeta potential, stability, and nanoparticle yield. Chitosan (CS) nanoparticles, serving as a control, were fabricated using the same procedure. The mucoadhesion of the nanoparticles was evaluated using the flow-through method after different incubation periods. The retention percentages of ACS nanoparticles were found to be significantly higher than those of CS nanoparticles, for all studied time intervals. An additional indication for the higher mucoadhesion of ACS nanoparticles was obtained from the mucin particle method, in which mucin and nanoparticles are mixed at different ratios, and an increase in particle size was detected. NMR data verified the presence of free acrylate groups on the ACS nanoparticles. Thus, the improved mucoadhesion could be due to a Michael-type addition reaction between the nanoparticles and thiol groups present in mucin glycoprotein, in addition to entanglements and hydrogen bonding. Overall, ACS nanoparticles exhibit enhanced mucoadhesion properties as compared to CS nanoparticles and could be used as vehicles for drug delivery systems to provide improved drug absorption and bioavailability.

Adhesives and sealants have become a significant part of our life. We use and work with these materials in all segments of human activities. Although multi-functional, the synthetic adhesives used today are inappropriate, in particular in human-focused areas, but they are still used due to their high adhesive strength and lack of alternatives [1].

With the increasing interest for biocompatible and biodegradable components for biomedicine, nanotechnology and tissue engineering, bioadhesives are becoming relevant and credible alternatives to current toxic and non-ecological adhesives.

Within bioadhesives, the ones produced by marine organisms offer impressive performances in water, the enemy of adhesion for synthetic glues, and thus have a huge potential to inspire the development of a new generation of biological, superior, adhesives for an increasing variety of high-tech applications.

Being inhabitants of wave-swept shores, sea urchins possess specialized adhesive organs, the tube feet, relying on chemical attachment to move and anchor to the sea floor. These organs are composed by a proximal motile stem and a distal attaching disc that encloses a duo-gland adhesive system, capable of producing separately adhesive and de-adhesive secretions, allowing sea urchins to attach and detach repeatedly.

Sea urchin tube feet and its secreted adhesive have been studied in the last two decades [2] using histochemistry, electron microscopy, biomechanics, differential protein expression, mass spectrometry, western-blotting, transcriptomics, in-situ hybridization and atomic force microscopy. The gathered knowledge is being used as inspiration for the production of sea urchin-inspired recombinant adhesive proteins for future biomedical applications (Fig. 1).

Fig1. Sea urchin inspired biomimetic adhesives.

Scaling of adhesion: shear forces and pad sliding reduce adhesion loss for large insects

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Climbing animals range over seven orders of magnitude in size and can produce strong adhesion on diverse substrates. Theory predicts that adhesion forces scale with the length or area of adhesive contacts. Therefore, supporting the body weight should become increasingly difficult for larger climbing animals. As pad size is approximately isometric within closely related taxa, how can larger individuals cope with the expected loss of relative adhesion?

We studied the scaling of contact area and adhesion in different-sized stick insects (Carausius morosus). When adhesion was measured for whole insects using a centrifuge, the scaling coefficient was much higher than for single-pad measurements. To investigate the mechanisms underlying this effect, we tested how shear forces affect the scaling of adhesion. Adhesion for single-pad perpendicular pull-offs without shear forces scaled with mass0.43 (CI 0.37-0.5), but the scaling coefficient increased dramatically to 0.94 (CI 0.79-1.12) when shear forces equivalent to one body weight were applied before pull-off. This higher coefficient was based on a large increase of adhesion with shear forces for large insects, but almost no change for small insects. These findings can be explained by the effect of pad sliding, which removes adhesive secretion from the contact zone, thereby increasing stress levels required for detachment. We experimentally varied the amount of sliding and its distribution among large and small insects and confirmed that sliding increases the scaling coefficient, helping to maintain the safety factor of larger climbing animals.
Involvement of sulfated biopolymers in adhesive secretions produced by marine invertebrates

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Many marine invertebrates use adhesive secretions to attach to underwater surfaces and different types of adhesion can be distinguished. Permanent adhesion involves the secretion of an adhesive that hardens with time and forms a durable cement. Non-permanent adhesion allows simultaneous adhesion and locomotion. Some organisms creep on a viscous film they produce and leave behind them as they move (transitory adhesion). Others attach firmly but only temporarily to the substratum, being able to attach and detach repetitively (temporary adhesion). Finally, instantaneous adhesion relies on single-use organs or cells and is used in functions other than attachment to the substratum requiring a very fast formation of adhesive bonds. Whatever the type of adhesion considered, functional chemical groups borne by the adhesive proteins and carbohydrates appear to play a key role in the adhesion of marine invertebrates. Among these functional groups, catechols, amines and phosphates have been shown to be of prime importance. The occurrence of sulfates as recurrent moieties in marine bioadhesives suggests that they could also play a role in the adhesion of the organisms producing them [1]. However, in most cases, they have only been detected histochemically in gland cells and their presence in the adhesive material remains speculative. Moreover, the nature of the molecules bearing the sulfate groups is not known with certainty.

In this study, we investigated the presence of sulfated biopolymers in five marine invertebrates representative of the four types of adhesion encountered in the sea: the mussel *Mytilus edulis* and the tubeworm *Sabellaria alveolata* for permanent adhesion, the limpet *Patella vulgata* for transitory adhesion, the sea star *Asterias rubens* for temporary adhesion, and the sea cucumber *Holothuria forskali* for instantaneous adhesion. First, total sulfate content was assayed in the adhesive material of three of these species and compared to values present in the literature. In the adhesive material of mussels, sea stars and sea cucumbers, sulfates amounted for about 1% of the glue dry weight, a value much lower than the 17% reported for the limpet *P. vulgata* [2]. We then used anti-sulfotyrosine antibodies and Alcian blue staining to investigate the presence of sulfated biopolymers in the adhesive secretions produced by the different organisms as well as to localize the cells producing them in the adhesive organs. The two methods presumably highlight different polymers, the former specifically labelling sulfated proteins and the latter staining sulfated proteoglycans and polysaccharides. Sulfated biopolymers were identified in the secretory cells and adhesive secretions of all species except in the tubeworm. In terms of adhesive mechanisms, sulfated proteoglycans appear to play a role only in non-permanent adhesion. In comparison with catechol or phosphate functionalities found in permanent adhesives, sulfates possess weaker coordination ability and do not adsorb strongly to mineral surfaces, especially at the pH of seawater [1]. Yet, organisms such as sea stars and limpets display an adhesion strength almost as high as that of organisms using permanent adhesion, which could be mediated by the cohesive role of sulfated macromolecules. In mussels and sea cucumbers, on the other hand, the specific arrangement of sulfate-positive cells in the adhesive organ and the localization of their secretion in the adhesive material suggest that sulfated biopolymers could rather have an anti-adhesive function, precluding self-adhesion.

Bio-Mimetic tissue adhesives – A journey from the academic lab to the operating room Tomer Fuchs

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It was brown Algae ability to adhere to rocks and vessels in the sea, which inspired an academic chemical engineering professor, Havazelet Bianco Peled, one of the organizers of ICBBA, to work intensively at her lab to study the mechanism of action and material compositions which provided the Algae with this unique ability to adhere in wet environment.

The science and understanding led to the idea that this knowledge could be translated into a medical tissue adhesive technology, which will mimic the Brown Algae adhesion and potentially save lives by stopping bleeding and preventing other surgical leak complications.

The journey from the early stage pure science aiming at understanding the magic of nature to an engineering effort focused on technology commercialization which is feasible from operational, scale up, material stability, shelf life, healthcare economics and many other aspects. This, in short, is the translation of discoveries and understandings into products - a fascinating process which requires teamwork, academic – industry collaboration, patience, focus and vision.

At Sealantis, with the backing of the Technion we were fortunate to build this team, and in a journey of 10 years translated the vision into two products which were already tested clinically on human patients and are now approved for sale in Europe.

The presentation will share the story of the path from the lab to the operating room, the key challenges, success factors and key learning from the journey of Sealantis.

Fig1. Seal-G – From the Sea to the Lab, From the Lab to the operating room……
Charging of material surfaces in aqueous electrolyte solutions is important to better understand interactions between biomaterials and surrounding tissue. In our work we studied the surface charge properties of Titania nanotubes and cerium nanoparticles using polyelectrolyte colloid titration measuring technique. High-resolution transmission electron microscopy imaging was used to determine the morphology of nanoparticles. A theoretical model based on the classical density functional theory coupled with the charge regulation method in terms of mass action law was developed to understand the experiments [1].

Acrylated Chitosan for mucoadhesive drug delivery systems

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The interest in mucoadhesive delivery of drugs constantly increases due to potential benefits over other delivery methods such as lower administration frequency, high epithelial permeability for many drugs and avoidance of some enzymatic degradation as a result of contact with the absorbing mucosa.

