of all the H- and L-chain mutations required for bnAb activity against the native CD4bs. Indeed, no neutralizing activity was detected for any of the 8 eOD-GT8 60mer−induced Abs (all with high affinity (Kd < 1 nM) for eOD-GT8 and low affinity (1 µM < Kd < 100 µM) for core-e−2CC Hxb2 N276D) that we tested against a panel of four viruses from clades A and B that included both WT and N276A mutant viruses with increased sensitivity to VRC01-class bnAbs (fig. S16). One design feature of eOD-GT8 is that it lacks the N276 glycan; removal of this glycan is a requirement for germline reactivity (17, 27). However, the N276 glycosylation site is conserved in 94.5% of HIV strains, according to an analysis of 3706 sequences from the Los Alamos HIV database (www.hiv.lanl.gov/). Induction of broad neutralization will probably require one or more boosting immunogens bearing a glycan at N276 so as to select mutants to accommodate that glycan (27). On the H chain of VRC01-class bnAbs, mutations in the CDR2, CDR1, FW1, and FW3 are likely required for maximum potency and breadth (24, 40), and native-like Env immunogens will probably be needed to select for these. In sum, boosting with a sequence of increasingly native-like antigens, and potentially including cocktails of different antigens within each boost to mimic the antigenic diversity of the CD4bs, will likely be needed to select the mutations required for VRC01-class bnAb activity. The mouse model presented here, as well as other newly developed VRC01-class knock-in mouse models (41), should aid us to test this notion and can be used to identify the antigens and boosting strategies that work best. Of note, we demonstrated here that a single immunization with the eOD-GT8 60mer induces VRC01-class antibodies with modest affinity for the core-e−2CC Hxb2 N276D monomer and 60mer, so these molecules represent promising candidates for the first boost. We are thus mapping the core-e−2CC HxB2 N276D monomer and 60mer, VRC01-class antibodies with modest affinity for immunization with the eOD-GT8 60mer induces to test this notion and can be used to identify the 8 eOD-GT8 60mer induced Abs [all with high affinity (Kd < 1 nM) for eOD-GT8 and low affinity (1 µM < Kd < 100 µM) for core-e−2CC Hxb2 N276D] that we tested against a panel of four viruses from clades A and B that included both WT and N276A mutant viruses with increased sensitivity to VRC01-class bnAbs (fig. S16). One design feature of eOD-GT8 is that it lacks the N276 glycan; removal of this glycan is a requirement for germline reactivity (17, 27). However, the N276 glycosylation site is conserved in 94.5% of HIV strains, according to an analysis of 3706 sequences from the Los Alamos HIV database (www.hiv.lanl.gov/). Induction of broad neutralization will probably require one or more boosting immunogens bearing a glycan at N276 so as to select mutants to accommodate that glycan (27). On the H chain of VRC01-class bnAbs, mutations in the CDR2, CDR1, FW1, and FW3 are likely required for maximum potency and breadth (24, 40), and native-like Env immunogens will probably be needed to select for these. In sum, boosting with a sequence of increasingly native-like antigens, and potentially including cocktails of different antigens within each boost to mimic the antigenic diversity of the CD4bs, will likely be needed to select the mutations required for VRC01-class bnAb activity. The mouse model presented here, as well as other newly developed VRC01-class knock-in mouse models (41), should aid us to test this notion and can be used to identify the antigens and boosting strategies that work best. Of note, we demonstrated here that a single immunization with the eOD-GT8 60mer induces VRC01-class antibodies with modest affinity for the core-e−2CC Hxb2 N276D monomer and 60mer, so these molecules represent promising candidates for the first boost. We are thus mapping the first steps in a sequential strategy for the rational induction of bnAbs against HIV.

REFERENCES AND NOTES

REPORTS

SOFTWARE ROBOTICS

A 3D-printed, functionally graded soft robot powered by combustion

Nicholas W. Bartlett,1,2,† Michael T. Tolley,2,† Johannes T. B. Overvelde,1 James C. Weaver,2 Bobak Mosadegh,4 Katia Bertoldi,4 George M. Whitesides,5,6 Robert J. Wood1,2

Roboticians have begun to design biologically inspired robots with soft or partially soft bodies, which have the potential to be more robust and adaptable, and safer for human interaction, than traditional rigid robots. However, key challenges in the design and manufacture of soft robots include the complex fabrication processes and the interfacing of soft and rigid components. We used mulitmaterial three-dimensional (3D) printing to manufacture a combustion-powered robot whose body transitions from a rigid core to a soft exterior. This stiffness gradient, spanning three orders of magnitude in modulus, enables reliable interfacing between rigid driving components (controller, battery, etc.) and the primarily soft body, and also enhances performance. Powered by the combustion of butane and oxygen, this robot is able to perform unthethered jumping.

