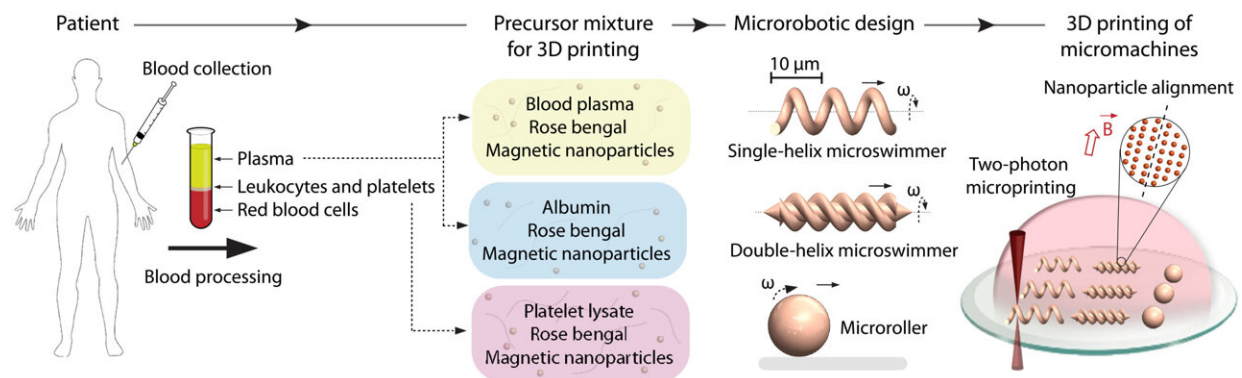


Personalized 3-D magnetic micromachines from patient blood-derived biomaterials

September 22 2021, by Thamarasee Jeewandara



A facile strategy for the 3D printed personalized micromachines from patient blood-derivable biomaterials. Harvested blood from the patient can be rapidly and robustly processed to obtain blood plasma, albumin, and platelet lysate. We use these biomacromolecules to prepare the microfabrication precursor mixtures containing the photosensitizer rose bengal and magnetic iron oxide nanoparticles for wireless powering and control. CADs of the micromachines are then realized by two-photon polymerization-based 3D printing. During the 3D printing process, we apply a uniform magnetic $B \rightarrow$ field in the direction perpendicular to the rotation axis of the micromachines to maximize the net magnetization by self-assembling the magnetic nanoparticles into directional chains. Credit: Science Advances, 10.1126/sciadv.abh0273

Wireless micromachines have [increased the scope for applications](#) in biomedicine, although their risks relative to minimal biocompatibility need be lessened. Most materials are not intrinsically biocompatible in