A new mucoadhesive polymer was synthesized by conjugating chitosan to poly(ethylene glycol)diacrylate (PEGDA) via the Michael type reaction. The product was characterized using NMR. Higher PEGDA grafting efficacy was observed with low molecular weight PEGDA (0.7 kDa), compared to long 10 kDa PEGDA. The acrylation percentage was calculated based on the reaction of ninhydrin with chitosan, and supported the qualitative NMR findings. The adhesive properties were studied by tensile test and rotating system involving detachment of polymer tablets from a fresh intestine sample. Chitosan modified with high molecular weight PEGDA presented improvement in mucoadhesive properties compared to both non-modified and thiolated chitosan. On the molecular level, rheology measurements of polymer/mucin mixtures provided additional evidence of strong interaction between modified chitosan and mucin glycoproteins. This new polymer shows promise as a useful polymeric carrier matrix for delivery systems, which could provide prolonged residence time of the vehicle on the mucosa surface. [1]

Figure 1 describes the preparation of Chitosan-PEGAc and the adhesion test between polymer tablet and small intestine sample. [1]

Fig1. Preparation of Chitosan-PEGAc and the adhesion test between polymer tablet and small intestine sample

New Bioadhesive based on Allyl Isothiocyanate by Chemical Vapor Deposition (CVD)

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Allyl isothiocyanate (AITC), a compound from of cruciferous vegetables and present in mustard, horseradish, and wasabi, has been recently described as antibacterial, antifungal and anticancerogenic activity\textsuperscript{1,2}. The use of derivate of isothiocyanate (ITC) in science is known for the ability to react easily with compounds with active hydrogens as hydroxyl and amino groups presents in some amino acids of the proteins. The fluorescein allyl isothiocyanate compound (FITC) is a common example of this use in our and a lot of others research groups because offers the possibility to observe, by microscopy optical techniques, the presence of cells and proteins in different samples.

In this work we have focused to create a reactive surface with ITC groups through the polymerization of a thin film of poly-allyl isothiocyanate (PAITC)(Figure 1), and study the effects on bacteria and cells. We have used two polymerization techniques as induced Chemical Vapor Deposition (iCVD)\textsuperscript{3} and Plasma Enhanced Chemical Vapor Deposition (PECVD)\textsuperscript{4} with an optimized conditions of monomer flow, pressure, temperature, time and duty cycle. We have used a metallic grid as mask to create a polymeric surface with a square pattern over a medical silicon to compare visually the reactivity of proteins, bacteria and cells between against both surfaces.

The PAITC thin film have been characterize with ATR, water contact angle, fluorescence microscopy, and viability cell and bacteria assays.

We have found an optimal method to create PAITC thin films, which are able to immobilize proteins, as human albumin, and shows a sensitive behavior by cells and bacteria.

Mucoadhesive camptothecin polymeric micelles as nanodelivery systems for oral chemotherapy to treat colorectal cancer

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Colorectal cancer (CRC) is among the cancers with highest prevalence and mortality worldwide. Conventional CRC chemotherapy is hindered by poor oral bioavailability, short duration of activity and difficulty to selectively target the tumor overcoming intestinal barriers. Our work proposes to address these inadequacies using nanotechnology to develop oral camptothecin-loaded mucoadhesive polymeric micelles for the treatment of CRC. We synthesized an amphiphilic graft copolymer through the grafting of oleic acid (OA) and methoxypolyethylene glycol (mPEG) in the chitosan (CS) backbone by a carbodiimide reaction. Also, mPEG was added to the system in the same way to improve its mucodiffusion when in contact with the mucus layer. The success of the reaction was confirmed by Fourier transform infrared spectroscopy (FTIR), hydrogen nuclear magnetic resonance analysis (\textsuperscript{1}H NMR), differential scanning calorimetry (DSC), gel permeation chromatography (GPC) and contact angle evaluation. mPEG-CS-OA micelles were produced by solvent evaporation method, and the critical micelle concentration was investigated by different techniques. The obtained micelles were of 305-nm mean particle size, narrow size distribution (polydispersity index of 0.373) and presented positive surface charge around 20 mV. The morphology of micelles assessed by transmission electron microscopy (TEM) revealed round and smooth surface, in agreement with dynamic light scattering measurements. The association efficiency was determined by high-performance liquid chromatography (HPLC) and these polymeric micelles will be tested in the near future in terms of toxicity, cell migration, cell cycle effect and apoptosis/necrosis quantification on colorectal cancer cell lines; penetration in intestinal cell monolayers and mucoadhesion on intestinal mucosa. Since CS is a natural polymer with mucoadhesive properties, we believe that developed polymeric micelles containing camptothecin will be useful in the future as a therapeutic strategy for CRC and other carcinomas.
Tree frogs use adhesive pads on each of their toes for adhering to smooth surfaces. In addition, each toe bears subarticular pads, proximal to the adhesive pads. However, their role in climbing has not been addressed so far. Here we investigated how tree frogs would utilise their adhesive pads and subarticular pads while climbing flat and cylindrical surfaces. In contrast to climbing flat surfaces, frogs increased the contact area on all limbs by engaging not just adhesive pads but also their subarticular tubercles on curved surfaces. Force measurements on individual pads showed that tubercles can withstand larger shear stresses than adhesive pads. SEM images of tubercles revealed a similar structure to adhesive pads including the presence of nano- pillars, though channels surrounding epithelial cells were less pronounced. The tubercles’ smaller size, proximal location on the toes and shallow cells make them probably less prone to buckling and thus ideal for gripping curved surfaces.
Cation – π interaction mediated mussel underwater adhesion

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Adhesive systems in many marine organisms are postulated to form complex coacervates (liquid–liquid phase separation) through a process involving oppositely charged polyelectrolytes. Despite this ubiquitous speculation, most well-characterized mussel adhesive proteins are cationic and polyphenolic, and the pursuit of the negatively charged proteins required for bulk complex coacervation formation internally remains elusive. In this presentation, a clue for unraveling this paradox by showing the bulky fluid/fluid separation of a single cationic recombinant mussel foot protein, rmfp-1, with no additional anionic proteins or artificial molecules, that is triggered by a strong cation–π interaction in natural seawater conditions, will be provided. With the similar condition of salt concentration at seawater level (>0.7 M), the electrostatic repulsion between positively charged residues of mfp-1 is screened significantly, whereas the strong cation–π interaction remains unaffected, which leads to the macroscopic phase separation (i.e., bulky coacervate formation). The single polyelectrolyte coacervate shows interesting mechanical properties including low friction, which facilitates the secretion process of the mussel. Our findings reveal that the cation–π interaction modulated by salt is a key mechanism in the mussel adhesion process, providing new insights into the basic understanding of wet adhesion, self-assembly processes, and biological phenomena that are mediated by strong short-range attractive forces in water.

Wood-based panels or composite wood panels are commodities used primarily in furniture manufacture and as materials for the construction and decorative improvement of buildings. Such products are produced by the application of adhesives, which bind the wood elements together to form the final panel products.

The adhesive resins and binders used for producing wood-based panels nowadays are synthesized from petroleum and natural gas derived chemicals. The increased concern about the environmental problems caused by petrochemicals, and the insecurity of the long-term availability of oil reserves, combined with the increases in oil prices have raised considerable interest in adhesives obtained from renewable bio-resources. The promising candidates should match the reactivity, applicability, bonding performance and cost requirements of the synthetic resins and outperform them in environmental acceptability and safety of use. Another challenge is the need to control and reduce the formaldehyde emission of panels to meet the requirements of regulations and end-use consumers.

CHIMAR team is a pioneer in research and development of bio-based adhesives and chemicals suitable for the industrial production of composite wood panels. Materials derived from the treatment and/or fractionation of renewable biomass resources, of biomass and lignocellulosic waste have been evaluated by CHIMAR and the corresponding bio-based adhesives have been assessed in the production of wood panels at lab, pilot and the most successful ones at the industrial scale, in each case in direct comparison with commercial adhesives.

The ultimate goal of this work is to provide evidence that sustainable binder alternatives can be used in making panels of commercial quality while at the same time maintaining the total cost of panel manufacturing at competitive levels.

Figure 1 illustrates reference and bio-based adhesive samples of phenol-formaldehyde (PF) type prepared at CHIMAR lab.

![Reference (left) and bio-based (right) PF resins. The latter was derived from partial replacement of the feedstock phenol with the liquid residue of biomass gasification process.](image)

The influence of surface free energy of the substrate on traction force by the seven-spotted ladybird beetles

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Some beetle species can walk freely on flat vertical surfaces such as smooth plant leaves. It is known that beetle adhesive setae are supplemented with a liquid secretion that is responsible for generating adhesion on various surfaces [1,2]. To understand the functional mechanisms behind the attachment systems of these beetles, we studied the effect of surface free energy of the substrate on the traction forces developed by the seven-spotted ladybird beetles *Coccinella septempunctata*(L.)(Fig.1 and 2).

The ladybird beetles were collected in Namiki-site of National Institute for Materials Science in Tsukuba city, Japan. The experiments were performed on four smooth substrates with different surface energies: (a)sodalime glass, (b)silicon wafer, (c)smooth polymerized low-viscosity epoxy resin plate, and (d)smooth polystyrene plate.

The experimental results showed that the forces developed by the beetles are proportional to the dispersion part of surface free energy of the substrates. Our findings show that the dispersion part of surface free energy plays significant role on attachment systems of the ladybird beetles *Coccinella septempunctata*(L.).

