



## PLASMA TECHNOLOGIES ADVANCING BIOMEDICINE AND SUSTAINABILITY

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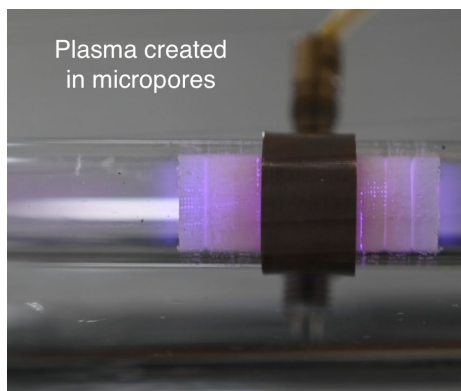
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When powered by renewable electricity, plasma processing technologies requiring minimal amounts of gaseous reactants and generating minimal waste can provide sustainable solutions to many materials and chemical processing needs. Here we present plasma processes that enable the creation of bio instructive and biomimetic surfaces for wide ranging applications in biomedicine, eliminating the need for multi-step wet chemical treatments.

Materials used in biomedicine are selected according to bulk properties, such as mechanical, electrical and optical, required for particular in-vivo and in-vitro applications. However, their surfaces almost always provide suboptimum biological microenvironments and do not promote the desired biological responses. In addition, they are often formed into geometries that are not appropriate for traditional line-of-sight low pressure plasma treatment modalities. Here, we will describe sustainable and readily scalable low temperature plasma surface modification processes, that enable resilient and tailorable biofunctionalization on all surfaces of complex, including microporous, fibrous or hollow-fiber-based, structures.

As cell behavior is directed by biochemical signals and local stiffness, our strategy is to immobilize biomolecules and hydrogels onto the cell contacting surfaces. Typical time scales of cell culture and tissue integration necessitate covalent immobilization to prevent biomolecule desorption and exchange with molecules in the aqueous environment. Energetic ion implantation into carbon-based surfaces or surface coatings creates buried radicals whose unpaired electrons migrate to the surface. At the surface these highly reactive radicals form covalent bonds with proximate molecules [1]. This basic strategy is extended to plasma synthesized nanoparticles and applied via capacitive coupling within the internal porosity of scaffolds and to microparticles in a packed bed configuration [2]. For structures created by 3D bioprinting which is not compatible with low pressures, we developed instead a localized atmospheric pressure plasma treatment to generate and covalently bond reactive groups to the surface which then react with side chain groups present on the surface of biomolecules [3]. A combination of these plasma activation processes is applied to microfluidics for organ-on-chip applications [4].



**Fig. 1.** Plasma treatment of scaffold for expansion of stem cells. Optimization of pressure as well as electrode size and location enables plasma within the micropores.

The reported plasma treatments were found to activate a range of materials and structures for spontaneous, reagent-free, covalent functionalisation with bioactive, cell-signaling molecules and hydrogels. Functional molecules that can be immobilized to create tailored, bio instructive cell microenvironments include, but are not limited to, oligonucleotides, enzymes, peptides, aptamers, cytokines, antibodies, cell-adhesion extra-cellular matrix molecules and histological dyes. The covalent immobilization occurs on contact via radicals or reactive groups on the plasma activated surfaces. Subsequent laser annealing can add conducting tracks allowing stimulation of electroactive cells without sacrificing optical transparency. Controlled application of the functional molecules via droplet dispensing or



contact printing enables the immobilization of biomolecular and hydrogel patterns onto the plasma activated surfaces.

Together these processes create a toolbox for fabricating bespoke biomimetic microenvironments that provide exquisite control in cell culture and tissue engineering. Commercialization is underway with expected impacts in personalized medicine, controlled tissue-integration, medical and environmental diagnostics, biosensing and nanomedicine.

#### References

- [1] PNAS., **108**, 14405-14410, (2011)
- [2] ACS Appl. Mater. Interfaces, **12**, 32163–74 (2020)
- [3] ACS Appl. Mater. Interfaces, **12**, 38730-43 (2020)
- [4] Adv. Funct. Mater., 2313664 (2024)