QUEEN MARY UNIVERSITY OF LONDON

SUPRAMOLECULAR WORLD

Edited by Xinqing Pang and Helena Azevedo

"Self-assembly in nature"

I. Collagen

Nature creates materials, such as wood or bone, with complex structures and incredible range of properties and functions[1]. These biological materials are made of small buiding blocks (proteins, polysaccharides, minerals) assembled in a hierarchical fashion across multiple length scales. The basic building blocks also possess a highly organized structure which derives from specific interactions at molecular level.

Supramolecular World will present examples of supramolecular structures in Nature where self-assembly is a fundamental feature[2]. This issue is focused on "Collagen", the fibrous protein in the matrix of our tissues.

Collagens are a family of extracellular proteins, being the most abundant proteins in the body (about 30% of the total body protein). Individual collagen molecules are made of three polypeptide chains that wrap around each other to form a superhelical cable (triple helix, Figure 1A). In each of the polypeptide chain, every third amino acid is glycine (Gly), the smallest amino acid that fits perfectly inside the helix, while the remaining amino acids are mostly proline (Pro) or hydroxyproline (Hyp), a modified version of proline (Figure 1B). Gly forms a kind of a small elbow packed inside the helix, and Pro and Hyp slighthly turn the chain back around the helix. In Figure 1B, a larger amino acid (alanine, Ala) is placed in the position normally occupied by Gly. In this case, the lateral side groups of Ala are protruding from the main chain.

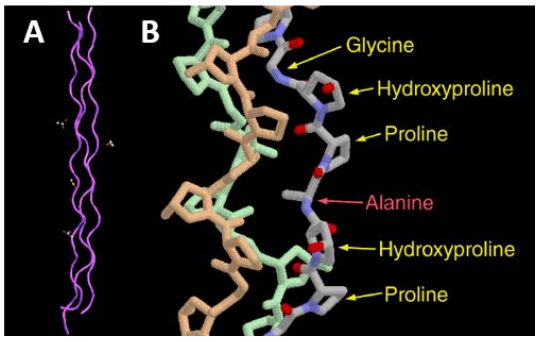


Figure 1 (A) Collagen triple helix (Structure genererated by Chem3D software using the PDB file 1bkv); **(B)** 3D view showing the packing of the repeating amino acid motif Pro-Hyp-Gly within the collagen triple helix (from Protein Data Bank, PDB).

Collagen molecules self-assemble in a hierarchical manner that spans from molecular to macroscopic levels (Figure 2A). First, the individual collagen triple helices self-assemble laterally in a stagerred arrangement forming fibrils with a D-band periocidity (~67 nm). This staggered array leads to the banding pattern seen in the collagen fibril under transmission electron microscopy (TEM, Figure 2B). The fibrils are further stabilized by the formation of covalent crosslinks iniated by speficic enzymes, wich further aggregate into fibres.

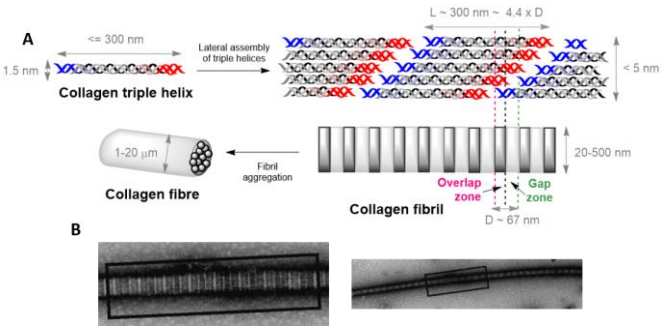


Figure 2 (A) Multi-step assembly of collagen fibres (adapted from 4). **(B)** TEM image of collagen fibril depcting the alternating dark-light patterns (adapted from 5).

Currently, there are 28 types of collagen (types I-XXVIII), but types I-V are the most common. Collagens provide the integrity of various tissues, forming strong fibres that strengthen tendons and composite materials with minerals in bones and teeth. In the cornea, collagen fibrils are kept at regular distances from each other to allow transparency and passage of visible light.

Because of its biological importance and intriguing hierarchical structure, collagen has fascinated scientists for many years. Self-assembly is a powerful technique for organizing molecular building blocks into complex structures. Using self-assembly approaches, researchers are now creating collagen-like peptides, synthetic molecules that resemble natural collagen, as recently reviewed by us[4].