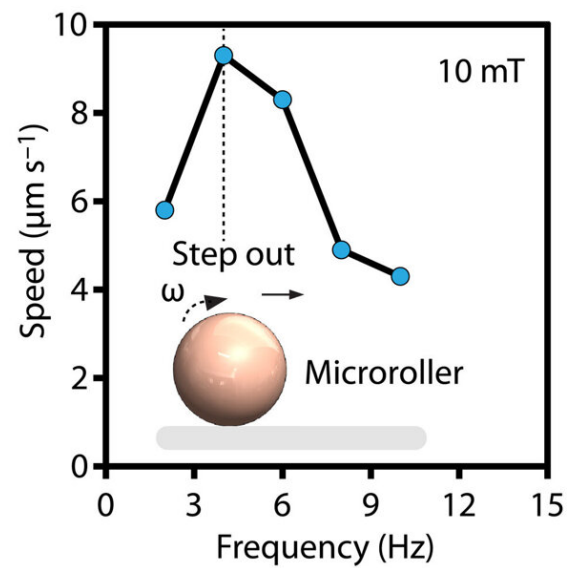
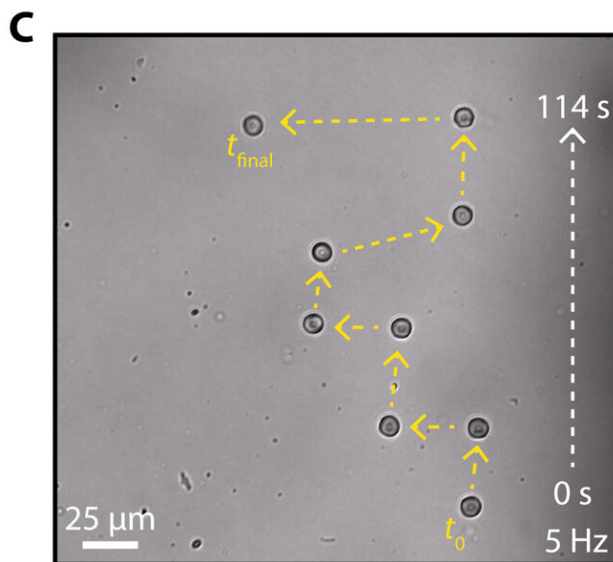
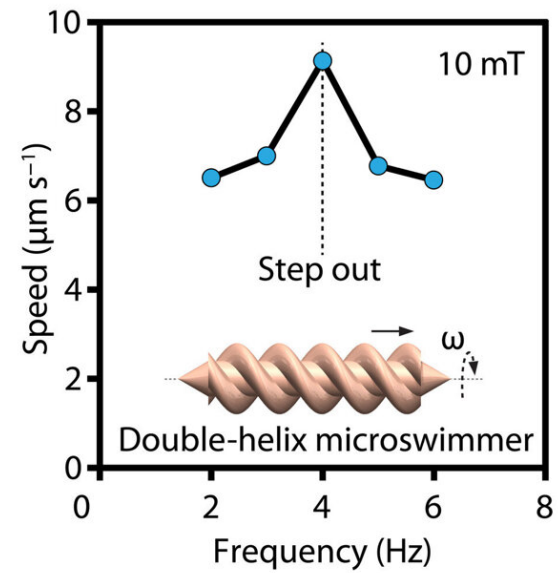
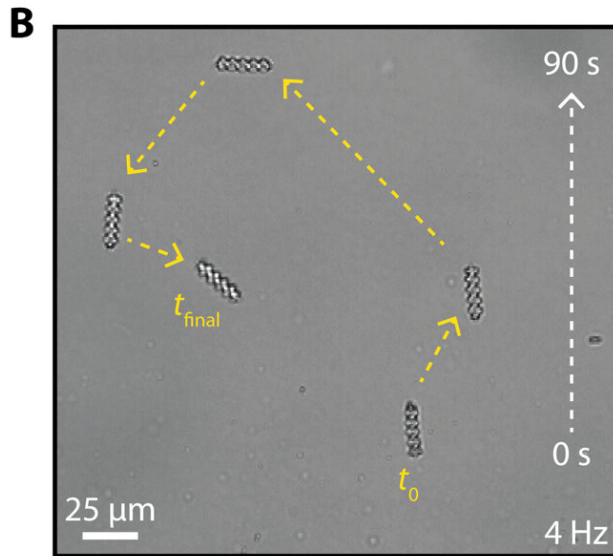
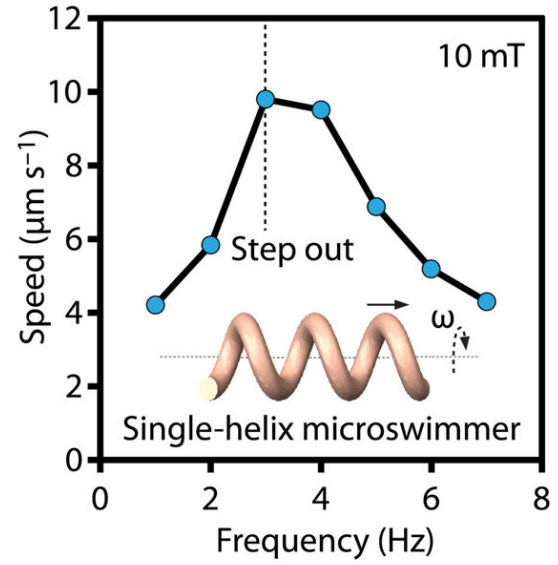
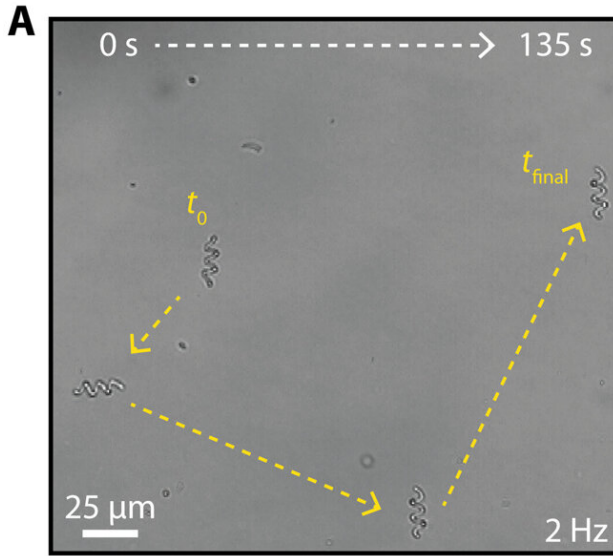
physiological environments. In a new report now published in *Science Advances*, Hakan Ceylan and an international research team in physical intelligence, biomedical engineering and medicine have proposed a personalized approach for patient blood-derived biomaterials as a fundamental construction fabric to influence biocompatibility. Ceylan et al. developed the 3D printed multiresponsive microswimmers and microrollers using magnetic nanocomposites of blood plasma, serum albumin protein and platelet lysate that responded to time-variant magnetic fields for controlled cargo delivery and release. The proteinaceous fabrics also allowed enzymatic degradability to lower the risks of long-term toxicity. The resulting product can influence the development of many future medical robots and devices made of autologous biomaterials to improve biocompatibility and smart functionality in biomedical applications.