References

Fig.1 the ladybird beetles *Coccinella septempunctata*(L.)  
Fig.2 Diagram of the experiment for measuring the traction force generated by tethered walking beetles.
Many marine organisms have the capacity to quickly and tenaciously adhere to slimy and dirty surfaces of widely different types, and under harsh conditions. The challenges involved in designing an adhesive system with these capabilities are considerable, and we believe that there are many useful insights to draw from nature in this respect. However, the chemistry of the adhesive interactions of marine organisms with surfaces are largely unexplored, with only a few organisms studied from this perspective, and there is also reason to believe that adhesive mechanisms and strategies differ considerably between the large number of adhering marine species.

Molecular biology tools can provide insights into the involved adhesive organs and proteins, but even in cases where the genomes or protein structures are known, the information is incomplete, and insufficient for a full understanding of the adhesion mechanisms. Post-translational modifications are common but rarely charted; for large proteins, the domains involved in surface attachment are unknown. Proteinaceous adhesives typically set within seconds to minutes after secretion, but the chemical reactions occurring during attachment, and their dependence on surface properties or environmental parameters remain to be identified. Hence, there is a need for in-situ chemical studies of marine adhesion processes, in order to properly understand the adhesion mechanisms.

An important reason why this is an unexplored area – despite the vast economic and environmental consequences of marine biofouling – is the difficulties involved in chemical investigation of the adhesive interfaces. We demonstrate that infrared attenuated total reflectance (IR-ATR) imaging can be used to probe the chemical properties of such adhesive interfaces \textit{in situ}, using two common fouling organisms as model systems; the barnacle \textit{Balanus improvisus}, and the Zebra mussel (\textit{Dreissena polymorpha}). We also discuss how some limitations can be overcome with surface-enhanced Raman scattering methods.
Session 9: Bioadhesion prevention

Peptide Self-Assembly into Functional Coatings

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Changing the chemical and physical properties of a surface is important for many fields. This includes the design of new medical devices, antifouling materials and smart surfaces. Surface chemistry and topography determine the interactions of biomolecules with an implant and therefore govern its fate in the body. It also controls the interactions of surfaces with other biological entities such as bacteria and cells that lead to the undesirable process of biofouling.

This lecture will present a new platform for the formation of functional coatings. The coating is based on simple peptides that self-assemble into a layer on various surfaces. The functionality of the coating is controlled by the sequence of amino acids of the peptide. This peptide-based coating can resist biofilm formation and direct cell attachment. It could be useful in hospitals to prevent health-associated infections, in water desalination facilities to arrest membrane blockage by biofouling and in the design of implants.
Relations between biofilm viscoelasticity and membrane biofouling: A case study of cellulose in the extracellular polymeric matrix

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Biological fouling, mainly bacterial originated, can be an acute problem in the operation of membrane based processes for water treatment, even when the water inlet contains low levels of nutrients. Microbial growth on the membrane surface has destructive influences, including a decrease in the permeate water flux, its quality and an increase in frequency of the membrane cleaning. This project aims to investigate in a controlled manner, if changes in the extracellular polymeric matrix (EPS) compartments will influence the biofilm-membrane relationship that is in charge for changes in membrane permeability and selectivity. A model component that was chosen to be investigated in the EPS matrix of the marine bacterium, Vibrio fischeri, is cellulose. We examine the effects of cellulose, contained in the EPS, on its coherence and viscoelastic properties. Also, we show how the extent of cellulose in the EPS influences reverse osmosis (RO) membranes performance, as a consequent reduction in permeate flux during the desalination process in a laboratory scale. We claim that there is a relation between the mechanical strength and elasticity that cellulose provides to the extracellular matrix and the decrease in membrane performance.

Three different strains of the marine bacterium V. fischeri were used: a wild type, and two isogenic strains, up- and down-regulating cellulose production and secretion. For that purpose, EPS was extracted from biofilm strains that were grown on polyamide surface, mimicking RO membrane. The extracted EPS was exploited to test its viscoelastic properties as well as to investigate the fouling extent of the three types of EPS on the RO membrane during the desalination process. EPS adherence and viscoelastic properties were evaluated in a quartz crystal microbalance with dissipation (QCM-D) monitoring technology. Complementing the QCM-D analysis, a positive correlation was found between cellulose expression and Young’s modulus of the biofilms using atomic force microscope (AFM). Observations of EPS species adherence to polyamide surfaces, mimicking RO membranes, denied the influence of cellulose on EPS deposition, however, QCM-D and AFM analyses have shown that with increase of cellulose content, a rising trend of the matrix rigidity was observed. These bacterial strains, altered in cellulose expression also showed interesting changes in biofouling of RO membranes during desalination process. Higher amount of cellulose has shown to reduce permeate flux attributed to increase in the biofilm matrix rigidity, which consequently, acquire the biofouling layer with higher resistance to shear stress providing thicker biofilm with higher hydraulic resistance. To our knowledge, this is one of the first reports in which, elastic properties of biofouling layers are shown to directly affect membrane performance.
Hybrid membrane bioreactor- powdered activated carbon (MBR-PAC) process for wastewater treatment

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The goal of this study was to evaluate performance of a membrane bioreactor (MBR), using powdered activated carbon (PAC) suspended in the mixed liquor suspended solids (MLSS) which entails adsorption-desorption-biodegradation processes. This MBR-PAC hybrid process provides a synergistic behavior as a solution for membrane biofouling in the MBR: The adsorption-desorption-biodegradation characteristics of the MBR-PAC reactor improve the stability of acclimated microbial community for biodegradation of recalcitrant organic compounds that can also acquire strong membrane fouling capabilities. The main hypotheses were that the MBR-PAC process would provide the MBR with higher microbial activity, stronger capacity to cope with certain shock loads of organic pollutants, and an alternative media for adsorption of organic foulants to the membrane surface, and as such, the presence of PAC may sequester organic fouling.

Two pilot-scale reactors were operated, one reactor was supplemented with suspended PAC and one was operated under similar conditions, without PAC. The feed to the reactors was comprised of synthetic-, domestic-, and olive oil mill-wastewater. The MBR operational parameters were registered daily, along with biological oxygen demand (BOD) and dissolved organic carbon (DOC) analyses that were measured weekly. The affinity of the main MBR components - the soluble microbial products (SMP) and extracellular polymeric substances (EPS) extracted from the MLSS - for a surface simulating ultrafiltration (UF) membrane (polyether sulfone (PES)) was determined using a quartz crystal microbalance with dissipation monitoring (QCM-D). Also, autopsies of the membranes were conducted at the end of the MBR operation.

The working hypothesis that supplementing the MBR with PAC would improve performance due to adsorption of certain foulants followed by their continuous desorption and biodegradation, was contradicted by the results of this study. Permeate flux and membrane permeability decreased faster in the MBR supplemented with PAC compared to the control reactor. Interestingly, the SMP and EPS originating from the PAC supplemented reactor were found to be more adhesive to the QCM-D sensor coated with PES. Notably, the SMP fraction, originated from the PAC reactor, which was collected towards the end of the reactor's operation, was found to have higher affinity to the PES-coated sensor mimicking the membrane surface. The autopsies results showed that the EPS from the biofilm on the membrane surface from the PAC reactor, had a bigger amount of polysaccharides, DOC and proteins compared to the control reactor. Furthermore, batch filtration of SMP solutions originating from the two MBRs through disks of UF membranes, corroborated the finding of reduced performance of the PAC supplemented MBR: a higher decline in membrane permeability was observed for the SMP of the PAC supplemented system. According to these effects of PAC on membrane fouling as well as affinity of the SMP fraction to a membrane mimetic surface, it seems that the addition of PAC to the MBR alters the distribution and type of organic compounds in the reactor. This effect of the PAC will be studied in the future and the reasons for the consequent reduction in membrane performance will be delineated. Probably, the activated carbon selects for certain refractory adsorbents, which remain in the aqueous phase and more significantly adsorb to the membrane and enhance fouling.
Figure 1. Adherence properties of SMP, extracted from the MBR, after runs with and w/o PAC provided as frequency shifts during SMP adhesion to PES coated QCM-D sensors. A background solution with ionic strength of 20 mM (17 mM NaCl + 1 mM CaCl2) was supplemented with SMP from MBR at 20 mg DOC/l was injected to an E4 QCM-D parallel flow cells (Q-Sense, SWEDEN) at a flow rate of 100 μl/min.
Biological adhesives produced by animals and plants are non-toxic, tissue compatible, and are able to function under wet conditions. However, little is known about the mechanisms underlying biological adhesives. We have characterized adhesion and release in our model system *Macrostomum lignano*. *M. lignano* is able to rapidly attach and detach from surfaces by means of a duo-gland adhesive system. First, we explored in detail the morphology of the duo-gland system which consists of an adhesive- and a releasing gland cell, and a modified epidermal cell, the ancho cell. Next; we used differential transcriptomes, in situ hybridization screening, RNA interference, combined with Mass Spectrometry, and Superresolution Microscopy to narrow down the number of adhesion- and release related genes to a handful of candidates. We now have identified two key adhesive proteins which result in a non-adhesive phenotype upon RNAi knock-down. We performed attachment assays and tested different molecules and surfaces regarding their interference with attachment and release. Negatively-charged molecules inhibited flatworm attachment, while positively-charged molecules impeded detachment. In addition, we found that *M. lignano* could not adhere to strongly hydrophilic surfaces. These results are incorporated into a model for temporary adhesion of *M. lignano*. We are currently expanding the characterization of adhesives to other flatworm taxa. We aim for understanding the fundamental mechanisms that mediate adhesion and release in flatworms.