1. Meyers MA, Chen P-Y, Lin AY-M, Seki Y (2008), Biological materials: structure and mechancial properties, Progress in Materials Science, 53: 1-206
2. Mendes AC, Baran ET, Reis RL, Azevedo HS (2013). Self-assembly in nature: using the principles of nature to create complex nanobiomaterials. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 5 (6): 582-612.
3. Hulmes D. (2008) Collagen Diversity, Synthesis and Assembly. In: Fratzl P. (eds) Collagen. Springer, Boston, MA, pp 15-47.
4. Banerjee J, Azevedo HS (2017). Crafting of functional biomaterials by directed molecular self-assembly of triple helical peptide building blocks. Interface Focus, 7 (6): 20160138.
5. Holmes DF, Graham HK, Trotter JA, Jadler KE (2001), STEM/TEM studies of collagen fribril assembly, Micron, 32: 273-285.

Presentations at QMUL workshop

Thank you to the Becer (SEMS) and van Hest group (Eindhoven University of Technology) for inviting us to participate in the workshop at Queen Mary University of London (17th October 2017).

- **Presentation:** Hyaluronan: a macromolecular template for self-assembling biomaterials - Helena Azevedo
- **Presentation**: Rational modification of peptide termini for controlled self-assembly: from functionalized surfaces to 3D biomaterials - Dominic Collis
- **Presentation:** Enzyme-assisted fibre-to-micelle transition controls presentation of cell-penetrating peptides in self-assembled nanostructures - Yejiao Shi

Workshop at QMUL, October 2017

Invited lectures:

- *29 January 2018* H. S. Azevedo, Interfacial Self-assembly of Peptides: from Molecularly Engineered Surfaces to Soft Biomaterials, Department of Chemistry, University of Reading, UK.
- *14 December 2017* H. S. Azevedo, Displaying Functionality into Biomaterials through Self-assembly, the IOP workshop Self-Assembly, Recognition, and Applications (SARA) 2017, University of Lincoln, UK.
- *1 November 2017* H. S. Azevedo, Molecular Biomaterials for Targeted Therapies, Centre for Inflammation and Therapeutic Innovation (CiTI) launch Symposium, Queen Mary University of London, London, UK.

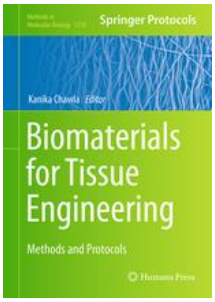
Presentations at national and international conferences/meetings

- D.W.P.Collis, E. Radvar, G. Yilmaz, C. O'Malley, Y. Shi, C. R. Becer, H. S. Azevedo, Engineering biomaterials through functionalisation of peptide termini, Peptide and Protein Science Group Early Stage Researcher Meeting, 14 September 2017, University of Durham, UK.
- E. Radvar, Y. Shi, H. S. Azevedo, Fabrication of Biomaterials by Self-assembly of Rationally Designed Peptides with Biomacromolecules, 16th Iberian Peptide Meeting/4th ChemBio Group Meeting, 5-7 February 2018, Barcelona, Spain.
- D. W. P. Collis, G. Yilmaz, C. O'Malley, C. R. Becer, H. S. Azevedo, Design and Synthesis of Neoglycopolymers Mimicking Hyaluronan, Bordeaux Polymer Conference, 28-31, May 2018, Bordeaux, France.
- Y. Shi, J. Banerjee, D. S. Ferreira, H. S. Azevedo, Insights into the MMP-1 Degradability of Self-assembled Peptide Amphiphile Nanostructures: the Role of Supramolecular Cohesion, Third International Conference on Peptide Materials for Biomedicine and Nanotechnology, 16-18 July 2018, London, UK.

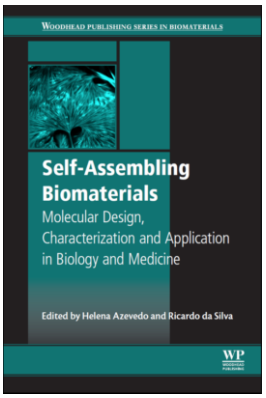
Recent and upcoming publications

- M. Hartweg, C. J. C. Edwards-Gayle, E. Radvar, D. W. Collis, M. Reza, M. Kaupp, J. Steinkoenig, J. Ruokolainen, R. Rambo, C. Barner-Kowollik, I. W. Hamley, H. S. Azevedo, C. R. Becer, Ugi Multicomponent Reaction to Prepare Peptide-peptoid Hybrid Structures with Diverse Chemical Functionalities, Polymer Chemistry 2018, 9:482-489.