Wireless micromachines

Mobile and wireless micromachines are [minimally invasive for targeted therapies](#) in medicine. Despite their advanced design, fabrication and remote control, their interaction dynamics are usually unknown. As a result, deploying such micromachines in the body for long periods of time can pose substantial safety risks due to [counteracting efforts](#) to eliminate the product. Elimination depends on the construction material, time of exposure and the engineering design, which can activate defense cascades in vivo. To minimize the risk of [cytotoxicity](#) and the immune response, Ceylan et al. proposed a personalized approach with patient blood-derived biomacromolecules to form biocompatible micromachines. The personalized strategy for micromachine development can influence the design of a variety of medical robots and devices in the future for enhanced biocompatibility and intelligent functionality.

Concept and fabrication process

During the experiments, Ceylan et al. focused on blood components such as plasma, albumin and platelet lysate to develop the micromachines. Using [two-photon polymerization](#) based three-dimensional (3D) printing, the team fabricated a variety of medical micromachines with intricate features. The methods allowed highly complex 3D computer-aided designs with sub-micron features. The scientists developed micromachines from blood-harvested materials by creating a precursor mixture of rose Bengal and magnetic iron oxide nanoparticles. They then applied the fabrication approach on common and promising medical micromachine designs, including [single helix microswimmers](#) and [microrollers](#) at the microscopic length scale. The team optimized the laser intensity during 3D printing and developed a double-helix microswimmer array with varying laser intensities, and then viewed them under fluorescence microscopy to observe the high-fidelity printing process.



