Supplementary Information

Heterogeneous silicon mesostructures for lipid-supported bioelectric interfaces

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Materials and Methods

Synthesis of mesostructured silicon (Si). Mesostructured Si materials were prepared by chemical vapor deposition (CVD) of Si inside mesoporous silica (SiO$_2$), followed by hydrofluoric acid (HF) etching to remove the template. Four types of mesoporous silica templates were adopted for the synthesis of mesostructured Si, including wheat-like SBA-15, rod-like SBA-15, sphere-like SBA-15, and KIT-6. Mesostructured Si synthesized from wheat-like SBA-15 was used for all the characterizations and applications shown in the main figures.

Wheat-like mesoporous silica SBA-15 was synthesized according to a previous report$^1$. Briefly, Pluronic P123 (Sigma-Aldrich, USA) was dissolved in a hydrochloric acid (HCl) (Sigma-Aldrich, USA) solution. Next, tetraethyl orthosilicate (TEOS) (Sigma-Aldrich, USA) was added and the mixture was stirred at 35 °C for 24 h. The chemical composition of the reaction mixture was 4 g P123: 0.04 mol TEOS: 0.24 mol HCl: 6.67 mol H$_2$O. The mixture was then aged hydrothermally at 100 °C. Finally, the powders were filtered, dried and calcined at 500 °C for 6 h.

Rod-like SBA-15 was synthesized following a previous report$^2$. 4.0 g of P123 was first dissolved in a mixture of 30 g of deionized (DI) water and 120 g of 2 M hydrochloric acid (HCl) by stirring at 35 °C overnight. 8.5 g of TEOS was then added to the aqueous solution under vigorous stirring. The mixture was stirred for 5 min before being kept under static condition at 35 °C for 20 h. The product was aged at 100 °C for another 24 h. After filtering and washing with water, the final product was dried and calcined at 550 °C for 6 h.

Sphere-like SBA-15 template was made based on a previous report using cetyltrimethylammonium bromide (CTAB) as a co-surfactant and ethanol (EtOH) as a co-solvent$^3$. In a typical synthesis, 3.0 g of P123 was dissolved in 60 mL of 1.5 M HCl while 0.6 g CTAB (Sigma-Aldrich, USA) was mixed with a separate 25 mL of water. After both surfactants have been dissolved, two solutions were mixed together and 20 mL of 100% EtOH (Thermo-Fisher Scientific, USA) was added to the mixture. 10 mL of TEOS was then added dropwise to the above mixture solution of surfactants under vigorous stirring (~500 rpm). After stirring at 35 °C for 45 min, the mixture was kept static under 75 °C for 10 h and aged at 100 °C for another 24 h. The product was filtered, washed, dried and calcined at 550 °C for 6 h.

The synthesis of KIT-6 template followed a previous report using n-butanol (BuOH) as a co-solvent$^4$. 6 g of P123 was dissolved in 217 g of DI water and 11.8 g of concentrated HCl (37%). 6 g of BuOH (Sigma-Aldrich, USA) was added under stirring at 35 °C. After 1 h stirring, 12.9 g of TEOS was added at 35 °C to make the molar ratio as TEOS : P123 : HCl : H$_2$O : BuOH = 1 : 0.017 : 1.83 : 195 : 1.31. The mixture was left under stirring for 24 h at 35 °C, and subsequently heated for 24 h at 100 °C under static conditions. The solid product obtained after hydrothermal treatment was filtered and dried at 100 °C without washing. The template was removed by calcination at 550 °C for 6 h.
Next, the as-synthesized mesoporous SiO$_2$ powder was loaded close to the bottom of a small quartz tube (diameter: ~1.5 cm), which serves as the inner reactor. The inner tube containing SiO$_2$ template was then placed into the center of an outer quartz tube (diameter: ~2.5 cm) for CVD. Si was deposited at 500 °C and 40 Torr using silane (SiH$_4$) as the Si precursor and hydrogen (H$_2$) as the carrier gas. In a typical synthesis of mesostructured Si, we used 200 mg of SiO$_2$ template, with flow rates of H$_2$ and SiH$_4$ set at 60 and 2 standard cubic centimeters per minute (sccm), and a total CVD duration of 120 min. Subsequent HF (Sigma-Aldrich, USA, 48%) etching for 5-10 min was used to remove the template at room temperature. The etched samples were filtered, rinsed with DI water, isopropanol (IPA) and dried in air. The final product is in brownish powered form.

**Electron microscopy.** Mesostructured Si was sonicated in IPA, and then dispersed onto Si wafers (Nova Electronic Materials, USA, p-type, 0.001 Ω·cm) for scanning electron microscopy (SEM) (Carl Zeiss, Germany, Merlin FE-SEM) and over copper grids (Ted Pella Inc., USA, Lacey Formvar/Carbon, 200 mesh) for transmission electron microscopy (TEM) (FEI, USA, Tecnai F30). The high-angle annular dark field (HAADF) scanning transmission electron microscope (STEM) images were recorded using an aberration corrected STEM (JEOL, Japan, JEM-ARM200CF). The electron-dispersive X-ray spectroscopy (EDX) maps were collected simultaneously with HAADF images using the same microscope equipped with an Oxford X-Max$^N$ 100TLE windowless SDD X-ray detector (Oxford Instruments, UK). For *in-situ* heating TEM study, samples were dispersed on molybdenum grids (Structure Probe Inc., USA, Holey Carbon, 200 mesh) and imaged using a JEOL JEM-3010 (JEOL, Japan) with a double-tilt heating stage (Gatan Inc., USA, Model 652). The temperature ramping was set as 50 °C/min from ambient to 900 °C. Images were taken at room temperature, and at 10 min, 30 min, 60 min, 90 min and 120 min time points at 900 °C.

**Nitrogen sorption measurements.** Nitrogen sorption isotherms were collected on a Micromeritics ASAP 2020 (Micromeritics, USA) surface area and pore size analyzer at 77 K. Pore size distribution was calculated in the Micromeritics ASAP2020 software package (assuming slit pore geometry), using a non-linear density functional theory (NLDFT) model. All samples were degassed at 180 °C overnight prior to experiment. For all measurements, ultra high purity (UHP) grade helium (He) and nitrogen (N$_2$) were used.

**Small angle X-ray scattering (SAXS).** SAXS measurements were conducted at the 12ID-B station at the Advanced Photon Source (APS), Argonne National Laboratory (ANL). The wavelength of the X-ray beam was 0.8856 Å, and the beam size was 0.20(H) × 0.03(V) mm$^2$. The detector for SAXS measurements was the Pilatus 2M (DECTRIS Ltd., Switzerland). The exposure time was set to 1 s for all measurements and the sample-to-detector distance was about 2 m, which allows covering scattering momentum transfer, $q$, up to 1.0 Å$^{-1}$. The $q$ value calibration was performed using silver behenate prior to measurements. The isotropic 2-D images were converted to 1-D scattering profiles using the Matlab software package developed
at the beamline. For static SAXS measurements, powder samples were sandwiched with kapton tapes and loaded onto the sample holder. For in-situ heating SAXS measurements, samples were first pelleted and loaded in a Linkam TS1500 heating stage (Linkam Scientific Instruments Ltd., UK). The sample chamber of the heating stage was sealed and purged with N\textsubscript{2} during the whole heating process. The temperature ramping rate was set as 60 °C/min and the first temperature set point was 800 °C. After reaching the set point, the temperature was fixed at 800 °C for 20 min, 900 °C for 20 min and 1000 °C for 20 min, respectively. SAXS data were collected every 38 s. For in-situ stability assays in aqueous systems, 1× phosphate buffered saline solution (PBS) or 0.60 mg/mL collagen hydrogel were added into individual quartz capillary tubes (O.D.,1.5 mm), respectively. Powders were subsequently added into the tubes and mixed with solution or gel to form suspensions at room temperature. Data were collected every 30 min in the first 6 h and every 2 h in the last 6 h.