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Probing the permanent adhesion of barnacle cypris larvae

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The permanent adhesion of larvae to surfaces is a pivotal point in the barnacle life cycle, as the free-swimming organism commits to a sessile existence. So, while mechanisms of surface selection and settlement by barnacles are of ecological interest, they are also a target for more applied research. In the context of marine biofouling, a multi-billion-dollar industry, cyprids (the settling larvae) are of particular interest as the colonizing stage of barnacle communities.

Larval settlement is arguably the most logical point of intervention for fouling control strategies, although development of coatings that can resist barnacle adhesion clearly requires far better knowledge of the cyprid adhesion mechanism than is currently the case. It is also possible that the adhesion systems of adult and larval barnacles are related, although evidence for this remains circumstantial. If this relatedness exists, the adhesion of larvae may represent a more straightforward experimental system for compositional analysis of the adult glue, since in larvae a discrete and highly localized deposit is released externally. In the adult form, the adhesion process occurs progressively during the growth cycle and involves the sequential secretion of numerous components between the basis of the animal and the surface.

For a combination of these reasons, understanding cyprid adhesion remains a focus for our antifouling research. Recent data suggest that both lipids and carbohydrates, as well as proteins, may be important in the adhesion process and have received little research attention to date. If these are functional components, then the implications for hypothesis-driven development of non-fouling coatings could be significant. This talk will discuss the dynamics of cyprid attachment to surfaces and the composition of the secreted material, including advances in our understanding of the complex morphology on the surface.
The salivary glue secretion (Sgs) produced by mature larvae of the fruitfly, *Drosophila melanogaster*, is a mixture of 8 unique proteins which, when solidify, serves to affix the freshly formed puparia to a substrate (e.g. glass wall in a culture vial) in an upright position. Salivary glands (SGs) produce a large amount of the mucinous glue-containing secretory granules which display a strong periodic acid-Schiff (PAS) positive reaction. Under transmission electron microscope, the Sgs proteins synthesized inside the SG cells tend to form Golgi-derived electron-dense secretory vesicles that then fuse into larger granules. Various authors have studied secretory granules in *D. melanogaster* and some other species and have described several different infrastructural elements within the granules. Towards the end of the last larval instar, the steroid hormone ecdysone is released into circulation and induces a complex response that leads to the initiation of metamorphosis. In the SGs, this is accompanied by a series of polytene chromosome puffs that reflect a cascade of transcriptional regulation, and the secretion of the glue by exocytosis. These 8 unique *Drosophila* proteins, varying between 7 and 140 kDa in size, are encoded by the genes named *Sgs*-1, *Sgs*-3, *Sgs*-4, *Sgs*-5, *Sgs*-5bis, *Sgs*-7, *Sgs*-8, and *Eig71Ee*. Although strong glycosylation was expected in most of the Sgs proteins even before their amino-acid sequence was known, only Sgs-3 initially showed motifs that conclusively supported the contention that it is heavily O-glycosylated. Later, detailed sequence analysis of Sgs-4 and Sgs-1 supported the view that they too are O-glycosylated (Furia *et al.*, 1992; Roth *et al.*, 1999). The Sgs-5 appears to have just single N-glycosylation and a single O-glycosylation sites, and the both Sgs-7 and Sgs-8 are not glycosylated at all. At the time of maximum synthesis, these Sgs proteins comprise for 25-30% of the total protein content of the salivary glands, with each salivary gland cell containing 2500-3000 individual secretory granules ranging from 0.2 to 2.5 or even 3.0 μm in diameter. Here we will present data on further physico-chemical properties of individual Sgs glue proteins, and will indicate how these properties can affect function of these proteins and the glue as a whole.

In addition, for the first time here we provides an evidence that in contrast to previous expectations, into lumen exocytozed Sgs-glue has micellar fibrous-like spongy character that allows its fast hydration prior to expectoration. After Sgs-glue is released and solidified, its surface have uniformly smooth appearance, however its internal composition beneath this surface is rather structured and complex showing multilayered infrastructure resembling trabecular network. More interestingly, the released glue has ability to trap and immobilize various microorganisms including bacteria and yeasts, thus providing puparia the first line of defense against microbial invasion.
Tick attachment cement – first characterization of a potential tissue glue

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Ticks, that are known to pierce through vertebrate skin for blood uptake, often do not only rely on their mouthparts for anchoring, but additionally produce a sticky secretion called cement [1]. Due to its potential to bond to humid and even wet tissue and its suggested biocompatibility, the material is of interest for medical glue research, intending to replace toxic ones and to enable new fields of application.

In the current study we investigated the attachment cement of the ixodid species *Dermacentor marginatus*, harvested from artificial feeding units (Figure 1) and analyzed by morphological, physical, and bioanalytical methods as well as cell biological assays. Morphological methods included high-resolution stereo microscopy, various histochemical stainings, lectin and immunohistochemical reactions and electron microscopy. Amino acid quantification by GC-EI-MS/MS (gas chromatography electron ionization tandem mass spectrometry) and protein identification by 1D electrophoresis and LC-ESI-MS/MS (liquid chromatography electrospray ionization tandem mass spectrometry) were performed. Pull-off tests using a surface force apparatus revealed the adhesiveness and physiological viability assays the cytocompatibility.

The cement firmly adhered to the silicone membrane of the feeding unit, forming a compact, slightly elastic mass. Macroscopic analysis showed a ring-like deposition on the upper side and a droplet-like secretory material on the down side of the membrane. Histochemistry indicated lipids (Oil Red), proteins (Biebrich Scarlet) and a certain amount of carbohydrates (PAS) distributed in a particular pattern in the cement droplets. Negative staining for catecholes (Arnow staining) revealed that the cement is based on a DOPA-independent mechanism. Amino acid quantification confirmed the absence of DOPA, and found glycine as the most abundant amino acid followed by leucine and serine. Protein analysis gave hints for proteins also found in other adhesive species (terrestrial and marine). Cell culture assays showed good cytocompatibility without any adverse effect on the cells.

The current findings indicate that the cement is a feasible candidate for a biomimetic glue template to develop a tissue adhesive with new bonding mechanisms, good biocompatibility and satisfactory adhesive strength.

Fig 1. Male *Dermacentor marginatus* adhering to a piece of artificial silicone membrane of the *in vitro* feeding unit. The tick is piercing through the membrane with its mouth parts and secreting adhesive cement material on the upper and lower side of the membrane.

A 3D numerical model for membrane delamination

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Biological attachment structures are usually studied using single or multiple peeling models, which involve one-dimensional tapes or contacts [1]. This approach is oversimplified for many practical problems, since the adhesive behaviour of a large number of complex two-dimensional structures (e.g. spider web anchorages) is still poorly explained. Here, we develop a model to simulate the detachment of a membrane attached to a surface. To do so, we use a 3D numerical model based on two-dimensional contacts coupled with the substrate using a 3D coupled cohesive law [2]. Our goal is to better understand the mechanical behaviour of the biological adhesives with complex geometries or material anisotropies by analyzing the interaction between the stress distributions at the interface and in the membrane itself. Results show how parameters can be adjusted to optimize or tune the pull-off force for different loading scenarios, highlighting the relationship between the pull-off force and the length of the delamination front.

Fig1. 3D plot of a discretized adhesive elastic membrane represented while delamination is occurring.

The expansion of genes encoding silk adhesives in the greater wax moth, *Galleria mellonella*

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Lepidopteran silk represents a heterogeneous family of structural proteins produced by altered larval labial glands called silk glands. Information on the molecular structure of silk proteins is limited to a handful of species. We found that *G. mellonella* silk has a higher proportion of soluble proteins than that of *B. mori* or *A. yamamai*. In order to detect all major components in the silk of *G. mellonella*, we used silk gland transcriptome sequencing and identified 27 candidate cDNAs encoding putative secretory proteins that may represent novel silk components. Eight of these candidates were confirmed by proteomic analysis or by N-terminal Edman sequencing. The association of several other candidates with silk was supported by sequence similarity with known silk proteins and northern blotting. Our results show that *G. mellonella* adhesive sericins form the largest subfamily among silk proteins. The pattern of branching in a sericin phylogenetic tree is in agreement with the birth-and-death model of evolution. We also found that *G. mellonella* silk glands produce seroins, mucins, protease inhibitors, imaginal disc growth factor and several abundant but unknown low molecular weight proteins. Profound changes in the number of soluble silk components and their remarkable divergence reflects fast adaptation of these insects to different environments.

![Fig1. Scanning microscopy of the outer side of *G. mellonella* cocoon, scale 10 µm](image)

Electropolymerization of biomimetic polydopamine films for biosensing applications

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Polydopamine films have been extensively explored to mimic the bioadhesive properties of mussels to wet surfaces [1, 2]. Oxygen-driven polymerization in slight basic solutions, has been the common method to coat a wide range of surfaces with these biomimetic polymeric films. Indeed, polydopamine coatings have been employed pursuing many different purposes, namely self-healing [3], antifouling [4] and (bio)sensing applications [5]. The immobilization of biomolecules, through their amine groups, is expected to occur at the reactive quinone moieties by Michael addition or Schiff-base reactions [6]. Nevertheless, it is commonly accepted that chemical growth of these type of polymeric films yields heterogeneous and poorly conducting matrices. A range of chemical oxidants have been explored to rational tailor the overall quality of dopamine films [4]. Herewith we propose an alternative electrochemical approach to prepare reproducible and functional hybrid polydopamine/enzyme films.