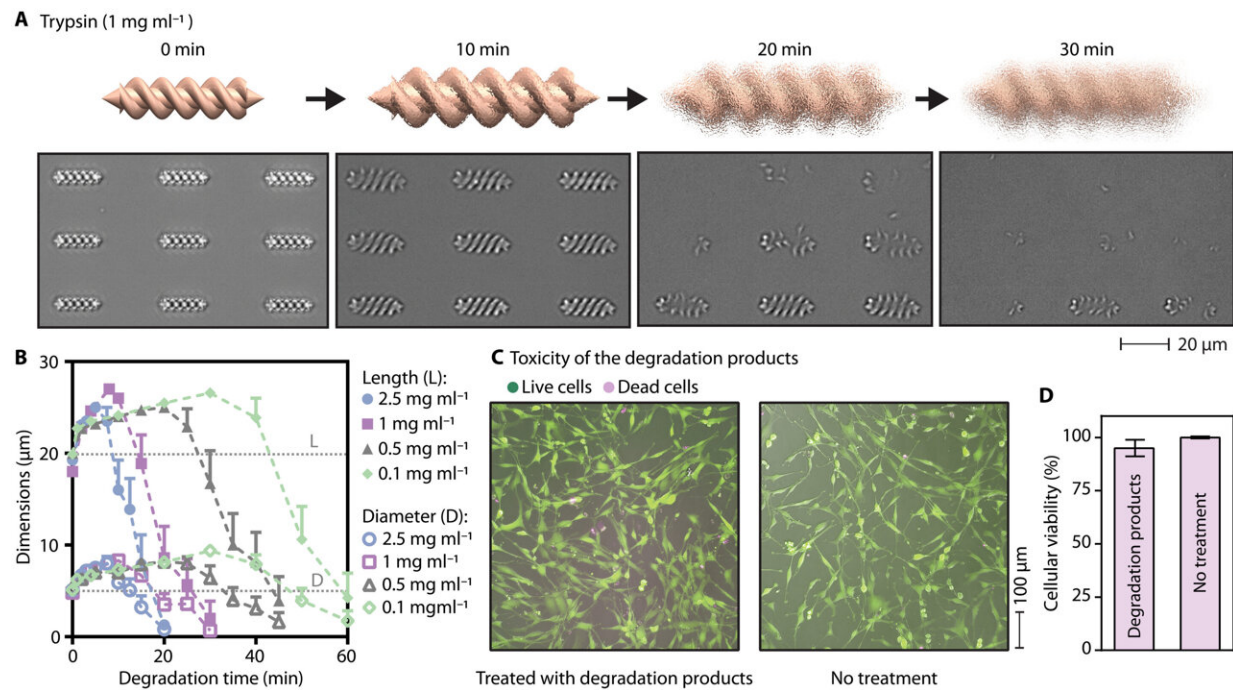
Magnetic torque–based actuation and steering of the micromachines. Swimming trajectories and step-out frequencies of albumin microswimmers with varying designs: (A) A single-helix microswimmer, (B) double-helix microswimmer, and (C) microroller. The step-out frequencies are determined by stepwise increasing the actuation frequency. Credit: Science Advances, 10.1126/sciadv.abh0273

Magnetic actuation to steer the micromachines and properties of biodegradability

Ceylan et al. used rotational magnetic fields with a custom designed [Helmholtz coil](#) electromagnetic system mounted on an inverted microscope and observed how the single- and double-helix microstructures converted rotational motion into translational motion based on their [asymmetric body shape](#). Meanwhile, microrollers converted the rotation into directional mobility based on [nonslip contact](#) with the surface. By increasing the magnetic nanoparticles loaded into the micromachines, Ceylan et al. facilitated fast locomotion of the micromachines. In addition to that, biodegradability of the medical micromachines also formed an essential aspect for long-term biocompatibility of the devices. For example, after explanting the micromachines, they should ideally dissolve in nontoxic soluble compounds, since an extended presence of nondegradable micromachines can result in [chronic inflammation](#). To accomplish this, Ceylan et al. used [trypsin](#) as a model protease, or degrading enzyme, to understand the enzymatic degradability of micromachines. The scientists noted the degradation mechanisms and observed how the albumin microswimmers underwent rapid swelling followed by complete dissolution of their constituent hydrogel network under a variety of