Transmission X-ray microscopy (TXM). Absorption full-field nano-computed tomography (nano-CT) was performed on the new transmission X-ray microscope at sector 32-ID of APS in ANL. Mesostructured Si was first mounted onto a micromanipulator installed in a focused ion beam (FIB) system (FEI, USA, Nova 600 NanoLab). The micromanipulator was secured on a custom-built holder for data collection. Acquisition was conducted with a monochromatic beam tuned at 8 keV. The condenser and the objective lens used are diffracting optics developed in-house. X-rays are focused to the sample thanks to a beam-shaping condenser (BSC), i.e., a mosaic of diffraction gratings organized in concentric rings. The round BSC can collect a large portion of the beam with its diameter of 1.6 mm. Gratings in each rings have spacing decreasing down to 60 nm at the optic periphery. A 180 µm large Fresnel zone plate with 60 nm outer most zone width was used as a microscope objective lens in order to magnify radiographs of the sample placed on a high accuracy air-bearing rotary stage. With a distance CCD-sample set to 3.4 m, a magnification of ~47 was obtained. The X-ray detection system corresponds to an assembly comprising a scintillator (LuAG), a 5× microscope objective, a 45° mirror and a low noise fast CCD cooled at -40 °C. The voxel width obtained in this geometry was 27.6 nm and the field of view was about 70 × 60 µm\textsuperscript{2} while the illumination coming from the BSC was a disk slightly larger than 70 µm. The true spatial resolution given by the zone plate is ~60 nm. 3D reconstructions were performed with the software Tomopy (http://www.aps.anl.gov/tomopy/), an open source Python based toolbox for the analysis of synchrotron tomographic data.

The 3D iso-intensity surfaces were constructed and visualized using Amira 5.5 (FEI Visualization Sciences Group). Segmentation of intra- and inter-granular voids was carried out based on intensity. Inter-granular voids were assigned to intensity value less than -0.00015. Intra-granular voids were determined manually by choosing low intensity regions within particles slice by slice using a magic wand tool.

Atom-probe tomography (APT). Mesostructured Si particles were transferred onto Si microposts using a micromanipulator installed in a focused ion beam (FIB) system (FEI, USA,
Nova 600 NanoLab). Samples were then mounted and milled into needle-like microtip specimen for APT characterization. The APT was run in an ultraviolet (UV) laser-assisted local-electrode atom-probe (Cameca, USA, LEAP 400XSi). Surface atoms from a microtip were evaporated with an applied voltage of 1-6 kV and the assistance of a 30 pJ UV (wavelength $\lambda=355$ nm) laser pulsing at 250 kHz frequency. The mass-to-charge ($m/z$) ratios of individual evaporated ions and their corresponding ($x, y, z$) coordinates in space were recorded with a position sensitive detector. The samples were held at 30 K and $2 \times 10^{-11}$ Torr during APT experiments. The 3D reconstructions and data analyses were performed using Cameca’s Integrated Visualization and Analysis Software (IVAS) 3.4 code. Typical regions of both Si nanowires (Fig. 2c, left panel) and micro-bridges (Fig. 2c, right panel) were cropped from Fig. 2b using a region-of-interest (ROI) tool in IVAS. A series of Si isoconcentration surface from 50 at.% to higher concentrations were created for both regions (Fig. 2e), i.e., nanowires and micro-bridges until no isoconcentration surface with higher atomic concentration could be created. Proximity histograms (Fig. 2d) were calculated using the 60% Si isoconcentration surface of the dataset in Fig. 2b, and included information of both Si nanowires and inter-connecting micro-bridges. For histogram shown in Fig. 2e, the number of Si atoms per Si concentration interval was calculated by subtracting the total number Si atoms enclosed within one isoconcentration surface from the precedent isoconcentration surface. For example, the number of Si atoms that is 50-51 at.% is the difference between the total Si atoms enclosed in 50% isoconcentration surface and that in 51% at.%. The Si concentration distribution was plotted by calculating the relative frequency of the number of Si atoms per Si atomic concentration.

**Electrical measurements.** Mesostructured Si particles were gently sonicated in IPA and dispersed onto Si substrates (Nova Electronic Materials, 600 nm oxide, $p$-type, 0.001 $\Omega \cdot$cm) with photo-lithographically patterned gold electrodes. Electrical contacts onto individual Si particles were made with an FIB system (FEI, USA, Nova 600 NanoLab) by depositing platinum (Pt) wires with a built-in gas-injection system (GIS). The electrical conductance measurements were evaluated using a dual-channel source-meter (Keithley 2636A) and a probe station (Rucker & Kolls, Model 680A). The particles were then removed from the interconnects by sonication and the conductance was subsequently measured as controls.

**Atomic force microscopy (AFM) measurements.** Force curves were collected using an Asylum MFP-3D AFM (Asylum Research, USA) with ACTA (AppNano, USA, nominal spring constant 40 N/m) probes in air and AC240 (Olympus, Japan, nominal spring constant 2 N/m) probes in liquid. Prior to measurements, the inverse optical lever sensitivity and cantilever spring constant were calibrated following vendor’s standard procedures. For all measurements, mesostructured Si particles were first transferred onto Si substrates (Nova Electronic Materials, USA, $p$-type, 0.001 $\Omega \cdot$cm). Prior to solution phase AFM experiments, samples were also soaked in $1 \times$ PBS solution at room temperature for ~2 h. Force curves were recorded by loading at a rate of 1$\mu$m/s up to an indentation depth of ~10 nm, followed by unloading at the same rate. For both measurements in air and in fluid, ten particles were chosen to take force curves by making
indentations on random sites over the particle surfaces. The total number of data points is \(n=138\) for the sample in air and \(n=94\) for the sample in liquid. Asylum Research software was used for data collection and analysis. Oliver-Pharr method was used by fitting the range between 25% and 75% of maximum indentation of the retraction curve. The as-calculated value was reduced Young’s modulus \(E_c\), which was comprised of the indenter and sample’s Young’s modulus (\(E_i\) for indenter, \(E_s\) for sample) and Poisson ratio (\(\nu_i\) for indenter, \(\nu_s\) for sample) by \(1/E_c=(1-\nu_i^2)/E_i+(1-\nu_s^2)/E_s\). The indenter’s Poisson’s ratio was 0.17 and its Young’s modulus was 150 GPa, for both Si cantilevers. The sample’s Poisson's ratio was chosen as 0.10 from literature\(^5\). Based on the equation, \(1/E_c=(1-\nu_i^2)/E_i+(1-\nu_s^2)/E_s\), it is noted that even an appreciable deviation in the Poisson’s ratio will not introduce significant error into the calculated sample modulus\(^5\).

**Ultraviolet-visible (UV-vis) spectroscopy.** Prior to measurements, mesostructured Si powders were soaked in \(1\times\) PBS for 0 h, 2 h, 12 h and 24 h. After filtration and rinsing with DI water, samples were re-dispersed in IPA and drop casted over glass slides and air dried. The thickness of the Si films was \(~20\ \mu\text{m}\), as determined by profilometer (Bruker, USA, Dektak XT-S). Diffuse reflectance UV-Vis spectra were collected on a Cary 5000 UV-Vis-NIR spectrometer (Varian, USA) equipped with a diffuse reflectance accessory (DRA). The acquired diffuse reflectance spectra were converted to Kubelka-Munk functions defined as \(F(R) = (1-R)^2/2R\), where \(R\) is reflectance. Tauc plots were then plotted to calculate band gap energies.

**Raman spectroscopy.** Prior to measurements, mesostructured Si powders were soaked in \(1\times\) PBS for 0 h, 2 h, 12 h and 24 h. Raman spectra were recorded using a LabRAM HR evolution system (Horiba, Japan), with samples immersed in PBS solutions.