In this work, a one-step electrode bio-functionalization through the potentiostatic polymerization of dopamine in the presence of the enzyme Laccase is presented. The morphology, optical and electrochemical properties of polydopamine/Laccase modified carbon electrodes were accessed by atomic force microscopy, ellipsometry and cyclic voltammetry. The catalytic activity of modified surfaces was evaluated by chronoamperometry and optimized for 2,2’-azino-bis-(3-ethylbenothiazoline-6-sulphonic acid) (ABTS) detection, a well-known substrate of Laccase. The effective one-pot procedure proposed in this work is successfully investigated in the detection of phenolic compounds (e.g. caffeic acid, rosmarinic and gallic acid). There is a clear improvement of the analytical parameters achieved for the one-step modified electrodes regarding those prepared in two steps: immobilization of Laccase on chemically or electrochemically pre-synthesized polydopamine films, highlighting the prospective applicability of these interfaces in biosensors.

Characterization of the temporary adhesive of the sea urchin *Paracentrotus lividus* by Atomic Force Microscopy

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Biological adhesives commonly present complex hierarchical structures from the micrometric to the nanometric scale, in contrast to synthetic adhesives. Within marine adhesives, interest has been mostly focused on permanent ones whereas non-permanent adhesives have been comparatively less studied. To our knowledge, the nanostructure of temporary adhesives has been investigated in marine flatworms, barnacle cyprids, freshwater cnidaria and echinoderms such as sea cucumbers and sea stars [1, for review]. In this work, Atomic Force Microscopy (AFM) was used to perform a nanoscale characterization of sea urchin temporary adhesives. Our results reveal a similar topography for the adhesive imaged under dry and native conditions (seawater) being characterized by a honeycomb like meshwork of threads made of globular nanostructures. Higher adhesion forces up to 50 nN were obtained under dry conditions, whereas in seawater adhesive forces up to 500 pN were recorded. Under native conditions sawtooth force–extension curves were observed suggesting the presence of a functional amyloid, as also supported by a positive Thioflavin-T labelling. These results indicate that sea urchin temporary adhesives most likely contain proteins with amyloid quaternary structures or rich in beta-sheets, probably contributing to increased cohesiveness. This work thus extends our knowledge on sea urchin adhesive composition and mechanical properties essential for the engineering of biomimetic adhesives.

Fig1. Adhesive material deposited by the tube feet of *Paracentrotus lividus*: a) AFM image observed in air; b) histological staining with Thioflavin-T; and c) force-distance retracting curve obtained in seawater. Adapted from [2].

The aim of this study was to investigate the effect of acrylate modification on the mucoadhesion of chitosan at the nanoscale. Nanoparticles were fabricated from acrylated chitosan (ACS) via ionic gelation with tripolyphosphate and were characterized in terms of size, zeta potential, stability, and nanoparticle yield. Chitosan (CS) nanoparticles, serving as a control, were fabricated using the same procedure. The mucoadhesion of the nanoparticles was evaluated using the flow-through method after different incubation periods. The retention percentages of ACS nanoparticles were found to be significantly higher than those of CS nanoparticles, for all studied time intervals. An additional indication for the higher mucoadhesion of ACS nanoparticles was obtained from the mucin particle method, in which mucin and nanoparticles are mixed at different ratios, and an increase in particle size was detected. NMR data verified the presence of free acrylate groups on the ACS nanoparticles. Thus, the improved mucoadhesion could be due to a Michael-type addition reaction between the nanoparticles and thiol groups present in mucin glycoprotein, in addition to entanglements and hydrogen bonding. Overall, ACS nanoparticles exhibit enhanced mucoadhesion properties as compared to CS nanoparticles and could be used as vehicles for drug delivery systems to provide improved drug absorption and bioavailability.

Evaluation of mucoadhesive polymeric nanoparticles as a delivery system for cherry extracts polyphenols

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This study aims at evaluating the efficacy of nanoparticles (NPs) as vehicles for the oral administration of antioxidants present in Tuscan cherry extracts (CE). Previous studies reported NPs aptitude for internalization by endothelial cells as well as improvement of entrapped polyphenols antioxidant activity. The total phenolic content (TPC) and the antioxidant capacity of CE were measured. CE-loaded NPs based on two different chitosan (Ch) derivatives, i.e., quaternary ammonium-Ch (QA-Ch) and S-protected thiolated QA-Ch conjugates, were prepared by ionotropic gelation with hyaluronan. The NPs size is not significantly different for the two formulations (300 nm range) and the CE entrapment efficiency in NPs is always around 70% with no difference between the two NPs type. Human Umbilical Vein Endothelial Cells (HUVECs) viability was evaluated by WST-1 assay and reactive oxygen species (ROS) production was detected after H2O2-induced oxidative stress. Free CE polyphenols treatments showed a reduction in oxidative stress and ROS production. In vitro permeation studies were performed in Ussing-type chambers with excised rat jejunum as substrate. A permeation enhancement ratio of 1.5 was found with either NPs type. The results of the present study demonstrate the CE ability to protect the endothelial cells from oxidative stress. Moreover, CE loaded-NPs enhance CE absorption also thanks to their ability to protect CE degradation in the GI.

Mucoadhesive alginate pastes with embedded liposomes for local oral drug delivery

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Oral cancers are extremely common among adults with increasing incidences due to human papillomavirus, while treatment modalities are limited. This study aims to develop a new oral mucoadhesive delivery system based on the combination of alginate and liposomes (Fig. 1). The polymer provides adhesion properties and induces local release of the drug-loaded carriers, while the liposomes protect the drug from degradation and improve its absorption into the cells. Three hybrid alginate/liposomes delivery systems were investigated: a hybrid paste, which presented excellent adhesive capabilities, yet fast burst release of 90% after 2 h; a hybrid hydrogel, demonstrating controllable release rates of 5%, 30% or 60% after 2 h but poor mucoadhesive properties. These findings led to the development of a hybrid cross-linked paste. Polymer retention studies demonstrated that 80% of the crosslinked paste was retained on tongue tissue compared to 50% retention of the non-cross-linked pastes, verifying its superior mucoadhesion. The hybrid cross-linked paste presented controllable release rate of 20% after 2 h. Alginate paste incorporating doxorubicin loaded liposomes presented similar release rates and were highly effective in promoting cancer cell death. Thus, our innovative formulation, including both desired characteristics of mucoadhesion and sustained liposomes release, is an important milestone in the development of a new potential treatment for oral cancer. [1]

Fig1. mucoadhesive delivery system based on the combination of alginate and liposomes.
Development of lipid based liposomes for adhesive patches

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Introduction Targeted drug delivery systems are used to minimize the adverse effects of the pharmaceutical agents while maintaining the high local drug concentrations. One of drug delivery system forms is liposomes – lipid based spherical particles [1]. Vancomycin hydrochloride (VANKA) is used in the treatment of inflammations and bacterial infections and in this study was used as a model drug. Plasma has all the essential characteristics to be an excellent support biomaterial – to interface with biological systems for the purpose of treating or replacing any type of tissue or organ. Fibrin sealants fabricated from human plasma are effective tissue adhesives that are biocompatible and biodegradable [2].

Materials and Methods The liposomes were synthesized using a thin film hydration method and 3 dehydration-rehydration (d-r) cycles. The liposome double-layer structure consists of 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) and cholesterol in molar ratio 2 : 1. The dry lipid film was hydrated with water or VANKA solution (c=250 μg/mL). The distribution of liposome sizes by d-r cycles was determined by laser diffraction granulometry method. To obtain the plasma, blood was centrifuged for 10 minutes at 3000 rpm (Compact Star CS 4). For preparation of the fibrin sealant composites antifibrinolytic agent tranexamic acid (Amchafibrin 500mg/5ml; Rottapharm) was dissolved in the human plasma, calcium gluconate (Calcium Sopharma 8,94mg/ml; Sopharma) and liposomes were added afterwards. Release of VANKA was determined in the phosphate saline buffer with UPLC.

Results Obtained liposomes are round, regardless of d-r cycles, but they tend to agglomerate by reducing free energy and taking a thermodynamically more stable condition see Figure 1. The size distribution of all obtained liposome compositions has a positive asymmetry and the modal interval is 0.01 – 0.5 μm and the d-r cycles result in an increase in small size liposomes due to the osmotic pressure on the liposome double layer. After lyophilization liposomes stick and fuse together due to static charges and separation of cholesterol molecules [3, 4]. The release of VANKA from liposomes in fibrin sealant composites showed burst release in the first 2 – 4 h followed by sustained release of VANKA.
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Adhesion of self-adhesive resin cements

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Objective: The aim of the present study was to evaluate the retentive strength of two self-adhesive resin cements used for the cementation of fiber posts into root canals.

