Vascularized Biomaterials for Rapid Soft-Stiff Transitions in Medical Devices

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Statement of Purpose: Materials with the ability to rapidly manipulate their stiffness are attractive components in biomedical devices. Rapid actuation of rigid-compliant transitions can be useful in intra-vascular surgical devices to negotiate vascular tortuosity without causing damage to the vascular walls. In polymers, stiffness transitions are observed by manipulating the spatial bulk temperature. In bulk form factors, the heat conduction length scales in polymers determine the characteristic time scale for glassy to rubbery transitions, which is a critical figure of merit for biomedical applications. Reducing the characteristic diffusion length scales will dramatically reduce the time for phase switching in bulk materials. In order to decrease the characteristic length scales in bulk materials, a "biomimetic" material design with the incorporation of synthetic vascular networks in the material bulk is proposed. It is hypothesized that synthetic microfluidic networks in bulk polymers will accelerate stiffness transitions by reducing the characteristic length scale of thermal diffusion. An initial demonstration of this strategy was performed by studying stiffness transitions in synthetic poly(1,3-diamino-2-propanol-*co*-polyol sebacate) (APS) elastomers with embedded microfluidic networks. Stiffness transitions were triggered by the glassy-rubbery relaxation of APS polymeric networks due to diffusion of plasticizer (water) into the bulk. This stiffness transition can be indirectly interpreted by measuring the shape-memory response kinetics.

Methods: Shape-memory microfluidics were fabricated through sequential replica-molding and lamination of microfabricated APS films [1]. A temporary shape was induced in APS microfluidic films by heating the films to 75 ^{o}C and straining them by 11.21 ± 0.31% at a rate of 1 mm min^{-1}. The temporary shape was fixed by cooling the strained APS devices to 20 ^{o}C while under applied tension. The strain recovery rate of APS elastomers in response to dynamic hydration was recorded (Pro Webcam C910, Logitech, Fremont, CA, USA) in three modes of operation: (1) supply of water from an external bath, termed "static" operation; (2) supply of water through the embedded vascular network, termed "perfused" operation; (3) supply of water into APS networks through both "static" and "perfused" modes, termed "perfused+static" operation.

Results: APS elastomers are a class of synthetic crosslinked poly(ester amide)s that exhibits utility in the field of tissue engineering [1]. APS exhibits a Young's modulus of 4.58 ± 0.404 MPa at temperatures $T > T_g$ and 540 ± 32.1 MPa at temperatures $T < T_g$. Fully hydrated and dehydrated APS networks exhibit T_g of -8.3 and 37 ^{o}C, respectively. This enables heating or hydration to be used as stimuli for stiffness transitions and shape recovery. Shape recovery kinetics for all modes of operation were compared and it is observed that perfusion assisted delivery of water into the bulk APS devices substantially accelerates shape recovery kinetics compared to non-perfused modes of water delivery. Perfusion assisted delivery reduces shape recovery time scales to 4.2 ± 0.12 hours from 8.0 ± 0.26 hours in the case of non-perfused delivery methods. Finite element simulations can accurately predict the shape recovery kinetics of APS shape-memory microfluidics operating in all three modes of stimuli delivery.

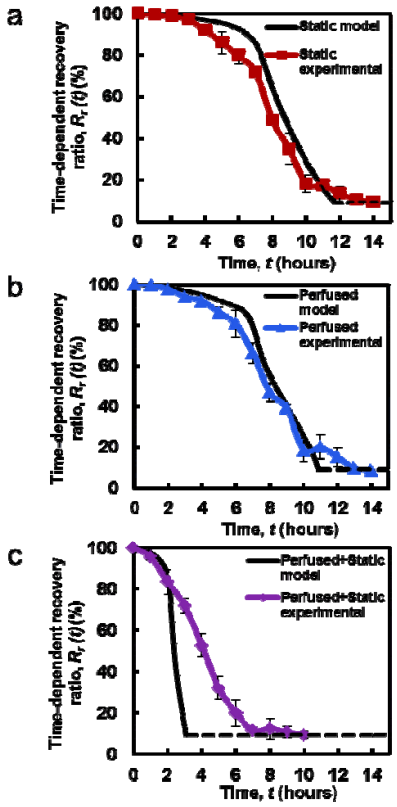

Figure 1. Comparison of theoretical vs. experimental time-dependent strain recovery ratio $R_r(t)$ for the device operated in (a) static mode, (b) perfused mode, and (c) perfused+static mode. $R(t)$ is defined as $R_r(t) = \frac{\varepsilon_u(t) - \varepsilon_o}{\varepsilon_u} \times 100$ where ε_o is the original length of the device, $\varepsilon_u(t)$ is the time-dependent deformation length of the device during hydration and ε_u is the deformation length of APS samples after removal of applied stress.

Conclusions: This study demonstrates that the reduction of the characteristic diffusion length scales in APS by the incorporation of a "biomimetic" vascularized material design accelerates stiffness transitions. This strategy can be utilized in other materials to trigger rapid phase transitions in large form factors. Future work will focus on engineering novel vascular devices with multiple addressable dynamic stiffness regions to negotiate vascular tortuosity.

References: [1] (Wang J, Bettinger CJ, Langer RS. Organogenesis. 2010;6;212.)