**Cell/Si interface imaging.**

**A. High-pressure freezing and freeze-substitution.** Human umbilical vein endothelial cells (HUVEC) were first seeded on a transwell with 96 permeable supports (Corning Inc., USA, polyester membrane, pore size, \(1.0\mu\text{m}\)) and cultured in Medium 200 (Life Technologies, USA) until reaching confluency. Mesostructured Si particles (~0.01 mg) were added to the transwell, which settled down within 15 min. The polyester membrane was peeled off from the well and transferred to an aluminum planchet, with excess space filled with 1-hexadecene (Sigma-Aldrich, USA). Samples were frozen in a Baltec HPM 010 high-pressure freezer (Technotrade, USA) and then freeze-substituted in 0.25% glutaraldehyde (Electron Microscopy Sciences, USA) and 0.1% urinal acetate (Electron Microscopy Sciences, USA) dissolved in anhydrous acetone (Electron Microscopy Sciences, USA), using an automated freeze substitution machine (AFS2, Leica Microsystems, Germany). The temperature increased from \(-180 °C\) to \(-80 °C\) in 12 h and stayed at \(-80 °C\) for 72 h. The temperature was then ramped from \(-80 °C\) to \(-20 °C\) over 12 h. Samples were washed with anhydrous acetone three times at \(-20 °C\), then transferred to \(4 °C\), held overnight, and warmed to room temperature. Samples were then infiltrated with increasing concentrations of epoxy resin in anhydrous acetone (low viscosity Spurr, Ted Pella Inc., USA, 20%, 25%, 33%, 50%, and 100%; v/v) and finally solidified at \(60 °C\) for 24 h. Epoxy sections of
~100 nm were cut using a ultramicrotome (Ultracut E, Reichert-Jung, USA) collected on copper grids (Electron Microscopy Sciences, USA, 200 mesh). Sections were stained with 2% (w/v) uranyl acetate and 0.5% (w/v) lead citrate (Electron Microscopy Sciences, USA). Samples were imaged using a Tecnai F30 TEM (FEI, USA).

B. Chemical fixation. HUVECs and mesostructured Si mixture were prepared in the same way for freeze substitution on transwell membranes. The samples were fixed with 2% glutaraldehyde and 4% paraformaldehyde (Electron Microscopy Sciences, USA) in 0.1 M sodium cacodylate buffers (Electron Microscopy Sciences, USA) overnight at 4 °C. The samples were then washed three times with sodium cacodylate buffers for 5 min each time. After replacing with 1% osmium tetroxide (Electron Microscopy Sciences, USA) in sodium cacodylate buffers and incubating for 60 min, the samples were washed twice with sodium cacodylate buffers for 5 min each time. Maleate buffers (Electron Microscopy Sciences, USA, pH 5.1) were then used to rinse the samples for 5 min. The samples were subsequently stained with 1% uranyl acetate in maleate buffers for 60 min. After the staining, the samples were washed three times with maleate buffers with 5 min each time. The following dehydration process involves a series of washing steps with increasing concentrations of acetone in maleate buffers (25% 2×5 min, 50% 2×5 min, 70% 2×5 min, 95% 2×5 min, 100% 3×15 min; v/v). The infiltration process was performed in the same way as that used in freeze-substitution method (epoxy in anhydrous acetone, 20%, 25%, 33%, 50%, and 100%; v/v). The final epoxy resins were solidified at 60 °C for 24 h. Epoxy sections were cut, stained and imaged in the same way as those used for freeze substitution.

In vitro Si degradation. A series of samples with 50 µg, 100 µg and 300 µg mesostructured Si in 1 mL of 1× PBS solution were incubated at both room temperature and 37 °C. An aliquot of 0.5 mL solution was removed at different time points from each tube and diluted with 4.5 mL 2% HNO₃ and subjected to analysis by inductively coupled plasma optical emission spectroscopy (710 ICP-OES, Agilent Technologies, USA). 0.5 mL of fresh PBS solutions were added back each time to all tubes. For each group of samples, 5 independent tests were performed (i.e., n = 5).

Calcium imaging. HUVECs were first cultured on petri dishes to reach a confluency of ~80% before experiments. Cells were stained with 1 µM Fura-2 AM (Life Technologies, USA) for 30 min and washed three times with a HEPES-buffered Tyrode’s solution (119 mM NaCl, 5 mM KCl, 25 mM HEPES, 2 mM CaCl₂, 2 mM MgCl₂, 6 g/L glucose, pH 7.4). Solid silicon particles were prepared by mechanically grinding of a silicon wafer (Silicon Quest, USA, p-type, 1-10 Ω cm). Both mesostructured and solid Si particles were immersed in HEPES-buffered Tyrode’s solutions overnight before applying to the stained cell cultures. About 0.01 mg of Si particles were delivered and allowed to settle down for about 5 min to form interfaces with cells. Glass pipettes with tip diameters of ~1.5 µm were pulled in a flaming/brown type micropipette puller (P-97, Sutter Instruments, USA). Micropipettes were filled with the same Tyrode’s solution as the bath and controlled with a motorized micromanipulator (PatchStar, Scientifica, UK).
general, only particles sitting on cell bodies, with lateral sizes of ~5 µm, were chosen. Glass pipettes were approached vertically using the micromanipulator and the pipette resistances were monitored in real time. The contact point was determined by the time where a transient or steady increase in the pipette resistance was observed. After making contact with the particles, pipettes were lowered by another 1 µm and held still for 20 s before retraction. During the whole process, fluorescence images were collected using an upright microscope (BX61WI, Olympus, Japan) equipped with an EM-CCD camera (C9100-13, Hamamatsu Photonics, Japan). Images from excitation wavelengths at 340 nm and 380 nm were taken every 1 s. Ratiometric information was obtained from the images collected at 340 nm and 380 nm, and was used for quantitative analysis in MetaFluor software (Molecular Devices, USA). The amplitude and the slope of the ratio changes after mechanical perturbation were defined in Fig. 3e, and statistically compared between porous/mesostructured/amorphous and solid/single crystalline Si samples. The amplitude was calculated as a ratio between the peak ratiometric difference and the baseline. The slope was determined by linear fitting of the range between 25% and 75% of the maximum from baseline.

**Cytotoxicity assays.** HUVEC (Life Technologies, USA), C2C12 cells (ATCC, USA) and human aortic smooth muscle cells (HASMC) (Life Technologies, USA) were seeded in 96-well plates and settled down for 1 d prior to applying mesostructured Si particles. The particles were added to make the final concentration as 0.1 mg/mL in each well. In the positive control groups, no particles were added. On days 1, 3, 5, 7 of the co-culture with Si particles, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (Life Technologies, USA) were added and the mixtures were incubated for 4 h at 37 °C. Dimethyl sulfoxide (DMSO) (Thermo Fisher Scientific, USA) was added to dissolve the as-formed formazan after all the solutions were removed. After 10 min incubation at 37°C, the absorbance of the DMSO solution in each well was recorded with a multi-plate reader (Tecan Group Ltd., Switzerland, Infinite 200 PRO) at 570 nm. For each group, n=8.

**In vivo Si biocompatibility and degradability.** The animal protocol used for this study was in accordance to the policies of the University of Chicago and were approved by the Institutional Animal Care and Use Committee (IACUC). Young adult male CD® IGS rats weighing 226~250 g were ordered from Charles River Laboratories (USA) and housed in pairs in a 6 AM–6 PM light dark cycle. Mesostructured Si and sodium carboxymethyl cellulose (CMC, MW ~250,000, Sigma-Aldrich, USA) were sterilized by UV irradiation for 24 h. Si particles were suspended in 1% CMC solution of 1× PBS and sonicated for 1 h before being loaded into 1 mL syringes under sterile conditions. CMC was added as a stabilizing agent to prevent the aggregation and sedimentation of mesostructured Si particles in saline, and it is biocompatible. Anesthesia was induced briefly, prior to injection, with isoflurane in 100% oxygen. Each rat received one subcutaneous injection of 5 mg mesostructured Si in 0.5 mL of 1% CMC. 1 day, 7 days and 21 days after the injection, four rats were sacrificed at each time point for examination. Tissues retrieved from the necropsy were fixed in 10% neutral buffered formalin (Sigma-Aldrich, USA),
embedded in paraffin, sectioned, and stained with hematoxylin and eosin for histological examination using standard techniques and then reviewed by a pathologist.

**Artificial lipid bilayer experiments.**

**A. Experimental setup.** An inverted microscope (Zeiss IM35, Germany) was used with a 10×/0.25 NA and a 40×/0.55NA lens to deliver focused laser pulses with spot sizes in diameter of ~40 µm and ~10 µm, respectively. The beam of the diode-pumped solid-state (DPSS) laser (UltraLaser, Canada) was modulated with an acousto-optic modulator (NEOS Technologies, USA), controlled by transistor-transistor logic (TTL) pulses, delivered individually or in trains of pulses at desired frequencies by a custom-made circuit board. Voltage- and current-clamp protocols were done by an Axopatch 200B amplifier (Molecular Devices, USA), controlled by a personal computer (PC) through a digital-to-analog converter (Innovative Integration SBC-6711-A4D4, USA) with an in-house program control. Analog data were low-pass filtered by an 8-pole Bessel filter (Frequency Devices 950L8L, Canada), converted into digital signal by the same board and acquired by a PC. Patch pipettes were pulled in a CO\textsubscript{2} laser micropipette puller (Sutter Instruments P-2000, USA) and polished in a custom-made microforge for a final resistance of 2-4 M\textOmega when filled with adequate solution. For the temperature measuring experiments, the resistance of a positioned patch pipette was monitored and recorded by an OC-725A amplifier (Warner Instrument, USA). Experiments to measure capacitance change were carried out with a sinusoidal command voltage using a function generator (Krohn-Hite 1200A, USA).