Materials-Methods: Twenty extracted non-carious human maxillary central incisors, with fully developed apices extracted for periodontal reason were used for this study. After endodontic treatment, glass fiber posts were cemented with two types of self-adhesive resin cements (RelyX U200, 3M ESPE, and Maxcem Elite, Kerr). Four until six sections of 1 mm were cut perpendicular on the post from each specimen using a diamond saw starting 1 mm coronal from the tip of the post. Post sections were tested on push out bond strength using universal testing machine. Mean values of push-out bond strength for each group and root region (cervical, middle and apical) were calculated. Data were statistically analyzed with one-way ANOVA and Tukey’s test (p<0.05). Failure modes were evaluated using optical microscopy and scanning electron microscopy.

Results: Without being statistically significant, the bond strength of RelyX was higher (8.23±4.46 MPa) when compared to that of Maxcem Elite (6.52±3.68 MPa). Significant differences (p<0.05) were observed between the apical and cervical regions. More frequent (>60%) adhesive failures at the resin cement-dentine interface were observed

Conclusions: The mean push-out bond strength of teeth samples containing RelyX U200 was higher than that observed for Maxcem Elite. Increases in cement thickness in the cervical third may account for the lower push-out bond strength values obtained in comparison to the middle and apical thirds in both groups.

Keywords: PUSH-OUT BOND, SELF-ADHESIVE RESIN CEMENTS, adhesives
Acrylated Chitosan for mucoadhesive drug delivery systems

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The interest in mucoadhesive delivery of drugs constantly increases due to potential benefits over other delivery methods such as lower administration frequency, high epithelial permeability for many drugs and avoidance of some enzymatic degradation as a result of contact with the absorbing mucosa.

A new mucoadhesive polymer was synthesized by conjugating chitosan to poly(ethylene glycol)diacrylate (PEGDA) via the Michael type reaction. The product was characterized using NMR. Higher PEGDA grafting efficacy was observed with low molecular weight PEGDA (0.7 kDa), compared to long 10 kDa PEGDA. The acrylation percentage was calculated based on the reaction of ninhydrin with chitosan, and supported the qualitative NMR findings. The adhesive properties were studied by tensile test and rotating system involving detachment of polymer tablets from a fresh intestine sample. Chitosan modified with high molecular weight PEGDA presented improvement in mucoadhesive properties compared to both non-modified and thiolated chitosan. On the molecular level, rheology measurements of polymer/mucin mixtures provided additional evidence of strong interaction between modified chitosan and mucin glycoproteins. This new polymer shows promise as a useful polymeric carrier matrix for delivery systems, which could provide prolonged residence time of the vehicle on the mucosal surface. [1]

Figure 1 describes the preparation of Chitosan-PEGAc and the adhesion test between polymer tablet and small intestine sample. [1]

Biofilm is an accumulation of microbes on surfaces. The first step of biofilm formation involves bacterial cells adhesion to the surface and is critical for their survival under changing environments. The mechanism of attachment is mediated by extracellular organelles: flagella and pili. Due to its size, the investigation of flagella involvements in the attachment to the substrate is more clear compared to pili. Here, we present the adhesion of organelles of single bacterial cell to different surfaces. To study the various interactions involved in the process we used functionalized self-assembled monolayers coatings. Using atomic force microscopy (AFM) we obtained high resolution images, consisting of data that can be interpreted to provide information on elasticity and adhesion of bacterial cell to the surface.

Fig 1. AFM adhesion, stiffness and height image of *E. coli* bacteria cell on -CH₃ functionalized surface.
Bioadhesion in the Ascidian *Ciona intestinalis* specially the adhesive secreting collocytes

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Marine bioadhesion research has increasingly inspired the design of biomimetics for tissue compatible glues in the medical field and antifouling compounds for shipping and aquaculture. Tunicates (ascidians) are not only important, because of their phylogenetic position, being the sister group to vertebrates, but also ecologically they are one of the major biofoulers massively populating artificial surfaces like ship hulls causing serious damage. In recent years, it therefore became of great interest to understand how bio-adhesion is functioning in ascidians.

In our lab, we use the ascidian *Ciona intestinalis* as model organism to study the adhesive properties of their larvae. Recent research demonstrated that larval adhesion organs (papillae) of *Ciona intestinalis* mainly consist of glue secreting collocytes, papillary neurons and supporting cells. However, the exact secretion mechanism, and the involved molecules are still not fully described. Recently, we performed serial-section electron microscopy and confocal imaging of the *Ciona* papillae with various marker combinations to document each cell type and numbers precisely, their subcellular and molecular characteristics [1]. Furthermore, we successfully established CRISPR/Cas9 towards loss of function analyses of papillae morphogenesis genes. Finally, we plan to biochemically analyses (Protein pulldown, Mass-spectrometry) candidate adhesion proteins in parallel to their functional analysis.

![Fig1. Scheme of the papillar cell types and their discriminating markers of *Ciona intestinalis.*](image)

Adhesion of sea cucumber Cuvierian tubules: Identification and characterization of adhesive proteins

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Cuvierian tubules form a specialized defense system occurring in some species of sea cucumbers. Indeed these long sticky tubules are able to entangle potential predators in a matter of seconds [1]. As it is the case for other bioadhesion systems, their adhesive consists mostly of proteins. Cuvierian tubules, however, stand apart because of their instantaneous adhesion without the necessity for curing [2]. We identified the proteins present in the glue from the Cuvierian tubules of *Holothuria forskali* by mass spectrometry combined to transcriptomic analyses. This first approach allowed the establishment of a list of 105 protein candidates. As glue samples are contaminated by connective tissue remnants, some of these proteins may not be involved in adhesion. We therefore also extracted proteins directly from the granular cells, the Cuvierian tubule adhesive cells, and identified them using the same combination of proteomic and transcriptomic analyses. The list of 51 major proteins from granular cells was then compared to the list of proteins present in the glue, yielding a short list of 34 adhesive proteins and/or precursors. The mRNAs encoding for these adhesive protein candidates were then localized by in situ hybridization on Cuvierian tubules transverse and longitudinal sections. One putative adhesive protein was also selected for the production of anti-peptide antibodies. Immunohistochemical labelling was observed at the level of the granules from granular cells as well as in the tubule print material, confirming the involvement of this protein in the instantaneous adhesion of the tubules. The sequence of this first identified adhesive protein from the Cuvierian tubules of *H. forskali* comprises 115 amino acids but is still incomplete. This partial sequence contains 4 EGF-like domains that might be implicated in protein-protein interactions within the adhesive material.

Localization and characterization of *Asterias rubens* adhesive proteins

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Adhesive secretions are used by a large diversity of marine invertebrates, in which four types of adhesion (permanent, temporary, transitory and instantaneous) are usually recognized. Over the last 30 years, individual marine adhesives have been investigated extensively, notably the permanent adhesive of mussels. Indeed, they provide an interesting design paradigm for engineering biomimetic glues with potential applications in biomedicine. The adhesive of sea stars, although it represents an interesting model for temporary adhesion, has been less studied. Sea stars use their adhesive secretions to attach strongly to the substratum and to pry open the mussels on which they feed. Their secretory organs are the tube feet or podia, in which two types of adhesive cells co-secrete a blend of adhesive proteins to form the adhesive layer joining the tube foot to the substratum [1]. This layer is left on the surface as a footprint after detachment and is composed of a structural meshwork deposited on a thin homogenous film. To date, only one adhesive protein, the sea star footprint protein 1 (Sfp1) has been characterized in asteroids. This protein is translated from a single mRNA and then cleaved into four subunits displaying specific protein, carbohydrate and metal-binding domains. It was localized in the tube foot adhesive epidermis and more specifically in only one type of adhesive cells [2]. After secretion, it can be found at the level of the fibrillar meshwork of footprint where it forms the structural core of the adhesive material.

Recently, a tube foot transcriptome and a footprint proteome were combined, which allowed to obtain the sequences of all footprint specific proteins in the species *Asterias rubens*. A list of 34 putative Sfps was retrieved in this way [3]. However, they are presumably not all involved in adhesion. The aim of this study is therefore to further characterize these different proteins. First, the transcripts coding for the Sfps were analysed in silico. Then, their expression site in the tube foot has been localized by in situ hybridization (ISH), an expression in the adhesive epidermis being indicative of a function in temporary adhesion. Double ISH experiments have also been conducted in order to map the Sfps to adhesive cell type 1 or 2. Based on these results, a few candidate proteins will be selected for the production of polyclonal antibodies. Using immunohisto- and immunocytochemistry, will be used to confirm the ISH results but also to locate the Sfps in the footprints (in the meshwork vs in the homogenous film). All of these results will provide an overview of the role of Sfps in sea star temporary adhesion.


Evolution of temporary adhesive proteins in sea stars

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Sea stars are able to quickly and repeatedly attach and detach themselves with their hydraulic tube feet. Long thought to be 'suckers', the tube feet indeed contain a duo-gland adhesive system, where adhesive glands secrete the proteinaceous glue and a different gland type produces a de-adhesive substance. Upon voluntary detachment the adhesive material stays attached to the substrate as a footprint, consisting of a structural meshwork on a thin homogenous film. In recent years, the structural characteristics and adhesive composition have been investigated in the forcipulatid species Asterias rubens. Transcriptomic and proteomic analyses revealed the presence of 34 proteins within the footprints of this species [1]. To date, one large (3853 aa) adhesive protein, the sea star footprint protein 1 (Sfp1), has been characterized and was localized in the meshwork of the footprints [2].