Robots are typically composed of rigid components to promote high precision and controllability. Frequently constructed from hard metals such as aluminum and steel, these robots require large machining equipment and an intricate assembly process. In contrast, recent work has explored the possibility of creating soft-bodied robots (7–6) inspired by invertebrates such as cephalopods (7–9) and insect larvae (10), as well as vertebrates, including snakes (11) and fish (12). The use of compliant materials facilitates the development of biologically inspired robotic systems (13) that are more adaptable (14), safer (15, 16), and more resilient (17) than their fully rigid counterparts.

The design and fabrication of soft robotic systems, however, present significant engineering challenges (18, 19). The bodies of soft robots are typically fabricated in custom-designed molds and require multiple assembly steps (20) or lost-wax techniques (21) to embed actuation. The molds used to create these soft robots are complex and time-consuming to make, especially for prototype designs that are fabricated in small numbers and are constantly evolving. Additionally, some applications (such as ones
We used a multimaterial 3D printer (Connex500, Stratasys) to directly print the functional body of a robot that employs soft material components for actuation, obviating the need for complex molding techniques or assembly (24). The robot body is composed primarily of two nested hemispheroids. The flexible bottom hemispheroid features a small depression that provides an initial volume into which oxygen and butane are injected. Ignition of the gases causes a volumetric expansion (25, 26), launching the robot into the air (Fig. 1, A and B). The top hemispheroid has a modulus of elasticity that ranges over three orders of magnitude (from approximately 1 MPa to 1 GPa) through a stepwise gradient of nine different layers, creating a structure that transitions from highly flexible (rubber-like) to fully rigid (thermoplastic-like). In addition to providing a mechanical interface for the rigid control components, the rigid portion of the top hemispheroid also prevents undesired expansion locally and focuses the energy of combustion into the ground, enhancing the jumping efficiency. Pneumatic legs, which use a nested hemi-ellipsoid design similar to that of the main body, surround the central explosive actuator and are used to tilt the body before a jump, controlling the direction of locomotion. This separation of power and control actuators simplifies actuation and gives greater control over direction.

In order to simplify prototyping, we chose a modular design with a rigid core module containing the control components (which are expensive and change infrequently during design iteration of the body), connected through a predefined interface to the body of the robot (Fig. 1C). This modularity enables efficient iteration of the robot body design, as well as rapid replacement in the case of destructive testing. The core module contains a custom circuit board, high-voltage power source, battery, miniature air compressor, butane fuel cell, bank of six solenoid valves, oxygen cartridge, pressure regulator, and an internal network of channels to facilitate interfacing between the components as necessary (fig. S1, A and B). The core module is mechanically attached to the rigid portion of the body with a layer of high-strength mushroom-head fasteners. Otherwise, it interfaces with the body only through four tubes (three pneumatic tubes for the legs and one tube for fuel delivery to the combustion chamber) and two wires (which produce the spark in the combustion chamber).

Characterization of nine 3D-printed materials with a set of mechanical tests informed the design of the 3D-printed rigid/soft robot. We performed qualitative twisting experiments to gain an intuitive understanding of the response of the various materials (Fig. 2A). Mechanical testing on a universal testing machine (Instron 5544, Instron) yielded quantitative values of material properties (supplementary text). This information was used to simulate the operation of the robot using finite element analysis (FEA) software, which allowed us to compare the relative efficiency of jumping robots with different
material distributions. Further simulations allowed us to examine the differences in stress concentrations as a function of material distribution (fig. S2). The results from these studies revealed that, when compared to an abrupt material transition, the incorporation of a graded interface could achieve a 30% reduction in maximum stress upon tensile loading, reaching a value comparable to the maximum stress observed in a soft, single-material model. Although a perfectly smooth gradient from rigid to flexible would have been ideal, the capability of the fabrication technique was limited to a stepwise gradient of at most nine materials. The actuation strategy necessitated a flexible bottom hemispheroid, whereas the off-the-shelf control components required a rigid housing; however, the stiffness distribution of the top hemispheroid was unconstrained. Thus, to determine how the material properties of the top hemispheroid would affect jumping, we simulated three cases: (i) a flexible top with a small rigid portion to mount control hardware, (ii) a top featuring a stiffness gradient from fully flexible to fully rigid, and (iii) a fully rigid top (Fig. 2B and movie S1). Simulations showed that the flexible top was inefficient at directing the energy of combustion into the ground and propelling the robot, suggesting weak jump performance. As expected, the simulated rigid top robot produced the highest ground reaction force, whereas the gradient top robot exhibited a performance between the two extremes.