**B. Lipid bilayer formation.** Asolectin lipids (25 mg/mL in chloroform, soybean polar lipid extract, Avanti Polar Lipids, USA) were smoothed in a test tube to form a thin film, and then dried inside a nitrogen desiccator for about an hour before use. The film was dissolved in n-decane (Thermo-Fisher Scientific, USA) in order to produce a lipid mix with final concentration 25 mg/mL. A custom-made upper chamber containing a 300 µm diameter hole for planar lipid bilayer formation was used and placed in a glass-bottomed lower chamber. Typically, 1 µL of the lipids in n-decane was deposited on the upper chamber hole and let dry for about 15 minutes. Afterwards both chambers were filled with bilayer bath solution (in mM: KCl 90, HEPES 10; pH 7.4). Each chamber was then connected to the patch amplifier headstage through Ag/AgCl hemicells via salt bridges made with 1% ultrapure agar (USB Corp., USA) melted in a solution containing 1M N-methyl-D-glucamine (NMG) (Sigma-Aldrich, USA) and 10 mM HEPES, pH 7.4. A lipid bilayer was painted with an air bubble held by a pipette tip. The formation of the lipid bilayer was monitored under voltage clamp by observing the current responses to a 1V/s voltage ramp. The recording electrode was connected to the lower chamber and the reference electrode was connected to the top chamber. Data was low-pass filtered at 50 kHz by the 8-pole Bessel filter and sampled at 200 kHz.

The material was grinded and sonicated to roughly spherical shape of ~ 1-2 µm in diameter. Approximately 0.01 mg of mesostructured Si particles were delivered into the upper bath solution and allowed to settle down for about 5 min. Most of the particles sank to the bottom of
the upper chamber and made contact with the bilayer. The laser power was adjusted by a set of neutral density filters manually. The laser pulse frequency and duration were controlled by the in-house software and external custom-made hardware. For these experiments we used the 10× objective lens which produced a laser spot size approximately 40 µm in diameter.

C. Capacitance measurements. Briefly, the current responses of the bilayer were recorded when a 5 kHz sinusoidal carrier voltage signal was concurrently used as the voltage command, while Si-based film was illuminated by the laser pulses. Upon stimulation, if the bilayer impedance was altered, the magnitude and the phase of the output current would change. Since the impedance is inversely related to the capacitance, an increase in bilayer capacitance due to a temperature rise would lower the impedance, resulting in an increase of output current with the same phase angle with respect to voltage. After low-pass filtered at 20 kHz and sampled at 100 kHz, the sinusoidal current output signals were rectified, and low-pass filtered at a cutoff frequency of 2 kHz. The difference of the current outputs, with and without the laser stimulation, reflects the capacitance change in the bilayer.

D. Local temperature measurements. During the bilayer stimulation experiment, a pipette electrode (2~4 MΩ) filled with bilayer bath solution was placed adjacent to the stimulation site. As the solution inside the pipette was the same as in the bath, the effect of liquid junction potential is diminished, i.e., no ionic gradient across the pipette tip. The resistance of this temperature-monitoring electrode was recorded. After the stimulation experiment, the temperature-monitoring electrode was placed carefully into a chamber with bilayer bath solution pre-heated to about 50 °C. A thermocouple was positioned close to the pipette tip. A calibration curve was constructed, based on the pipette resistances in the range of 50 to 20 °C. Subsequently, the calibration curve was used to estimate the temperature change from the pipette resistances values recorded earlier.

E. Capacitive current recording. Capacitive currents were recorded in voltage-clamp mode. A laser pulse was delivered to the preparation 300 ms after the voltage was jumped from a holding potential of 0 mV to the desired voltage. The amplifier output was low-pass filtered at 50 kHz and sampled at 200 kHz.

Dorsal root ganglia (DRG) neurons experiments.

A. DRG culture. DRGs were extracted from decapitated P1-P3 Sprague-Dawley rats and were placed immediately in Dulbecco’s modified eagle medium (DMEM) (Life Technologies, USA) on ice. The ganglia were transferred to a 0.25% solution of trypsin (Worthington, USA) in Earle’s balanced salt solution (EBSS) (in mM: NaCl 132, KCl 5.3, HEPES 10, NaH₂PO₄ 1, glucose 5.5; pH 7.4) and placed for 20 min in a 37 °C shaker. Afterwards, the cells were centrifuged and the supernatant was replaced with EBSS added with 10% fetal bovine serum (FBS) (ATCC, USA). After mechanically dispersing the cells with pipetting, they were centrifuged and the supernatant was replaced with DMEM containing 5% FBS. Next, cells were seeded into poly-L-lysine (PLL) (Sigma-Aldrich, USA) coated glass-bottom Petri dishes, and
allowed 30 min for cell adhesion. Finally, the dishes were flooded with DMEM supplemented with 5% FBS, 100 U/ml penicillin (Sigma-Aldrich, USA), and 100 µg/ml streptomycin (Sigma-Aldrich, USA), and incubated at a 37 °C chamber with 5% CO₂ until used for experiments. The DRG neurons are ready for use in about 3 hours and can be used for experiment for about a week.

The animal protocol used in this step was in accordance to the policies of the University of Chicago and were approved by the Institutional Animal Care and Use Committee (IACUC).

**B. Electrophysiology.** Before the experiment, supplemented DMEM in the Petri dish with DRG neurons was rinsed three times with recording solution (in mM: NaCl 132, KCl 4, MgCl₂ 1.2, CaCl₂ 1.8, HEPES 10, glucose 5.5; pH 7.4). About 0.01 mg of mesostructured Si particles were delivered and settled for approximately 5 min. In general, we visually selected a DRG neuron with a single particle (size: ~ 2 µm) attached to the soma for patching. Desired neurons were patched with a ~2 MΩ pipette, filled with pipette solution (in mM: NaCl 10, KCl 150, MgCl₂ 4.5, EGTA 9, HEPES 10; pH 7.3). Voltage recordings were made in current clamp mode. Every three seconds, a 1 ms suprathreshold amplitude current injection was delivered to the neuron to assess its excitability and followed by a 1 ms laser pulse, 300 ms later. We used the 40× objective lens for these experiments, therefore a 10 µm diameter laser spot was delivered to the preparation. Then we determined the minimal power enough to elicit action potentials (APs) and applied it in trains of laser pulses at different frequencies. Spike responses elicited by either individual pulses or pulse trains were low-pass filtered at 5 kHz and sampled at 20 kHz.

**C. Data analysis.** Spike latency was calculated as the time between the onsets of the light pulses and the spike peaks. Jitter was calculated as the standard deviation (SD) of spike latencies, measured either across all the spikes throughout a spike train (throughout trial jitter), or for individual spike across different trials of trains (trial-to-trial jitter). Specifically, we collected 21 spikes at each frequency, and repeated 4 times. To calculate ‘throughout trial jitter’, we took SDs of latencies throughout 21 spikes in a single trace, followed by averaging them over 4 trials, To calculate ‘trial-to-trial jitter’, we took SDs of latencies for one specific spike (e.g., the second spike in the train) in 4 independent trials, followed by averaging them throughout 21 spikes in a single trace. For all latency and jitter analyses, light pulses which failed to elicit a spike were ignored.

Fast Fourier transform was performed on representative traces for each frequency in OriginPro. Area-based return map, \( A_n - A_{n+1} \) \( (A_n \) is the area of the \( n^{\text{th}} \) induced neuronal signal)⁶, was obtained by plotting the integrated area for each signal (range: peak-10 ms ~ peak+10 ms) using a MATLAB code. Height-based return map was obtained using the amplitude values of each signal in MATLAB. At each frequency, 4 traces were analyzed. For each trace, analysis was performed for spikes from the 2⁰ to the 2¹st.