Among sea stars, the adhesive proteins have been solely investigated in the species A. rubens. Yet, polyclonal antibodies raised against footprint material of A. rubens led to a strong immunolabelling within the adhesive epidermis of thirteen other asteroid species, indicating conserved components [3]. A BLAST search with the protein sequence of A. rubens Spf1 in publically available sea star transcriptomes revealed a high conservation of this large protein throughout the Asteroidea phylogeny. These results were further confirmed with Sfp1 antibody staining on tube foot sections of various species.

While the research in A. rubens is ongoing, we further started to investigate temporary adhesion in the distantly related valvatid species Asterina gibbosa. The most recent molecular phylogeny of the Class Asteroidea supports a tree in which two main groups apparently diverged early in the evolution of sea stars [4]. According to this phylogeny, A. gibbosa and A. rubens could be considered as distantly-related species as they each belong to one of these two main sea star clades. In A. gibbosa a de novo tube foot-specific transcriptome was made and is currently used to identify adhesive and de-adhesive proteins. The species A. gibbosa was chosen due to its availability, small size, and uncomplicated and fast development under laboratory conditions. These features may allow functional testing of potential adhesive- and de-adhesive genes using RNA interference.

Extending the research on sea star temporary adhesion from A. rubens to more species, will help to identify conserved motifs and properties of the reversible adhesive and might facilitate the development of biomimetic, reversible glues.


**P16**

**Recombinant expression of barnacle cement proteins**

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The adhesive proteins of barnacle cement have huge potential as environmentally friendly adhesives due to their ability to adhere to a variety of substrates in aqueous environments. Of the four characterised barnacle cement proteins, cp19k has been shown to be one of the stickiest. The cp19k gene from *Pollicipes pollicipes* fused with a leader sequence for export to the periplasm and a hexahistidine tag for detection and purification was cloned into an *Escherichia coli* expression vector. Initial expression in *E. coli* BL21 resulted in low levels of insoluble protein. Co-expression of GroEL-GroES chaperones yielded a protein of expected molecular weight resulting in a total extract yield of 1 mg/L of *E. coli* culture. The adhesive properties of the protein were characterised by surface-coat analysis and by Surface Plasmon Resonance. Understanding the mechanisms behind adhesion in aqueous environments will further aid the development of the next generation of surgical sealants and adhesives.
3D Printing of Complementary Pre-Polymers for Oral Delivery

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Current 3D printing techniques of tablets involve destructive UV irradiation or high temperature that limit the use of sensitive drugs. Here, we describe a novel 3D printing technique based on two complementary liquid copolymers that are injected in a coordinate fashion to form a cross-linked 3D tablets. The successful synthesis of the pre-polymers were verified by ¹H-NMR and gel permeation chromatography (GPC). Tablets swelled about 400% over 3 hours followed by a moderate disintegration. In-vitro cytotoxicity studied on 3T3 fibroblast cells demonstrated the safety of the tablets for oral administration. Finally, tablets were loaded with Prednisone resulting in 100% drug loading efficiency and a controlled release. Release rate could be controlled by coating with Eudragit. Thus, this unique method can be empowered to form an efficient oral drug delivery system with controlled release pattern and may provide desirable traits for drugs susceptible to heat or irradiation and possibly to other biomedical applications.

Figure 1: Schematic illustration of double syringe 3D printing system and the formed porosive structure.
Understanding and tailoring peptide self-assembly for the formation of surface-modified antimicrobial particles

Abstract title

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Bacteria settling on surfaces are currently one of the greatest concerns for the supply of proper health, water and energy. Bacterial accumulation on medical devices and implants, impair their function and can lead to severe infections and even death. Materials addressing this phenomenon are called antifouling materials. Different materials have been developed in the last 50 years, however, no optimal solution has yet to be found.

Here, we describe the self-assembly of a short peptide into two different types of supramolecular structures, depending on the pH of the solution. These particles are designed to reduce bacterial adhesion and at the same time release biocidal compounds. By using NMR and molecular dynamics (MD), we determined the structures of the peptide monomers and showed the forces directing the self-assembly of each structure under different conditions.

When adhered to its surface, the peptide particles modify the chemical and physical characteristics of glass and confer it with the ability to resist biofouling. The inclusion of biocidal compounds (e.g. antibiotic, enzyme and anticancer drug) in the particles resulted in an improved antimicrobial activity of the surface.

This approach and the detailed understanding of the processes are relevant for developing new sterile surfaces for health-care systems, water purification devices, food packaging or any environment that suffers from biocontamination.

Reduced biofilm formation on strong hydrophobic coatings

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The current non-toxic biofouling control is based on the idea for creation of non-adhesive, low-fouling material surfaces, an approach including development of strong hydrophilic “water like” bioinert biomaterials. Strong/super hydrophobic low-energy surfaces are preferable in industrial and marine biofouling control because of their better stability in water media and reduced interactions with living cells.

Siloxane fouling release coatings are currently the only viable non-toxic commercial alternative to the toxic biocide antifouling paints. However, they only partially inhibit biofouling since the biofilms remain a major issue. Hutch amount current researches are devoted to the study the mono-specie and multi-specie biofilms formation aimed at bioadhesion prevention.

Here are presented several successful solutions in the reduction of mono- and multi-specie biofilms formation on marine siloxane coatings. Relationship coating’ surface characteristics – bacterial adhesion was studied. The most important pre-requisites of the “clean” surface were formulated.
Strong antibacterial effect of Ag/Cu doped TiO\(_2\) thin films on \textit{E. coli}

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As a commonly found bacterium in the digestive tract of animals and humans, \textit{E. coli} is a big challenge for the scientific community in endeavor to preserve the human society from the resistant strains, which cause illnesses in hundreds of thousands of people. In many cases, \textit{E. coli} exchanges genes and produces toxins, too. In result, these pathogenic strains have the ability to cause a novel form of disease after adhesion and invasion in the human body due to harmful interference with the cell metabolism and tissue.

In this presentation is demonstrated the strong antibacterial effect toward \textit{E. coli} of Ag/Cu doped TiO\(_2\) thin films obtained through radio frequency magnetron sputtering under different technological parameters. The effects of a Ag : Cu ratio and a film thickness were assessed on the interaction with \textit{E. coli}. Diffusion method was used as a preliminary screening assay. Industrial strain \textit{E.coli} 3548 NBIMCC was tested in a dynamic regime through optical density measurements and classical Koch’s method. The precise disinfection time was determined for all samples. SEM images give a representative view of the thin films morphology and the bacterial damages due to the contact with the tested nanocomposite materials. Strong elongation of the bacterial cells and complete destruction of the microorganisms can be viewed in the SEM image of the highest dopants concentration. An elongated lag-phase in the bacterial growth with the increase of the dopants concentration and the film thickness was established. Different mechanisms of the thin films action on \textit{E. coli} are suggested.
Gripping ease in southern green stink bugs

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The southern green stink bug Nezara viridula L. (Heteroptera, Pentatomidae) is highly polyphagous, preferring apically situated seeds and fruits on more than 150 plant species belonging to over 30 plant families all over the world. This forces them to move over highly variable terrains, including plant stems, leaves, pods, and buds, which requires efficient attachment [1].

Stink bugs have long slender legs and feet (tarsi) equipped with paired curved claws, paired soft adhesive pads (pulvilli), and flattened lanceolate hairs (setae), which arise ventrally on the first and second foot segments (tarsomeres). To characterize their attachment abilities, here we measured and analyzed the traction forces of bugs walking horizontally and vertically on hydrophilic and hydrophobic glass plates and rods [2].

The results demonstrate a clear contribution of tarsal flattened lanceolate hairs to the stink bug’s attachment. Higher traction forces are generated on a glass rod than on a glass Substrate hydrophobicity promotes the attachment, while the measured forces are up to 8 times lower when tarsal hairs are disabled. The combination of long, slender legs, smooth and hairy tarsal pads results in a remarkable attachment ability, which enables stink bugs to climb three-dimensional terrains and unstable apical plant parts, and supports their invasive behavior and global dispersion (Figure 1) [2].

Fig1. An adult southern green stink bug holding on the pubescent tomato leaf stem and leaf – a highly three-dimensional terrain.

New three-dimensional intestinal tissue engineering model as multifunctional platform for drug and nanoparticle absorption studies

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The drug development field is increasingly requesting for reliable tools for high-throughput analysis of drug absorption profiles. This work aims to establish and characterize a new tridimensional intestinal model encompassing epithelial cells laid over fibroblasts embedded in extracellular matrix, closely resembling the intestinal mucosa assembly. Immortalized cells will be used for the preliminary model set up, namely Caco-2 clone and HT29-MTX regarding the epithelial cells lines and CCD18-Co myofibroblasts embedded in ECM providing the 3D support. Different ECM materials (collagen type I, collagen type IV and laminin) will be used to access the growth of fibroblasts and the formation of an epithelial monolayer. Raji B cells will also be used to induce the differentiation of Caco-2 cells into M cells. After a full characterization of the model, CCD18-Co myofibroblasts will be replaced by primary fibroblasts and Caco-2 cells by enterocyte-like cells obtained from the differentiation of induced pluripotent stem cells (iPSCs) to improve the robustness and reproducibility of the model. The establishment of this model is expected to return new insights regarding the crosstalk between stromal and epithelial cells and the pharmacokinetic profile of any tested compound. It is foreseen that this model has potential to speed up the phases of drug development and improve the planning of animal experiments.
Biomechanical properties of fishing lines of the glowworm *Arachnocampa luminosa* (Diptera; Keroplatidae)

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Animals use adhesive secretions in highly diverse ways, such as for settlement, egg anchorage, mating, active or passive defence, etc. One of the most interesting functions is the use of bioadhesives to capture prey, as the bonding has to be performed within milliseconds and often under unfavourable conditions. While much is understood about the adhesive and biomechanical properties of the threads of other hunters such as spiders, barely anything is documented about those of the New Zealand glowworm *Arachnocampa luminosa*.