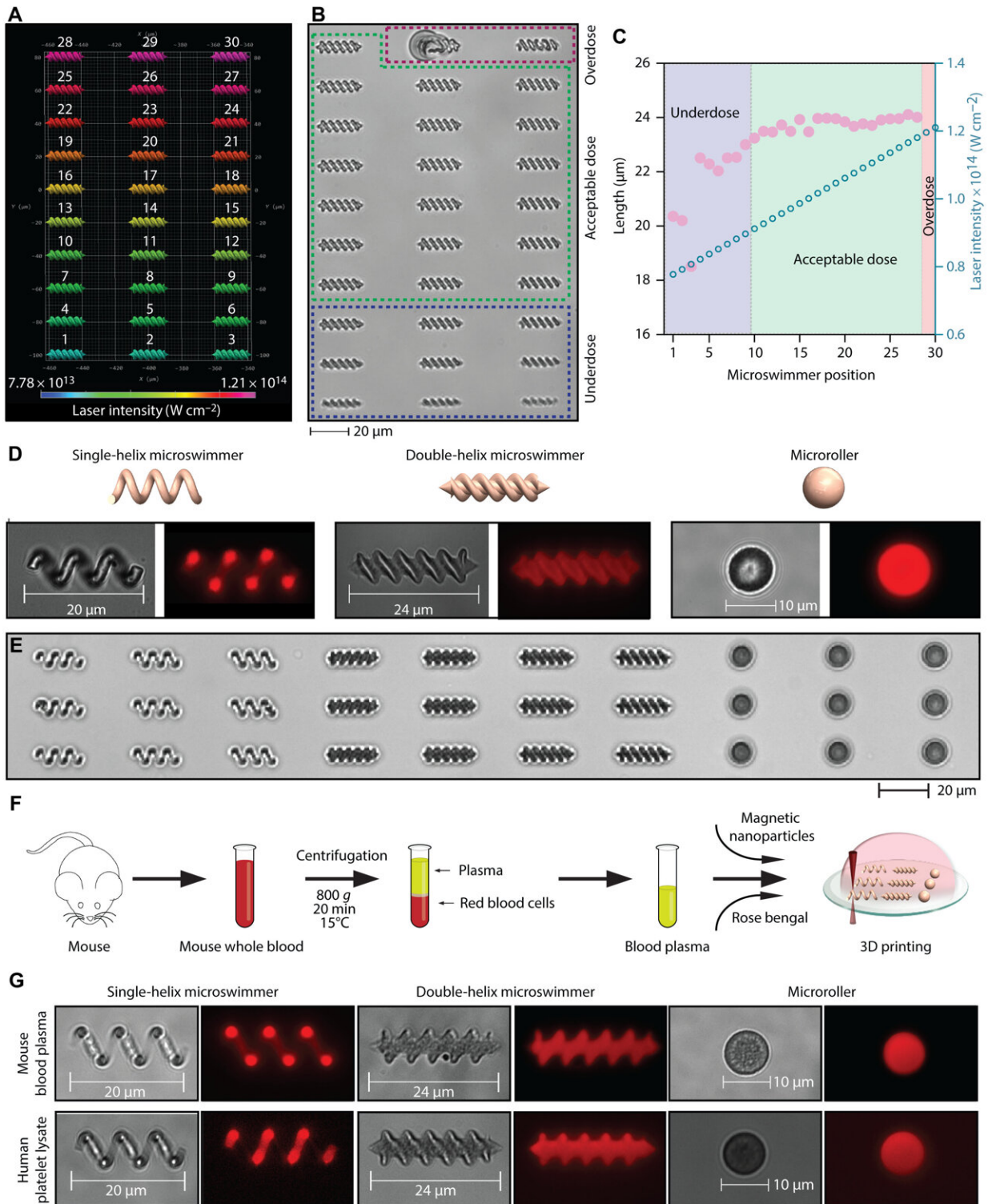
trypsin concentrations.

Cytotoxicity and pH-responsive shape memory behavior



Enzymatic degradation of the albumin microswimmers. (A) Enzymatic degradation observed under the time-lapse DIC imaging in the presence of trypsin enzyme at a concentration comparable to the pancreatic juice at 37°C . (B) An increase in the dimensions of albumin microswimmers during the degradation before the total collapse of the microswimmer fabric. (C and D) The biocompatibility of the degradation products of albumin microswimmers assessed by the viability of the exposed haMSCs at 24 hours. (C) Representative calcein acetoxymethyl ester/ethidium homodimer-1–stained fluorescence images of the exposed haMSCs. (D) The viability of the exposed haMSCs assessed based on the quantified intracellular adenosine 5′-triphosphate amount. Credit: Science Advances, 10.1126/sciadv.abh0273

The team further studied the biocompatibility of the micromachines by exposing cells to albumin microswimmers and to enzymatic degradation. The cytotoxicity tests detected the cellular membrane integrity and metabolic activity to indicate how the sensitive stem cells did not pose an acute toxic response. Since proteins also contain a variety of amino acid and carboxylic acid groups that can dynamically change the protonation state relative to the environmental pH, Ceylan et al. investigated albumin and platelet lysate microswimmers in the pH ranges of 2.5 to 12 and noted how the albumin microswimmers demonstrated shape memory behavior when the pH reverted to its original value. The products showed two-way [shape memory behavior](#) for stability and robustness in response to physiologically relevant extreme pH changes that are likely to occur in microenvironments.