- Q. Chen, A. Passos, S. Balabani, A. Chivu, S. Zhao, H. S. Azevedo, P. Butler, W. Song, Semi-interpenetrating Network Hyaluronic Acid Microgel Delivery Systems in Micro-flow, Journal of Colloid and Interface Science (2018), DOI link.



➢ Y. Shi, R. Lin, H. Cui, H. S. Azevedo, Multifunctional self-assembling peptide-based micelles for targeted intracellular delivery: design, physicochemical characterization and biological assessment, in Biomaterials for Tissue Engineering: Methods and Protocols Methods in Molecular Biology, vol. 1758, Ed. K. Chawla, Methods in Molecular Biology ISBN 978-1-4939-7741-3; in press.



➢ K. Shuturminska, C. O'Malley, D. W. P. Collis, J. Conde, H. S. Azevedo, Displaying biofunctionality on materials through templated self-assembly, in Self-Assembling Biomaterials: Molecular Design, Characterization and Application in Biology and Medicine, Eds. H. S. Azevedo, R. M. P. da Silva, Elsevier, 2018.

➢ "Self-Assembling Biomaterials: Molecular Design, Characterization and Application in Biology and Medicine", Eds. H. S. Azevedo, R. M. P. da Silva, Elsevier, 2018. ISBN 9780081020159. *Expected release date: April 1, 2018.*

New students joining the MHAtriCell Lab:

PhD student

Yichen Yuan: Supramolecular polymers for displaying sugars and peptides as ECM mimics, in collaboration with Dr Remzi Becer (SEMS).

PhD student

Xinqing Pang: Engineering the endothelial glycocalyx *in vitro* to study the mechanisms of hyaluronan regulation of vascular integrity in health and disease, in collaboration with Prof Wen Wang (SEMS).

Upcoming Conferences

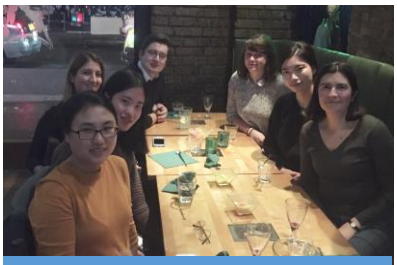
International events

- 16th Iberian Peptide Meeting - 4th ChemBio Group Meeting, 5th-7th February 2018, Barcelona, Spain. Link
- 35th European Peptide Symposium, 26th-31st August 2018, Dublin City University, Ireland. Link
- 29th Annual Conference of the European Society for Biomaterials, 8th-13th September 2018, Maastricht, The Netherlands

UK events

- RSC Biomaterials Special Interest Group Annual Meeting 2018, 10th-11th January, Bradford. Link
- RSC Carbohydrate group meeting, 12th-13th 2018, Keele University. Link
- 5th Annual Peptides Congress, 16th-17th April 2018, London. Link
- Peptide Materials Conference 16th-18th July 2018, London. Link
- IMAP 2018, the 8th International Meeting on Antimicrobial Peptides, 2th-4th September 2018, Edinburgh. Link

News



Celebration for Yejiao 2017

- Yejiao has passed her PhD viva on the 19th of October 2017. Congratulations Dr Shi! Yejiao will continue working in the group as PDRA under the Seed Award in Science "Supramolecular peptide nanotechnology for antimicrobial therapies" funded by the Wellcome Trust.
- Helena has been admitted as Fellow of the Royal Society of Chemistry (FRSC).
- Helena will visit Prof Kadriye Tuzlakoglu from Yalova University and other academics from universities in Turkey in April 2018, under The Distinguished Visiting Fellowships and Missions – Turkey funded by the Royal Academy of Engineering (RAE), to foster research collaborations in "Molecularly engineered biomaterials for the treatment of diabetic wounds".
- We have an open PhD position on "Self-assembled peptide droplet interfaces for simple screening of stem cell microenvironments and micromanipulation of colonies" in collaboration with Dr Gautrot's group (Link). Check the advert here or through website FindAPhd.
- Follow us on twitter @mhatricell Link

From back to front and left to right:
Dominic Collis, Clare O'Malley, Yichen Yuan, Yejiao Shi, Elham Radvar, Xinqing Pang, Helena Azevedo.

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