We carried out additional simulations to investigate the behavior of the three designs during the impact of landing (Fig. 2C and movie S1).

Fig. 2. Material tests and simulation results. (A) Qualitative twisting analysis comparing 3D-printed beams that are fully flexible, half rigid and half flexible, or transition gradually from rigid to flexible. These tests were performed to gain an understanding of how these materials respond, as well as to validate the numerical values of the material properties used in simulation. (Left) Material distribution of the beams. (Middle) Beams under torsion. (Right) Simulation of beams under torsion. (B) Jumping simulation. (Left) Ground reaction force as internal gases expand. (Middle) Pressure evolution inside the robot body as internal gases expand. (Right) Deformation state of rigid top, gradient top, and flexible top robot bodies at the initial state and the point of maximum simulated gas expansion. Line thicknesses indicate material stiffness. (C) Impact simulation. In the simulation, the robot strikes the ground at 45°. This angle was chosen as a particularly extreme loading condition and because it correlated with observations from jumping experiments. (Left) Reaction forces experienced by the three robots upon striking a solid plane under simulated conditions representative of actual testing conditions. (Right) FEA results of rigid top, gradient top, and flexible top robots, compared at 50 N.
The results indicate that the rigid top robot experiences a given reaction force (50 N) at a much smaller deformation than either the gradient or flexible top robots. Immediately upon impact, the rigid top robot experiences an abrupt increase in force, whereas the gradient top robot experiences a more moderate increase. The flexible top robot sees almost no increase, until the small rigid portion strikes the ground, initiating a rapid increase akin to that of the rigid top robot. Integrating the force-displacement curves (up to 50 N), we find that the rigid and flexible top robots only absorb 13 and 73% (respectively) of the impact energy that the gradient top robot absorbs. The increased energy absorbed by the gradient top robot during impact suggests that it will be most successful at distributing the impulse over a longer duration, therefore reducing peak stresses and providing the least violent landing.

By 3D-printing different test cases, we experimentally verified these simulation results. A jumping robot with a completely rigid top was able to jump 1.12 m untethered using 40 ml of butane and 120 ml of oxygen. Identical testing conditions on a gradient top robot produced a jump of 0.25 m. A flexible top robot was deemed impractical to print because of the predictions from FEA. As predicted by the simulations, the gradient top robot was less efficient at jumping. However, the gradient top robot was better able to withstand the impact of landing (Fig. 3A and movie S2). In one test, the body of the rigid top robot shattered upon landing, surviving a total of just five jumps; the gradient top robot survived more than twice that number of jumps and remained operational. Other nearly identical gradient top robots survived over 100 jumps (in 81% of these tests, we removed the core module from the body and delivered the combustion products and ignition sparks through a tether to simplify testing, reducing the system mass to about 50% that of the untethered system). To provide a direct comparison in landing behavior; the gradient top robot was additionally dropped from the maximum height achieved by the rigid top robot and successfully survived 35 falls (supplementary text). The stiffness gradient provides the necessary rigidity to transfer the impulse of combustion to generate effective jumping, and the compliance of the base absorbs and dissipates the energy of the landing impact. By trading the jumping efficiency of the rigid robot for an improved ability to survive landings, the gradient top robot demonstrated a greater overall robustness.