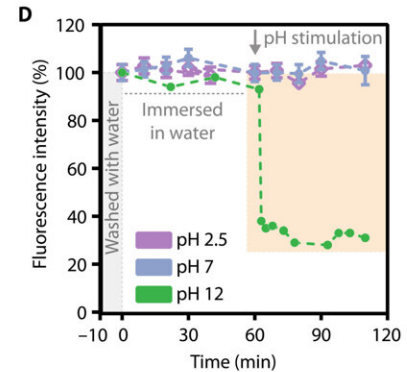
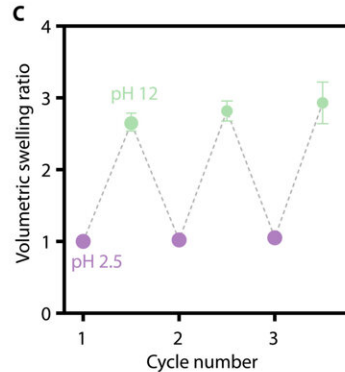
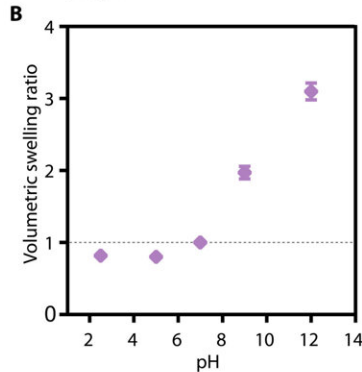
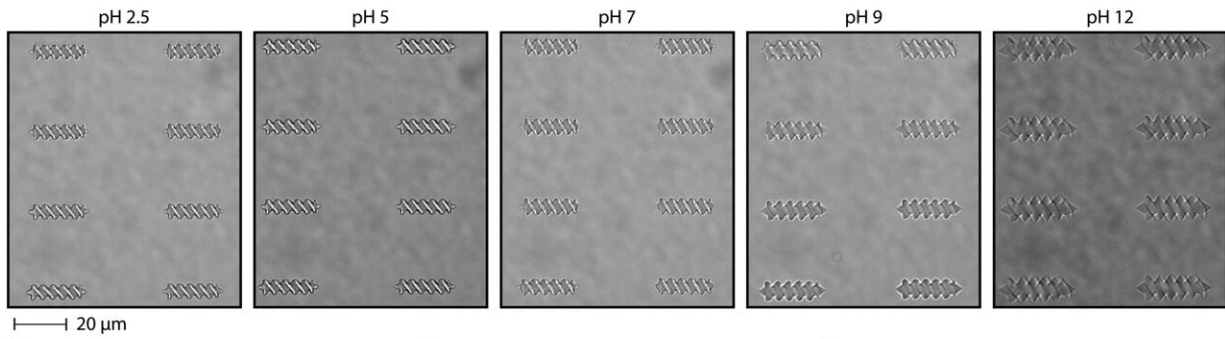
3D printed micromachines from bovine serum albumin, mouse blood plasma, and human platelet lysate. (A) A color-coded assignment of the systematically varied laser intensities for the fabrication of albumin microswimmer. (B) The

structural quality of the 3D printed albumin microswimmers assessed with differential interference contrast (DIC) imaging. (C) The length of the microswimmers measured as a function of the applied laser intensity. (D and E) DIC and fluorescence images of the 3D printed albumin-based micromachines. (F) Fabrication strategy of the mouse plasma micromachines. (G) DIC and fluorescence images of the 3D printed plasma and platelet lysate microswimmers. Credit: Science Advances, 10.1126/sciadv.abh0273