**Fabrication of patterned Si-based devices.** The device was fabricated on a Si substrate \((n\text{-type, 0.001} \sim 0.005 \ \Omega \cdot \text{cm, Nova Electronic Materials, USA})\). The fabrication process consists of two steps of photolithography. The first step yields mesostructured Si-covered SU-8 micro-pads. The
as-fabricated micro-pads were then connected by a second step of lithography. Briefly, one layer of SU-8 photoresist (SU-8 2002, MichroChem Corp., USA) was first spin-coated on the substrate, followed by baking at 65 °C for 2 min and 95 °C for 4 min, respectively. The SU-8 coated substrate was then photolithographically patterned and post-exposure baked at 65 °C for 2 min and 95 °C for 4 min. Mesostructured Si suspension in IPA was drop casted on the SU-8 layer and dried before developing in the SU-8 developer (MicroChem Corp., USA) for 4 min to reveal the micro-pad array. To connect the micro-pads, the as-formed isolated array was covered with another SU-8 layer. The second layer was baked at 65 °C for 2 min and 95 °C for 4 min. A mask aligner (EVG 620, EVGroup, Austria) was used to make the interconnections between micro-pads followed by post-exposure baking at 65 °C for 2 min and 95 °C for 4 min. The second layer was next developed using the SU-8 developer for 4 min. The final hard baking at 180 °C for 30 min is optional.
Theoretical analysis of light-induced bioelectric process.

The current generation in soft silicon/lipid bilayer system comprises several consecutive steps. Upon laser illumination, porous silicon absorbs photons and then converts light input into thermal energy by heating up itself and the surrounding buffer solution. Subsequently, the temperature increase of the buffer in the vicinity of both porous silicon and lipid bilayers alters the membrane capacitance. The rate of temperature increase but not the absolute temperature value dominates the capacitive current generation from lipid bilayers. The key processes are dissected quantitatively as below.

A. Photothermal heating.

We first simulated the laser-induced temperature dynamics in mesostructured silicon and buffer solution with COMSOL Multiphysics (COMSOL Inc., USA). In the lipid bilayer experiment, we applied mesostructured silicon particles into the upper buffer solution and let them settle down to form a quasi-continuous layer of silicon particles. We then illuminated a circular area (diameter \( \approx 40 \mu m \)) with 532 nm laser from the bottom of silicon film and probed the temperature profile using pipette resistance method from an adjacent point above the bilayer. For simulation, we adopted a three dimensional (3D) cylindrical geometry. Specifically, we simplified the mesostructured silicon particle layer as a thin slab of cylinder with a radius of 150 \( \mu m \) and a thickness of 15 \( \mu m \) (Fig. S25a). This layer was assumed to be packed compactly with mesostructured silicon particles with their internal channels/pores completely filled with water. On each side of the mesostructured silicon layer, we modeled the water phase as cylinders with a radius of 150 \( \mu m \) and a thickness of 200 \( \mu m \).

The laser energy can be absorbed by mesostructured silicon and the surrounding medium is subsequently heated up due to the heat conduction from silicon to solution. The spatiotemporal profiles for temperature within both silicon and buffer solution are governed by a time-dependent heat transfer equation (in cylindrical coordinates):

\[
\rho c_p \frac{\partial T}{\partial t} = \alpha (1 - R) I_0 e^{-\alpha z} + \frac{1}{r} \frac{\partial}{\partial r} \left( \kappa r \frac{\partial T}{\partial r} \right) + \frac{1}{r^2} \frac{\partial}{\partial \phi} \left( \kappa \frac{\partial T}{\partial \phi} \right) + \frac{\partial}{\partial z} \left( \kappa \frac{\partial T}{\partial z} \right),
\]

where \( T \) is the absolute temperature (K), and \( \rho, \ c_p, \ \kappa, \ R \) and \( \alpha \) are the density (kg/m\(^3\)), specific heat (J/kg·K), thermal conductivity (W/m·K), reflectance and absorption coefficient (m\(^{-1}\)) of mesostructured silicon \( (0 \leq z \leq 15) \) or water \( (z < 0 \ or \ z > 15) \). Since water is almost transparent at 532 nm, its \( \alpha \) value is set to 0. \( I_0 \) is the light power density (W/m\(^2\)). The surface of mesostructured silicon framework is oxygen rich and therefore hydrophilic. We consider a case in which water can wet completely the inner surfaces of the silicon mesostructures. In this scenario, heat conduction from silicon to water is facilitated due to the large interfacial area. We
used weighted arithmetic means to estimate corresponding physical properties of porous silicon, respectively.

\[ \rho_{pSi} = (1 - \phi)\rho_{Si} + \phi\rho_{water}; \]  
(2)

\[ \rho_{pSi}c_{pSi} = (1 - \phi)\rho_{Si}c_{Si} + \phi\rho_{water}c_{water}; \]  
(3)

\[ \kappa_{pSi} = (1 - \phi)\kappa_{Si} + \phi\kappa_{water}, \]  
(4)

where \( \phi \) is the volumetric porosity, which is 55% in this specific case, as estimated from nitrogen adsorption/desorption result.

Physical properties of amorphous silicon were taken from textbooks or literature as: \( \rho_{Si}=2330 \) kg/m\(^3\) (Supplementary ref. 7), \( c_{Si}=891 \) J/kg·K (Supplementary ref. 8) and \( \kappa_{Si}=1.61 \) W/m·K (Supplementary ref. 9). The final input values were calculated as follows: \( \rho_{pSi}=1598.484 \) kg/m\(^3\), \( c_{pSi}=2024.525 \) J/kg·K and \( \kappa_{pSi}=1.0545 \) W/m·K. Light absorption coefficient for mesostructured silicon is 203540 m\(^-1\) at 532 nm, which is estimated using the UV-vis reflectance \( (R=0.068) \) and transmittance \( (T=0.015) \) recorded at the same wavelength, \( T = [(1-R)^2\exp(-\alpha d)]/[1-R^2\exp(-2\alpha d)] \) (Supplementary ref. 10), where film thickness \( d \) is \( \sim 20 \) µm measured using a profilometer. The input laser power was 22.4 mW, with a spot diameter of 40 µm. We used 15 µm, a size comparable to the silicon film thickness, for the estimated distance between silicon top surface and micropipette tip where local temperatures were recorded. Initial and boundary conditions are defined as below, with the interfacial thermal resistance \( R_s \) of \( 10^{-8} \) K·m\(^2\)/W (Supplementary ref. 11).

\[ T(r, \phi, z, t = 0) = 300 \text{ K}, \]  
(5)

\[ T(r = 150 \text{ µm}, \phi, z, t) = 300 \text{ K}, \]  
(6)

\[ T(r, \phi, z = -200 \text{ µm}, t) = 300 \text{ K}; \]  
(7)

\[ T(r, \phi, z = 215 \text{ µm}, t) = 300 \text{ K}, \]  
(8)

\[ -\kappa_{pSi} \frac{\partial T}{\partial z} \bigg|_{(r, \phi, z = 0 \text{ µm})}^{(r, \phi, z = 0 \text{ µm})} = \frac{T_{pSi}(r, \phi, z = 0 \text{ µm}, t) - T_{water}(r, \phi, z = 0 \text{ µm}, t)}{R_s}; \]  
(9)

\[ -\kappa_{pSi} \frac{\partial T}{\partial z} \bigg|_{(r, \phi, z = 15 \text{ µm})}^{(r, \phi, z = 15 \text{ µm})} = \frac{T_{pSi}(r, \phi, z = 15 \text{ µm}, t) - T_{water}(r, \phi, z = 15 \text{ µm}, t)}{R_s}. \]  
(10)

By computing the Heat Transfer in \textit{COMSOL Multiphysics} (Solids Module), we simulated the spatiotemporal temperature profiles in both porous silicon and surrounding medium (\textit{Fig. S25b}). The output results recapitulate the experimental results (\textit{Fig. 4c}).
B. Depolarization current generation.