We analysed tensile properties of the fishing lines of the New Zealand glowworm *Arachnocampa luminosa* under natural and dry conditions and measured their adhesion energy to different surfaces. The capture system of *A. luminosa* is highly adapted to the prevailing conditions whereby the wet fishing lines only show a bonding ability at high relative humidity. Wet threads show a slightly higher breaking strain value than dried threads, whereas the tensile strength of wet threads was much lower.

The analyses show that the adhesion energy as well as breaking stress and strain values were very low in comparison to spider silk threads. As a functional explanation, the low tear strength for *A. luminosa* comprises a safety mechanism and ensures the entire nest is not pulled down by prey which is too heavy.
Relative roles of adhesion and gripping in climbing tree frogs

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Tree frogs can climb flat vertical surfaces by adhesion, but rate of ascent is increased on curved surfaces that allow gripping. Such adduction forces can occur both on narrow cylinders where individual digits wrap themselves around the cylinder and on larger diameter structures where outstretched limbs can reach sufficiently far around the cylinder to produce gripping forces (Hill et al., J exp. Biol. 221, jeb168179, 2018). In this study, direct measurements of such gripping forces were made on a force-measuring array consisting of 24 individual 3D force sensors, each with a resolution at the millinewton (mN) level, which were installed from top to bottom in four columns and six rows, with sensors in neighbouring columns staggered in height (Fig. 1). Three cameras were used to simultaneously record the climbing behaviours of animals (in these experiments tree frogs) on the cylinder-like force measuring array. We were thus able to simultaneously record the ground reaction forces of each of the four limbs of tree frogs (here six individuals of the Chinese gliding or flying frog, Rhacophorus dennysi, with forelimb spans in the range 163-201mm) climbing or descending both smooth and rough surfaces on a quasi-cylindrical structure with an overall diameter of 79mm. This poster describes the design of the individual force sensors, their installation on the climbing tower, and data on the use of a clamping grip by climbing frogs.

Figure 1: Force measuring array (a,b), climbing frog (c) and representative force data (d).
A library of novel photoswitchable adhesives for medical tape applications

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Switchable adhesion exhibits the ability to trigger adhesion in response to environmental changes, for example, temperature, light, pH, solvent, mechanics, and electro or magnetic field. The noteworthy functionality of switchable adhesives has been met with significant interest in many fields of material science and engineering and can find many useful and valuable applications, including the pain-free removal for wound dressing, simplification of separation for material recycle and easily repair or replacement of components in electronics.

In this project, our team has designed a novel photoswitchable adhesive for pain- and trauma-free medical tapes application. It is always a painful experience for patients to remove the bandages from the skin after the wound had healed. For those patients who have softer skins, the surface of skin (or hair) would be possibly peeled along with the medical tapes, which could cause serious skin trauma. With the help of photoswitchable adhesive, the peel force can be decreased over 50%. That new technology will help patients to peel the medical tape painlessly without causing skin injury. The next step of our team focuses on decreasing the peel force over 90% based on photochemistry principles and establish a startup for commercialization.
Functionalized Titanium Dioxide Nanoparticles for Targeting and Disrupting Amyloid fibrils

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Amyloidoses are a family of diseases characterized by abnormal protein folding that leads to aggregation. They accumulate to form fibrillar plaques which are implicated in the pathogenesis of Alzheimer, prion, diabetes type II and other diseases. Despite extensive research efforts devoted to plaque aggregates inhibition there is yet no cure for this phenomenon.

In recent years there has been growing interest in utilizing titanium and its alloys in biomedical applications. Various surface modification that produce porous, adhesive, bioactive coatings have been developed. Titanium oxides (titania) are also being developed for photothermal and photodynamic treatments.

Inspired by this, we set to explore the effect of functionalized titania nanoparticles in combination with external UV stimuli, as potential photothermal ablating agents against amyloids. Titania nanoparticles were coated with bi-functional catechol derivatives (dihydroxy-phenylalanine propanoic acid, noted DPA) to gain targeting properties. In conjunction with UV-radiation these nanoparticles may selectively destroy the vicinity of their target.

Titania modified 5 nm nanoparticles coated with DPA were further conjugated to the amyloid-targeting Congo Red (CR). These Titania-DPA-CR nanoparticles were found to target mature amyloid fibril of both amyloid-\textsuperscript{A}\textsubscript{β1-42} a.a) and prion peptide (PrP fragment, 106-126 a.a).

Moreover, irradiation of the peptides in presence of the modified nanoparticles decreased the aggregate content and oligomer fraction. This work provides new insights into the use of modified titania nanoparticles for amyloid plaque targeting and photothermal destruction. It may shed light on future modifications and functionalization of titania nanoparticles for different applications.

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Mixed mucoadhesive amphiphilic nanoparticles for the treatment of pediatric tumors of the Central Nervous System intranasal by administration.

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Central nervous system (CNS) tumors are the second most common pediatric malignancy and the leading cause of childhood morbidity and mortality due to cancer. High percentage of the CNS tumors in children are diffuse intrinsic pontine gliomas (DIPG). DIPG is a tumor with likely fully conserved blood-brain barrier (BBB), the anatomical barrier that controls the trafficking of endogenous (e.g., nutrients) and exogenous molecules (e.g., drugs) from the systemic circulation into the CNS. Due to the well-conserved BBB in the disease and the extremely low aqueous solubility of the candidate drugs, the bioavailability in the CNS after standard administration (e.g., intravenous, i.v.) could be compromised. The direct nose-to-brain transport pathway that bypasses the BBB is very promising to target nano-encapsulated drugs to the CNS. Interestingly, this transport mechanism is more efficient for particulate matter in the 100-300 nm size range than for drugs in solution. Thus, the implementation of a nanotechnology approach would be beneficial to improve the state-of-the-art treatment of DIPG. Many nanotechnology platforms are currently under investigation to improve the delivery of drugs. In this context, mixed mucoadhesive amphiphilic nanoparticles made of chitosan (CS) and poly(vinyl alcohol) (PVA) that were hydrophobized with poly(methyl methacrylate) (PMMA) blocks were synthesized and characterized to host high drug payloads and evaluate the potential of these nanocarriers to transport model anticancer drugs to the brain by the mucosal drug delivery thorough the intranasal (i.n.) pathway (Fig 1) and sustain its release over time. The size, size distribution and Zeta-potential of the nanoparticles was measured by dynamic light scattering and nanoparticles tracking analysis. Next, we investigated the transportation through Epithelium nasal model of our mucoadhesive nanoparticles and characterize by means of confocal microscopy and Image stream analysis.

Figure 1: Schematic representation of the mucosal delivery by i.n.

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Mucoadhesive poly(vinyl alcohol)-based nano-carriers as novel drug delivery system

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Mucosal tissues cover natural body cavities (e.g., gastrointestinal tract, nose, airways, eye and vagina) exposed to air and provide an epithelial barrier to the external environment. The mucous protects the epithelium from physicochemical, biological and mechanical insults. Moreover, mucus displays a porous structure that enables the penetration of small particulate matter. In this framework, a broad spectrum of materials have been investigated for the design of mucoadhesive nano-drug delivery systems with more prolonged residence time in the administration site and improved pharmacokinetic performance. Moreover, most of the polymeric nanoparticles (polymeric micelles-PMs) in clinical trials are for intravenous administration in the therapy of cancer. To extend their use to non-parenteral routes, polymeric nanoparticles should interact with mucus. Our research group investigates novel polymeric nanoparticles with greater stability and advanced features for efficacious mucosal drug delivery. In the frame of our work, we synthesized and investigated novel PVA-based amphiphilic nanoparticles for improved drug delivery. Polyvinyl alcohol (PVA) is a synthetic polymer, biocompatible, that can be crosslinked and stabilized with boric acid through non-covalent of borate anions and units of the polyol that are then, stabilized by H bonding between boron sites. Despite the presence of pendant hydroxyl groups that enable the interaction of macroscopic PVA systems with mucin, this polymer has not been previously explored in the production of mucoadhesive NPs. We recently reported on a novel type of amphiphilic poly(vinyl alcohol)-poly(N-isopropylacrylamide) mucoadhesive nanogel stabilized by selective non-covalent crosslinking and nano spray drying consolidation.¹ Now we are focusing on the development and full characterization of novel PVA-based nanoparticles that contain PMMA as the hydrophobic part. This polymer is hydrophobic at all temperatures and it has been approved as pharmaceutical by regulatory agencies such as the US-

Food and Drug Administration (US-FDA).