실크 피브로인의 전기적 • 광학적 디바이스 개발 및 응용

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1. 서론

✓ 실크 피브로인의 전기적 • 광학적 디바이스 개발 및 응용[1,2]

- 실크 피브로인 소재 기반 전기적 · 광학적 디바이스는 생체 적합적이면서 투명하여 최근 웨어러블 헬스 케어용 디바이스나 다양한 photonic devices 등에 응용성이 보고되고 있음.

- 최근 광학 · 전자 소자를 기반으로 하는 헬스 케어 디바이스의 구현은 시대의 패러다임으로 자리 잡고 있으며 생체 정보를 실시간으로 활용 및 조절하는 기술은 향후 IT 기술과 결합하여 큰 부가 가치를 창출할 수 있음.

- 이와관련 소자 제작 기술은 바이오 및 나노 기술과의 조합을 통해 빠른 속도로 발전하고 있으며, 특히 생체 내에서 직접 구동이 가능한 소자 연구가 많은 각광을 받고 있음.

- 인체 조직에 부착하거나 직접 삽입형 바이오 소자를 이용한 헬스 케어 플랫폼 제작 시 실크 피브로인의 생체친화성, 유연성 등의 특성을 가지는 바이오 고분자의 활용이 매우 중요함.

2. 연구 동향

✓ The optical properties of regenerated silk fibroin films obtained from different sources[3]

- 실크 피브로인은 광학적 성질이 우수해서 광학 소재로서의 관심이 증가하고 있음. Bobby mori, Antheraea mylitta, Samia ricini, and Antheraea assamensis와 같은 4종류의 누에에서 추출한 silk fibroin의 굴절률(refractive index)과 흡수 계수(absorption coefficient)를 조사함.

- 또한 단백질 분자량, 잔류 수분 함량, 결정성이 굴절률에 미치는 영향을 보사하였고 Cauchy 분산 법칙과 Urbach 흡수에 대한 변수를 각각 4가지 샘플에 대하여 조사하여 굴절률 차이를 이용한 all-protein slab waveguide 를 준비함.(표 참고)

- Spectroscopy를 통해 220nm~2000nm대역에서 absorbance를 측정되고 tyrosine amino acids에 의한 peak에 해당되는 270nm에서의 peak발견됨.
  300nm~2000nm에서 모든 silk fibroin의 absorbance가 매우 낮아 투명함.

- B. mori 의 silk film에서는 전체적으로 균일한 굴절률을 가지고 있고, silk film의 굴절률은 건조 시간에 따라(함유하는 물의 비율에 따라 (residual water)) 다른 값을 가짐. silk fibrion의 분자량은 굴절률에 큰 영향을 끼치지 않음

- 광학적 특성을 이용하여, Bobby mori와 Antheraea assamensis의 두 종류의 굴절률이 다른 silk-silk wave guide 를 만들었으며 이러한 경과를 이용하여 all-silk optical components 와all-silk biocompatible degradable sensors 제작이 가능함.

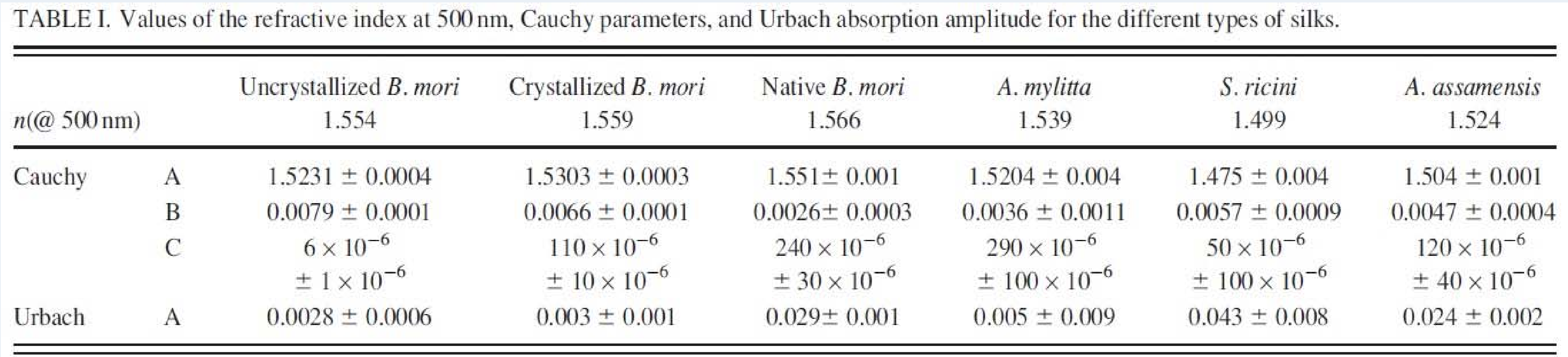


TABLE I. Values of the refractive index at 500 nm, Cauchy parameters, and Urbach absorption amplitude for the different types of silks.