The total membrane capacitance, consisting of the core capacitance of the bilayer and the in-series capacitance of electrical double layers on each side of the membrane, can be calculated using classical Gouy-Chapman-Stern (GCS) electrical double layer theory (Fig. S25c). The surface potentials on both sides of lipid bilayer, $\Phi_i$ and $\Phi_o$, can be used to calculate the mobile transmembrane charges, $Q = |\Phi_i - \Phi_o| \times C_{\text{bilayer}}$, where $C_{\text{bilayer}}$ is the core capacitance of the bilayer. The derivative of $Q$ over time represents the depolarization current following laser induced temperature change. The total membrane capacitance can be approximated by the ratio of the transmembrane charges and holding potential, $C_m = Q / V_m = C_{\text{bilayer}} \times |\Phi_i - \Phi_o| / V_m$. The details of the theory can be found in the previous publication\textsuperscript{12}. We want to emphasize that the rate of temperature change, rather than the maximum achievable temperature, is the cause for the observed capacitive current generation.
Figure S1 | Home-built CVD system for bottom-up synthesis of mesostructured Si. a, Overview of the experimental setup. Silicon precursor SiH₄ and carrier gas H₂ were pre-mixed and introduced to the tube furnace with temperature, flow rate and pressure controlled throughout the synthesis. Mass flow controllers, pneumatic valves, a pressure gauge, a tube furnace, and quartz tubes are labeled. An inner quartz tube with SiO₂ template was placed at the center of an outer quartz tube, where Si would be subsequently deposited. b, Zoom-in view of the double-tubing system. White SiO₂ template was placed near the bottom of the inner tube.
**Figure S2 | An inner quartz tube is a preferred sample container than an inner quartz boat.**

**a,** With an inner quartz tube, although the deposition time is longer (*e.g.*, 2 h), the sample morphology is uniform and there is a minimum sample loss (and correspondingly minimum contamination to vacuum system). An inner quartz boat has a much larger opening and allows shorter Si deposition duration (*e.g.*, 30 min). However, the sample uniformity is poor and some regions showed solid Si shell coatings (**b**). Green lines mark the open areas of two sample containers. **b,** SEM images of particles with solid Si shell coatings, formed in certain regions when an inner quartz boat was used as the sample container. The broken area (right) suggests that there were still nanowire bundles inside the shells. One significant issue with an inner quartz boat is the sample loss during Si deposition, which can contaminate the CVD system. We recommend using an inner quartz tube as the sample container.
Figure S3 | TEM (1st and 2nd columns from left) and SEM (3rd and 4th columns from left) images of mesostructured Si synthesized at various temperatures. a, 450 °C, b, 500 °C, c, 550 °C, d, 600 °C. The results from the growth at 500 °C showed the most uniform nanowire bundle-based morphology. Synthesis at 400 °C did not yield any product.
Figure S4 | TEM images of mesostructured Si synthesized at 500 °C for different durations. a, 0.5 h, b, 1 h. Their nanoscopic morphologies are similar to those of the standard sample (i.e., grown for 2h, Fig. 1), although the product yield is significantly lower, i.e. ~ 15 % (a) and ~ 57 % (b) of that collected for 2h.
Figure S5 | SEM (a) and TEM (b) images of rod-like mesostructured Si. The rod-like materials were synthesized through a static aging step. The width and length distributions (c) suggest decent shape uniformity.
Figure S6 | SEM images (a) and diameter distribution (b) of sphere-like mesostructured Si. The spheres were synthesized using cetyltrimethylammonium bromide (CTAB) as a cosurfactant and ethanol as a co-solvent.
Figure S7 | Size distributions of mesostructured Si particles. The wheat-like mesostructured Si aggregates can be grinded, sonicated and then filtered to achieve different size distributions. Typically, mesostructured Si particles were manually grinded in an agate mortar for ~30 min before being sonicated in IPA suspension and filtered through syringe filters with different pore sizes. **a**, A size distribution of Si particles that can pass ~ 5 µm pore-size filter, and are collected with a ~ 1 µm pore-size filter. **b**, A distribution of Si particles that can pass both ~ 5 µm and ~ 1 µm pore-size filters.
Figure S8 | Mesostructured Si is electrically conductive. Representative electrical device made from a single mesostructured Si particle shows a conductance of ~2.4 µS (black, left), measured with a probe station. Removing the Si particle by sonication made the device insulating (red, left), indicating that the measured conductivity came primarily from the Si particle between the pair of electrodes (left). An SEM image (viewed from 52° tilted angle) on the right shows the mesostructured Si particle and its contacts with Pt/C wires deposited in a FIB system.
Figure S9 | Mesostructured Si can be solution-processed and injected. a, The mesostructured Si can be molded (upper) after mixing with water to form clay-like pastes. The shaped part can be further indented (lower). White dots with different sizes (lower) mark the surface indentations with different depths. Scale bars, 1 cm. b, Mesostructured Si forms suspensions when mixed and sonicated with solvent (isopropanol, water, etc.) and can be drop-casted on substrates to yield continuous thin films (upper). SEM image of an as-deposited Si film (lower) shows interconnected gel-like network, reminiscent of xerogel surfaces. The individual particles exhibit rod-like morphology (yellow star, and the zoom-in view in yellow box) and characteristic curvature (magenta star, and the zoom-in view in magenta box), consistent with those in SBA-15 template. c, Mesostructured Si can be injected with syringe into a collagen hydrogel (left and middle panels, 2.98 mg/mL collagen). Only minor expansion of Si spots was observed after post-injection incubation at 37 °C for 18 h (right), indicating good retention of the material within fibrous biological matrix (right).
Figure S10 | Structural characterizations of mesostructured Si. a, Nitrogen adsorption/desorption isotherm shows a Type-IV characteristics. b, Typical TXM cross-sectional image, illustrating random intra-granular (blue lines) and inter-granular (black areas) voids in the material. These voids likely facilitate the trapping of light within the Si mesostructures, and may help reduce the Young’s modulus. c, Side-view TEM image shows aligned Si nanowire structure.
**Figure S11 | Mesostructured Si shows outstanding thermal stability.** In-situ TEM images taken at different time points during thermal treatment (900 °C), showing minimal destruction of ordered mesostructure up to 120 min (top and middle rows). SAED patterns indicate the formation of nanocrystalline domains during heating process (bottom row). White dashed box marks the zoom-in region for the images displayed in the second row.
Figure S12 | Thermal stability was corroborated with *in-situ* SAXS. Existence of diffraction peaks at high temperatures suggests the partial retention of the periodic structure although the broadened widths and decayed intensity indicate partial structural destruction. Temperature was ramped to 800 °C from room temperature and stayed at 800 °C, 900 °C and 1000 °C for 20 min (separated by white dashed lines).
Figure S13 | The synthesis of mesostructured Si is general. a, KIT-6 silica could be used as a template for mesostructured Si synthesis. SAXS profile of an as-casted Si shows a gyroidal lattice (space group, $Ia\overline{3}d$; lattice constant, 23.0 nm) with (211), (220), and (332) peaks, in accordance with the structure of KIT-6 template. b, Representative TEM images of the Si casted from KIT-6 template, showing ordered mesostructures.
**Figure S14 | EDX mapping suggests heterogeneous oxygen distribution.** a, HAADF STEM image of a free-standing Si mesostructure, showing ordered packing of individual nanowires. The structural integrity of the material suggests the existence of interconnecting micro-bridges which hold individual nanowires together. White dashed box marks the region for elemental mappings. b, EDX mapping of O (left, red), Si (middle, green) and the overlay of HAADF image and EDX maps (right) reveal alternating ordered spatial distribution of both elements. Scale bars, 200 nm (a) and 10 nm (b).
Figure S15 | APT sample preparation includes a series of fabrication steps. First, a particle of interest (mesostructured Si embedded in intact SiO\textsubscript{2} matrix) was picked up by a micromanipulator in a FIB system (left). Then, the mesostructured Si was placed on a micropost with the same micromanipulator and welded with Pt/C (middle). Green dashed box mark the zoom-in region with details of the micropost. Finally, the as-mounted particle was cut with a 30 kV Ga\textsuperscript{+} beam and sharpened with a 5 kV Ga\textsuperscript{+} beam into a final needle-shape morphology for APT characterization (right). White dashed box mark the region of interest that was analyzed with APT. Different layers of materials are indicated.
Figure S16 | APT reveals detailed structural and chemical heterogeneity within the mesostructured Si. a, Reconstructed 3D APT data, rendered in 65 at.% Si isoconcentration surfaces, show ordered Si nanowires and connecting micro-bridges. b, Histogram of angles between each micro-bridge and its connecting nanowires, showing a peaked distribution at ~90° ($n=34$). The quasi-orthogonal orientation of micro-bridges with respect to nanowires allows decoupling of the two components for separate analysis. c, A series of Si isoconcentration surfaces showing graded Si/SiO$_x$ interfaces and size-dependent heterogeneous distribution of O. In general, most micro-bridges that are shown in the 60 at.% isoconcentration surface disappears in the 75 at.% one. Green and pink dashed boxes marked the regions used to crop Si nanowire and micro-bridge dominant domains (Fig. 2c) for Si atomic concentration distribution histogram analysis (Fig. 2e).
Figure S17 | Ordered Si mesostructure can still be resolved after immersion in PBS for two days. a, In-situ SAXS data collected when mesostructured Si was placed in either collagen hydrogel (left) or PBS (right) over a time course of 12 h. No significant changes in peak position and width suggest the remaining Si material still has an ordered mesostructure network. b, Ex-situ SAXS data taken from mesostructured Si after immersing in PBS for 0 d (black) and 2 d (red), showing marginal differences in peak position and width. Given the ex-situ SAXS data were collected after the samples were dried, the results also suggest that drying process will not cause collapse of the mesostructures. The SAXS results corroborate those from Raman (Fig. 3b) and UV-vis (Fig. 3c) measurements, and suggest that despite degradation from surfaces, the remaining materials are still Si-based ordered mesostructures.
**Figure S18** | **Mesostructured Si shows surface degradation.**
a, Cross-sectional TEM image of two free-standing mesostructured Si particles. The sample was immersed in Tyrode’s buffer overnight prior to the imaging preparation. The interior of the particles showed ordered nanowire packing, consistent with the results from SAXS, and suggests that there would be a mechanism
to help preserve the particle’s internal ordered structures in saline. 