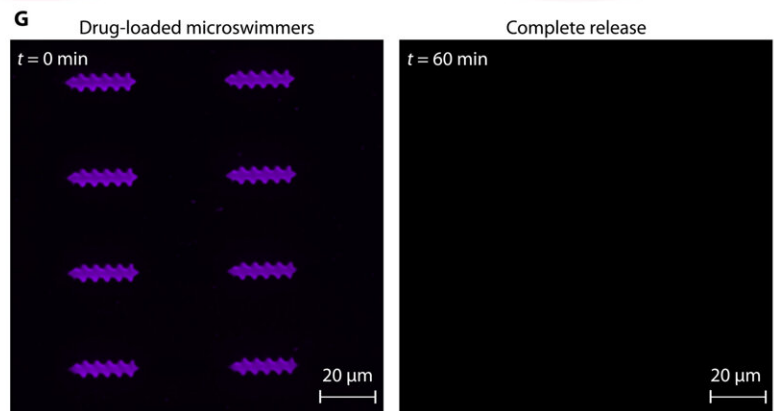
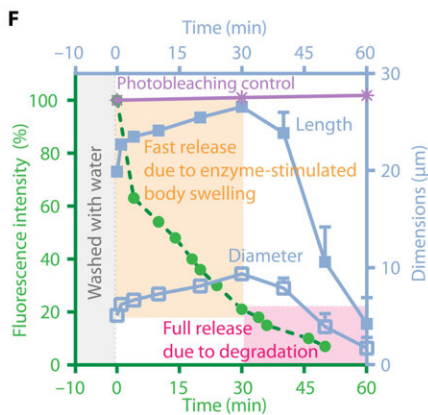
Stimuli-responsive cargo release

Drug delivery applications of medical micromachines also require [on-demand and on-target therapeutic release](#). For instance, smart material systems with responsiveness to external triggers and environmental changes can improve controlled cargo release. As a result, the pH and enzyme sensitive protein-based microswimmers served as environmentally responsive drug delivery and release platforms. As proof of concept, Ceylan et al. loaded a fluorescent small molecule drug analog and a deep red dye into a porous network of the albumin microswimmers and then tested the release of the molecule by probing the fluorescence intensity in the microswimmer relative to pH changes and enzymatic degradation in the physiological microenvironment. The team identified the inherent responsiveness to pH and proteases to tailor personalized micromachines for specific biomedical applications. The personalized robotic materials developed in this manner can affect the design of many medical robots and devices with improved biocompatibility.

A pH-responsive shape memory behavior



E Enzyme-mediated drug release



Stimuli-responsive shape memory albumin microswimmers. (A) pH-responsive albumin microswimmers. (B) The volumetric swelling ratio of the microswimmers as a function of pH. The swelling ratios are normalized to the initial volume at pH 7. (C) Two-way shape memory behavior of the microswimmers in response to pH change. (D) pH-stimulated, body swelling–driven drug release from the albumin microswimmers. (E) Trypsin–

stimulated two-step drug release dynamics from the microswimmers. (F) Trypsin-mediated cargo release kinetics at pH 7. (G) Representative fluorescence images of the drug-loaded microswimmers demonstrating the complete drug release with enzymatic degradation. Credit: Science Advances, 10.1126/sciadv.abh0273

Outlook

In this way, Hakan Ceylan and colleagues developed a new, protein-based micromachine with properties of pH sensitivity and enzyme degradability. They loaded iron oxide nanoparticles as magnetic transducers of the micromachines at [an acceptable level of safety](#). The study aimed to maximize the biocompatibility of materials while acknowledging the challenges of evading the immune system due to its synthetic constitution. Further investigations will assist them to also prevent [phagocytosis](#) of micromachines under a pathophysiological context.

More information: Hakan Ceylan et al, 3D printed personalized magnetic micromachines from patient blood–derived biomaterials, *Science Advances* (2021). [DOI: 10.1126/sciadv.abh0273](https://doi.org/10.1126/sciadv.abh0273)

Thomas Malachowski et al, Engineering nanoparticles to overcome immunological barriers for enhanced drug delivery, *Engineered Regeneration* (2020). [DOI: 10.1016/j.engreg.2020.06.001](https://doi.org/10.1016/j.engreg.2020.06.001)

Andre E. Nel et al, Understanding biophysicochemical interactions at the nano–bio interface, *Nature Materials* (2009). [DOI: 10.1038/nmat2442](https://doi.org/10.1038/nmat2442)

© 2021 Science X Network

Citation: Personalized 3-D magnetic micromachines from patient blood-derived biomaterials (2021, September 22) retrieved 20 March 2024 from <https://medicalxpress.com/news/2021-09-personalized-d-magnetic-micromachines-patient.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.