

## Fabrication of Collagen Based 3-D Complex Topologies via Electrochemical Compaction

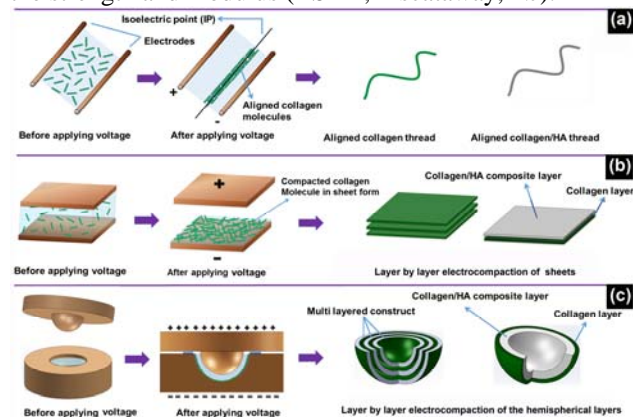
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**Statement of Purpose:** Fabrication of scaffolds with curved topographies is still a challenge in repair of tissues with complex geometries. A method which can fabricate a mechanically robust scaffold from biological proteins as complex topographies would be highly significant. Electrochemical compaction (ECOM) of aqueous monomeric collagen solutions have been shown to fabricate threads [1-3]. The purpose of this study was to demonstrate the potential of ECOM process in making compositionally varying and mechanically robust multilayered complex curved topographies.

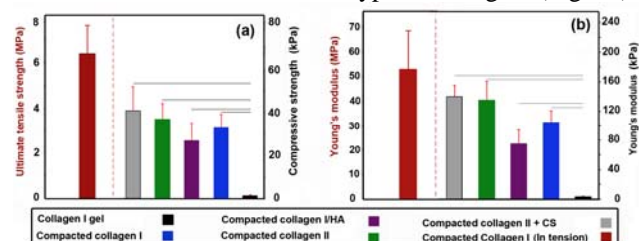
**Methods: Electrochemical Fabrication:** As presented schematically in Fig.1, electrochemical compaction method enables the fabrication of constructs in 1D, 2D and in 3D. It also provides the provision to use various types of collagen (I vs. II) collagen and secondary additives such as mineral particles or other biomolecules (such as GAGs). To make a hemispherical shell, a 12.5 mm diameter hemispherical indent was milled in a carbon electrode which was connected as the cathode. The indent was filled with type-I collagen solution (Advanced Biomatrix, CA). An aluminum ball of 10 mm diameter was positioned concentrically within the hemispherical indent, served as the anode. Electrical current compacts the molecules close to the cathode under the effect of mechanisms published before [1-3]. On the top of the electrocompacted pure collagen layer, a mixture of hydroxyapatite (HA) and type-I collagen solution (60% w/w HA) was compacted as the second layer. The highly complex structure of the nose was fabricated by molding liquid metal as electrodes.

**Effects of ECOM on Mechanical Properties:** Type-I or II collagen solutions were loaded between two parallel planar carbon sheet electrodes to obtain disc shaped sheets. Sheets were crosslinked in 0.625% genipin in 90% ethanol for 3 days, tested under tension (in-plane of the sheet) and compression (out of plane) at 1%/sec to obtain the strength and modulus (RSAII, Piscataway, NJ).



**Fig 1.** Schematic process of ECOM: (a) linear electrodes for making collagen threads, (b) planar electrodes for making 2-D multiphase construct, and (c) hemispherical or curvilinear electrode for making 3-D multiphase constructs.

**Results:** ECOM was able to pack collagen molecules  $17 \pm 2.6$  better than the standard collagen gel as determined by the volumetric measurements. Such packing has been shown to increase the efficiency of crosslinking [4]. As a result, the mechanical properties of electrocompacted sheet increased by  $27 \pm 7$  fold in comparison to collagen gel control made by using the same amount of collagen. Fig. 2a and b show the compressive stress and tensile strength of electrocompacted type I and II collagen sheets and also collagen gel. ECOM process was able to fabricate constructs with different compositions and geometries: collagen type II sheet incorporated with CS (Fig. 3a), a bilayered hemispherical construct with the concave layer of compact collagen I/hydroxyapatite and convex layer of pure compact collagen type I (Fig. b) and, a nasal construct made with type I collagen (Fig 3c).



**Fig 2.** Mechanical properties of ECOM products: (a) tensile and compressive stress of compacted type I & II collagen sheets, (b) Young's modulus of compacted collagen I and II sheets.



**Fig 3.** Product range attained by ECOM: (a) compacted collagen II incorporated CS, (b) semispherical scaffolds with HA-collagen (white) and pure collagen (black) layers standing alone, (c) nasal shell layer made by liquid metal nose-like electrodes.

**Conclusions:** Electrochemical compaction method is a solid freeform fabrication (SFF) method for making mechanically strong 3-D complex geometry constructs with a variety in composition and geometry relevant to targeted tissues and organs. The main advantage of this technique is its ability to produce complex products rapidly and directly from aqueous collagen solution which can contain other inclusion such as mineral particles, other biomolecules and bioinductive growth factors. Therefore, electrochemical compaction is a cutting-edge technology with significant potential to be used for the joints and craniofacial defects, and dental complications.

### References

- [1] Cheng et al., Biomaterials, 2008, 29(22), 3278-88.
- [2] Kishore et al., Biomaterials, 2012;33(7):2137-44.
- [3] Uquillas et al. Ann Biomed Eng, 2012;40(8):1641-53.
- [4] Uquillas et al., J Mech Behave Biomed, 2012;5: 176-189.