b, A segregated region with degraded fragments. The fragments still maintained nanowire morphology (green arrows) and, together with the fact that the particle interior was still ordered, suggests a surface degradation mechanism. 

c, A mesostructured Si particle enclosed within a plasma membrane bounded cavity. The degraded surface layer was confined in this cavity, instead of leaving the particles as seen in (a). Green dashed box marks a surface region for the zoom-in view on the right. The green arrows mark the degraded and fractured nanowire domains. 

d, A series of green arrows highlight a possible deformation at the Si/cell interface. 

e, Degraded pieces (green arrows) may help the adhesion of mesostructured Si onto cell membranes. Samples shown in c, d and e were prepared by chemical fixation method, instead of freeze-substitution as shown in a, b and Fig. 3d.
**Figure S19 | Intrinsic and induced chemical and structural heterogeneities enable multiple functions in mesostructured Si.** Freshly prepared mesostructured Si has intrinsic size-dependent chemical heterogeneity, where nanowires are rich in Si and micro-bridges contain more O (Fig. 2). The porous structures, the chemical heterogeneity, as well as the amorphous nature of Si, together promote a good photothermal effect. The material’s interior retains its structures and optical properties in buffer solution within days (Figs. 3b, 3c, S17, S18), which functions as a ‘heater’ upon light illumination. Within the ‘heater’, micro-bridges ‘support’ the Si-rich ‘heater filaments’, and the oxidized layers (SiOₓ, pink) over both the micro-bridges and nanowires slow down the reaction of Si with H₂O. The surface of the particle is degraded (Figs. 3d, S18c) and softer (Fig. 3a), which may ‘shield’ the interior by possibly blocking the nanoscale pores with the degraded species (Fig. S18c). This proposed shielding effect from the particle outer surface, as well as SiOₓ-enabled passivation of Si, may lead to the observed structure preservation in the particle interior (Fig. S18). The interface between mesostructured Si particle and plasma membrane shows local fragmentation (Fig. S18c, right). The Si/cell interface thus behaves as a less invasive ‘cushion’. The degradation/fragmentation of Si surfaces by water and possibly extracellular forces represents induced heterogeneity.
Figure S20 | Mesostructured Si is degradable in vitro. a, Mesostructured Si degradation curves in 1 mL of 1× PBS at 37 °C over time. Half of the solutions were taken out for ICP-OES analysis at each time point and 500 µL of fresh 1× PBS were added back each time. Different amount of initial mass of Si added are color coded as 50 µg (red); 100 µg (olive); 300 µg (navy blue). In general, the solution exchange protocol, i.e., the frequency of solution exchange and the volume of solution being exchanged each time, can affect the degradation rate. Additionally, larger Si/H₂O ratio yields slower degradation. Finally, the degradation rate drops significantly at the later stage in the tests of 300 µg sample, although fresh solution was added at each exchange point (navy blue). This is likely due to the Si oxidation into gel-like SiₓOᵧ(OH)ₜ₋₂₋z. b, Degradation curves under different temperatures. With the same amount of mesostructured Si added (100 µg), the sample degraded faster at higher temperature; red, 37 °C, blue, room temperature. For each group, n=5. The shaded areas denote the means ± 1 standard deviation.
**Figure S21 | Mesostructured Si shows less mechanical invasiveness to cells.**

**a,** Representative Fura-2 AM fluorescence recording from HUVECs before and after being mechanically perturbed by porous Si mesostructures (black) and solid Si particles (red). The particle sizes are \( \sim 5 \, \mu \text{m} \).