Further testing on the gradient top robot showed high resilience and good performance (Fig. 3B and movie S2). This robot autonomously jumped up to 0.76 m (six body heights) high and demonstrated directional jumping of up to 0.15 m (0.5 body lengths, 20% of jump height) laterally per jump (Fig. 3C and movie S2). Unlike previous combustion-powered soft jumpers that were either tethered (25) or achieved only a few untethered jumps due to inconsistent connection of electrical and mechanical components at the interface of the rigid and soft components (26), this design allowed for many successful jumps with a single soft robot (21 untethered jumps and 89 tethered jumps). Another jumper design has also shown the ability to perform multiple jumps, can operate on uneven terrain, and can even recover from landing in any orientation (27), although at the sacrifice of directional control. In our system, the high energy density of the fuels theoretically allows onboard storage of sufficient fuel for 32 consecutive jumps (supplementary text). The bodies were extremely robust, surviving dozens of jumps before they became unusable. The monolithic design has no sliding parts or traditional joints that can be fouled or obstructed by debris or rough terrain, and the nested design requires minimal deformation for actuation. As with previous jumping soft robots powered by combustion (25–27), and untethered systems exposed to direct flames (17), we did not observe significant damage to the soft (or rigid) body materials due to the brief
exposure to elevated combustion temperatures and flames. The fabrication of soft robots using multi-material 3D printing has numerous advantages over traditional molding techniques. This strategy promotes high-throughput prototyping by enabling rapid design iteration with no additional cost for increased morphological complexity. By allowing designers greater freedom, 3D printing also facilitates the implementation of good robotic design principles, such as modularity and the separation of power and control actuators. Beyond soft robotics specifically, the ability to print a single structure composed of multiple materials enables investigation into mechanically complex designs, without the drawbacks of complicated assembly or inconsistent manufacturing repeatability. One such design is a modulus gradient that eases the transition from soft to rigid components through stress reduction at the interface of materials mismatched in compliance. Although the materials available to this fabrication strategy are currently limited and perhaps best suited to the fabrication of prototype devices, future development of materials compatible with 3D printing will only enhance the relevance of this approach.

APPLIED PHYSICS

Mid-infrared plasmonic biosensing with graphene

Daniel Rodrigo,1 O deta Limaj,1 Davide Janner,2 Dordaneh Etezadi,1 F. Javier García de Abajo,5,3 Valerio Pruneri,2,3 Hatice Altug1∗

Infrared spectroscopy is the technique of choice for chemical identification of biomolecules through their vibrational fingerprints. However, infrared light interacts poorly with nanometric-size molecules. We exploit the unique electro-optical properties of graphene to demonstrate a high-sensitivity tunable plasmonic biosensor for chemically specific label-free detection of protein monolayers. The plasmon resonance of nanostructured graphene is dynamically tuned to selectively probe the protein at different frequencies and extract its complex refractive index. Additionally, the extreme spatial light confinement in graphene—up to two orders of magnitude higher than in metals—produces an unprecedented high overlap with nanometric biomolecules, enabling superior sensitivity in the detection of their refractive index and vibrational fingerprints. The combination of tunable spectral selectivity and enhanced sensitivity of graphene opens exciting prospects for biosensing.

If graphic has the potential to reshape the landscape of photonics and optoelectronics owing to its exceptional optical and electrical properties (1–3). In particular, its infrared (IR) response is characterized by long-lived collective electron oscillations (plasmons) that can be dynamically tuned by electrostatic gating, in contrast to conventional plasmonic materials such as noble metals (4–10). Furthermore, the electromagnetic fields of graphene IR plasmons display unprecedented spatial confinement, making them extremely attractive for enhanced light-matter interactions and integrated mid-IR photonics (11–14). Specifically, biosensing is an area in which graphene tunability and IR light localization offer great opportunities.

The mid-IR range is particularly well suited for biosensing, as it encompasses the molecular vibrations that uniquely identify the biochemical building blocks of life, such as proteins, lipids, and DNA (15). IR absorption spectroscopy is a powerful technique that provides exquisite biochemical information in a nondestructive label-free fashion by accessing these vibrational fingerprints. Nevertheless, vibrational absorption signals are prohibitively weak because of the large mismatch between mid-IR wavelengths (2 to 6 μm) and biomolecular dimensions (<10 nm). To overcome this limitation, high sensitivity can be achieved by exploiting the strong optical near fields in the vicinity of resonant metallic nanostructures (16–18); however, this comes at the expense of a reduced spectral bandwidth and is ultimately limited by the relatively poor field confinement of metals in the mid-IR (29).

Here, we report a graphene-based tunable mid-IR biosensor and demonstrate its potential for quantitative protein detection and chemical-specific molecular identification. Our device (Fig. 1A) consists of a graphene layer synthesized by chemical vapor deposition and transferred to a 280-nm-thick native silica oxide of a silicon substrate. Graphene nanoribbon arrays (width W = 20 to 60 nm and period P = 2W) are then patterned using electron beam lithography and oxygen plasma etching (20). A scanning electron microscope image and an atomic force microscope profile for typical samples are shown in Fig. 1, B and C. We apply an electrostatic field across the SiO2 layer through a bias voltage (Vf).

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30. Materials and methods are available as supplementary materials on Science Online.
34. ACKNOWLEDGMENTS

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SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/349/6244/161/suppl/DC1
Materials and Methods
Supplementary Text
Figs. S1 and S2
Table S1
References (28, 29)
Movies S1 and S2
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