**b,** Statistical analyses of the slope (left) and the amplitude (right). In general, porous and amorphous Si mesostructures yield smaller amplitudes and slopes in calcium response, comparing to solid single crystalline Si particles. \( p \)-values are from Mann-Whitney tests with \( n=44 \) for both sample groups.
Figure S22 | Mesostructured Si particles are biocompatible *in vitro*. MTT assays show minimal cytotoxicity when co-culturing mesostructured Si with different cell lines for up to 7 days (a, red, HUVEC; b, blue, C2C12; c, olive, HASMC, 0.1 mg/mL Si in all cell culture media). Data points are mean ± standard deviation, *n=8* for each group.
Figure S23 | Mesostructured Si is biocompatible and biodegradable in vivo. a, Photographs showing degradation of Si in the subcutaneous regions of adult male CD® IGS rats. No appreciable nodules were formed within the 3-week period. b-d, Hematoxylin and eosin (H&E) staining of the injection sites after 1 day (b), 1 week (c) and 3 weeks (d) periods. Images from 1
day post-injection (b) show diffused immune cell distribution. The channel-like void was created by the injection needle. Samples from 1-week post-injection (c) have defined boundaries of inflammatory responses. The total amount and density of Si particles, shown as black dots in the zoom-in views, are in general less than those in the 1-day post-injection samples (b). Samples from 3-week post-injection (d) exhibit least amount of Si particles and smallest areas of inflammatory regions. The arrows in (d) highlight remaining Si particles. There was no significant injury to surrounding tissues (e.g., muscle, blood vessels). There were no appreciable nodules developed during the test period. The animals did not show difficulty in moving, and no animal death occurred. For each group, n=4.
Figure S24 | Remotely controlled bioelectric interface based on mesostructured Si/lipid bilayer system. a-c, Local temperature (top), bilayer capacitance (middle) responses to laser pulses. Laser-induced charge-voltage ($Q$-$V$) curves (lines denote linear fits, bottom) are calculated from the depolarization current-time curves following laser pulses. In all panels, color denotes different laser energies (black, 0.5 ms; red, 1.0 ms; blue, 1.5 ms; olive, 2.0 ms, laser powers, (a) 5.32 mW; (b) 10.92 mW; (c) 22.4 mW, objective lens, 10×). All temperature and capacitance data were averaged from 50 traces. Capacitive currents and corresponding $Q$-$V$ curves are an average of 10 current traces. d, Pipette resistance over temperature calibration curve. Red line denotes a linear fit to the data.
Figure S25 | **Simulation model and equivalent circuit diagram.** a, 3D geometry model used for photothermal simulation of mesostructured Si. Blue cylinders mark water layers on both sides of Si layer (diameter, 300 µm; height, 200 µm). Dark grey cylinder denotes mesostructured Si being illuminated by green laser (diameter, 40 µm; height, 15 µm; laser wavelength, 532 nm). Light grey ring is the rest of mesostructured Si that is not illuminated. The probe location is at (0, 0, 30 µm), where the temperature profile was simulated. b, Simulated temperature dynamics recapitulates the experimental data, supporting the controllability of the photothermal effect. (c) Equivalent circuit diagram, illustrating the electrical model for lipid bilayer. Symbols are defined as follows: $V_m$ and $I_m$ are the holding potential and transmembrane current. $V_T$ and $g_T$ are the Thevenin equivalent potential and conductance of the membrane. $C_{\text{bilayer}}$ is the core capacitance of the lipid bilayer. $C_{\text{Stern}}^i$ and $C_{\text{Stern}}^o$ are the capacitance of the inner and outer Stern layers. $\Phi_i$ and $\Phi_o$ are the potentials right at the inner and outer surfaces of the bilayer. $\Phi_{\sigma,i}$ and $\Phi_{\sigma,o}$ are the battery potentials due to the fixed head group charges at the inner and outer bilayer surface.
Figure S26 | Mesostructured Si enables wireless control of the electrophysiology dynamics in DRG neurons. a, Peak voltage response (unit: mV) of a representative DRG neuron at different laser excitations indicates that laser pulses at 5.32 µJ can elicit reliable APs. Laser power was 5.32 mW with durations of 0.1 ms (black), 0.2 ms (red), 0.5 ms (blue), or 1.0 ms...
(olive). b, At high spike train frequency (e.g., 25 Hz), action potential (blue arrows) generation becomes less efficient, although a deterministic subthreshold depolarization (black arrows) remains evident. Green bars indicate when laser pulses are delivered. c, Successful rate, spike latency, trial-to-trial jitter and throughout trial jitter (see details in Materials and Methods) were analyzed for different pulse train stimulations. At frequencies higher than 15 Hz, the stimulation efficacy decreased as indicated by the reduced successful rates, delayed spike latencies and elongated jitters. Data points are mean ± standard deviation, analyzed from 21 pulses per trial, 4 trials per frequency.
**Figure S27** | **Control experiments suggest the role of Si.** a and b, Local temperature increases following laser illumination on single particles of both mesostructured Si (a) and SiO$_2$ template (b). Color denotes different laser energies (black, 3.29 µJ (a), 10.92 µJ (b); red, 6.58 µJ (a), 110 µJ (b); blue, 16.45 µJ (a), 550 µJ (b); magenta, 1100 µJ (b); olive, 32.9 µJ (a), 5500 µJ (b), objective lens, 40×). c, Comparison of temperature dynamics between mesostructured Si and SiO$_2$ template when illuminating with similar laser energies (black, 9.87 µJ, Si; red, 10.92 µJ, SiO$_2$). Negligible temperature change could be observed for SiO$_2$. d, Temperature calibration curves for pipette resistances measured for both Si (left) and SiO$_2$ (right) systems. Red lines denote linear fits to the data.
Figure S28 | Return maps reveal the evolution of cellular output patterns. a, Area-based return maps calculated at each input frequencies and the overlay show a gradual transition from focused to partitioned/diffused patterns. Areas were obtained by integrating the voltage with respect to time, $t$, from $t$ of peak voltage -10 ms to $t$ of peak voltage +10 ms. b, Height-based return maps at each input frequency. Heights were calculated as the difference between the peak and the holding voltages. All return maps were analyzed from the 2nd to the 21st spike per trial, 4 trials per frequency.
Figure S29 | Glass micro-pipette can be used to manipulate individual mesostructured Si particles to form deterministic biointerfaces. HUVEC was used in this demonstration. Both particle position and number can be controlled in this way. Scale bars, 50 µm.
Figure S30 | Mesostructured Si particles can be patterned over large areas. a, Fabrication schematics. b, A photograph of a patterned array where Si regions are black micro-pads with SU-8 interconnects. c and d, Optical micrographs showing the zoom-in views of the Si micro-pads before (c) and after (d) SU-8 interconnects were made, recorded from 3 different areas. Scale bars, 2 mm (b) and 200 µm (c and d).
| Length scale | Structural | Chemical | Mechanical | Optical | Thermal | Electrical |
|--------------|------------|----------|------------|---------|---------|------------|
| atomic       | Amorphous matrix |          | Compared to crystalline Si, amorphous phase has lower Young’s modulus. | Compared to crystalline Si, amorphous phase has larger absorptivity. | Compared to crystalline Si, amorphous phase has lower thermal conductivity/diffusivity. |          |
| < 2 nm       | Random micro-bridges | O-rich  | Hydration and degradation of ultrathin O-rich micro-bridges can help produce soft surface layers in saline. |          | O-rich components can improve thermal stability. |          |
| ~ 10 nm      | Ordered nanowire arrays | Si-rich | The porous framework can reduce Young’s modulus. | The porous framework can improve light trapping. | The porous framework can lower thermal conductivity/diffusivity. |          |
| 0.2 ~ 1 μm   | Irregular inter- and intra-granular voids |          |          |         | Provide long-range electrical conductivity |          |
| The whole particle (1 ~ 10 μm) | Multi-scale structural heterogeneity | Size-dependent chemical heterogeneity | Young’s modulus is 2.3 orders of magnitude less than that of bulk Si. | • Fast photothermal effect that induces capacitive currents for lipid bilayer-supported bioelectric interfaces. | • Thermally stable | Electrically conductive across single particles |

**Table S1 | Characteristics of mesostructured Si.** The new amorphous Si-based material has structural and chemical heterogeneities and is suited for remotely-actuated bioelectric interface.
Supplementary References:

1. Zhao, D. Y., Feng, J. L., Huo, Q. S., Melosh, N., Fredrickson, G. H., Chmelka, B. F. & Stucky, G. D. Triblock copolymer syntheses of mesoporous silica with periodic 50 to 300 angstrom pores. *Science* **279**, 548-552, doi:10.1126/science.279.5350.548 (1998).

2. Sayari, A., Han, B. H. & Yang, Y. Simple synthesis route to monodispersed SBA-15 silica rods. *Journal of the American Chemical Society* **126**, 14348-14349, doi:10.1021/ja0478734 (2004).

3. Katiyar, A., Yadav, S., Smirniotis, P. G. & Pinto, N. G. Synthesis of ordered large pore SBA-15 spherical particles for adsorption of biomolecules. *Journal of Chromatography A* **1122**, 13-20, doi:10.1016/j.chroma.2006.04.055 (2006).

4. Kleitz, F., Choi, S. H. & Ryoo, R. Cubic Ia3d large mesoporous silica: synthesis and replication to platinum nanowires, carbon nanorods and carbon nanotubes. *Chemical Communications*, 2136-2137, doi:10.1039/b306504a (2003).

5. Bellet, D., Lamagnere, P., Vincent, A. & Brechet, Y. Nanoindentation investigation of the Young's modulus of porous silicon. *Journal of Applied Physics* **80**, 3772-3776, doi:10.1063/1.363305 (1996).

6. Kaplan, D. T., Clay, J. R., Manning, T., Glass, L., Guevara, M. R. & Shrier, A. Subthreshold dynamics in periodically stimulated squid giant axons. *Physical Review Letters* **76**, 4074-4077, doi:10.1103/PhysRevLett.76.4074 (1996).

7. McGuire, G. E. *Semiconductor materials and process technology handbook*. (William Andrew Publishing/Noyes, 1988).

8. Zink, B. L., Pietri, R. & Hellman, F. Thermal conductivity and specific heat of thin-film amorphous silicon. *Physical Review Letters* **96**, doi:10.1103/PhysRevLett.96.055902 (2006).

9. Cahill, D. G., Katiyar, M. & Abelson, J. R. Thermal conductivity of a-Si: H thin films. *Physical Review B* **50**, 6077-6081, doi:10.1103/PhysRevB.50.6077 (1994).

10. Kovalev, D., Polisski, G., BenChorin, M., Diener, J. & Koch, F. The temperature dependence of the absorption coefficient of porous silicon. *Journal of Applied Physics* **80**, 5978-5983, doi:10.1063/1.363595 (1996).
11 Barisik, M. & Beskok, A. Temperature dependence of thermal resistance at the water/silicon interface. *International Journal of Thermal Sciences* **77**, 47-54, doi:10.1016/j.ijthermalsci.2013.10.012 (2014)

12 Shapiro, M. G., Homma, K., Villarreal, S., Richter, C. P. & Bezanilla, F. Infrared light excites cells by changing their electrical capacitance. *Nature Communications* **3**, doi:10.1038/ncomms1742 (2012).