		Uncrystallized *B. mori*	Crystallized *B. mori*	Native *B. mori*	*A. mylitta*	*S. ricini*	*A. assamensis*
n(@ 500 nm)		1.554	1.559	1.566	1.539	1.499	1.524
Cauchy	A	1.5231 ± 0.0004	1.5303 ± 0.0003	1.551± 0.001	1.5204 ± 0.004	1.475 ± 0.004	1.504 ± 0.001
	B	0.0079 ± 0.0001	0.0066 ± 0.0001	0.0026± 0.0003	0.0036 ± 0.0011	0.0057 ± 0.0009	0.0047 ± 0.0004
	C	6×10^{-6} $\pm 1 \times 10^{-6}$	110×10^{-6} $\pm 10 \times 10^{-6}$	240×10^{-6} $\pm 30 \times 10^{-6}$	290×10^{-6} $\pm 100 \times 10^{-6}$	50×10^{-6} $\pm 100 \times 10^{-6}$	120×10^{-6} $\pm 40 \times 10^{-6}$
Urbach	A	0.0028 ± 0.0006	0.003 ± 0.001	0.029± 0.001	0.005 ± 0.009	0.043 ± 0.008	0.024 ± 0.002

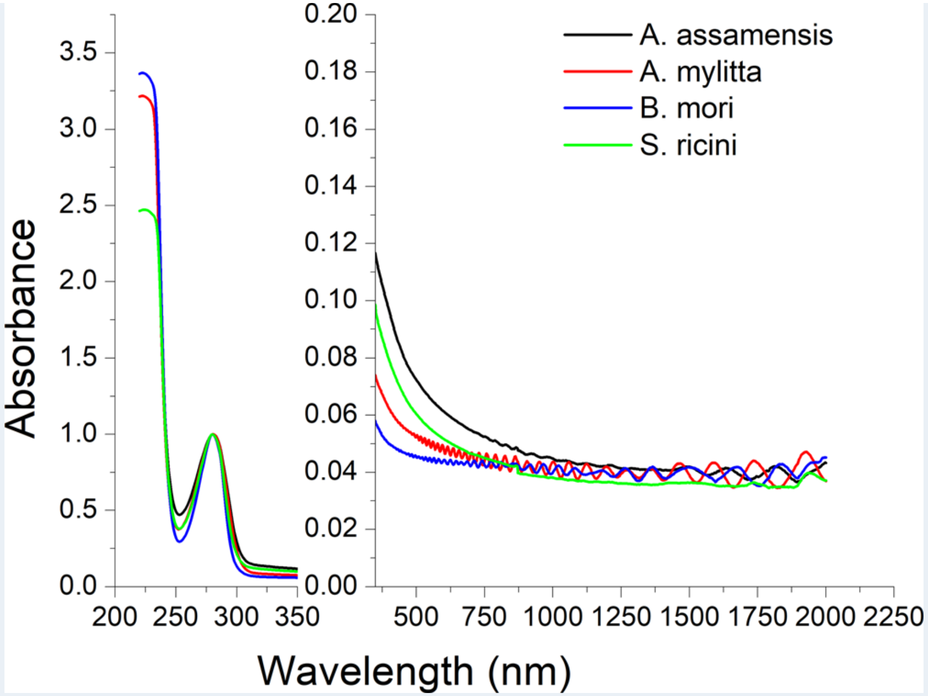


FIG. 1. Normalized absorption of free standing films of film prepared from B. mori silk (blue), A. mylitta (red), S. ricini (green), and A. assamensis (black) silks. Data were normalized to the 270 nm tyrosine absorption to take into account difference in thickness.

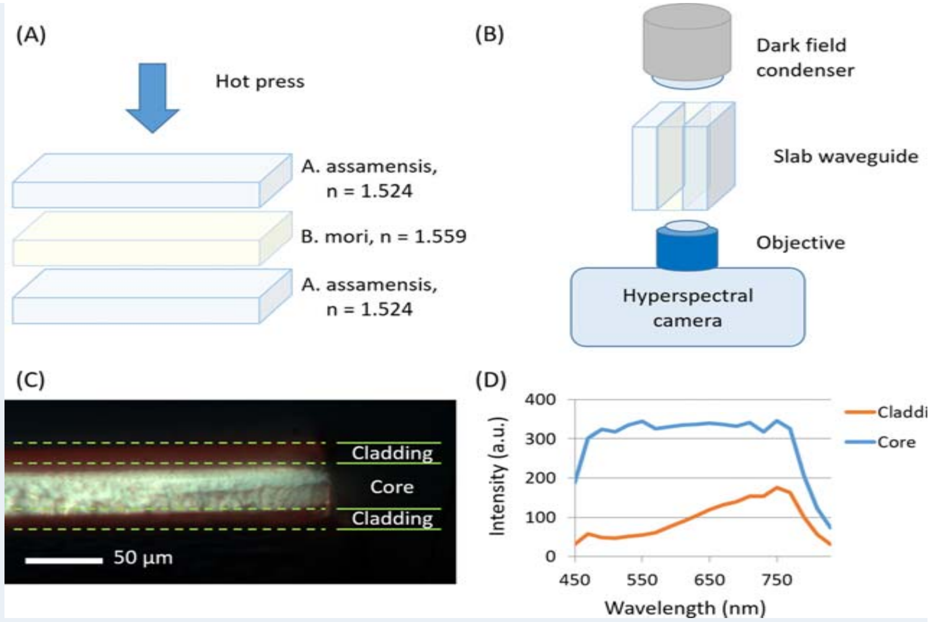
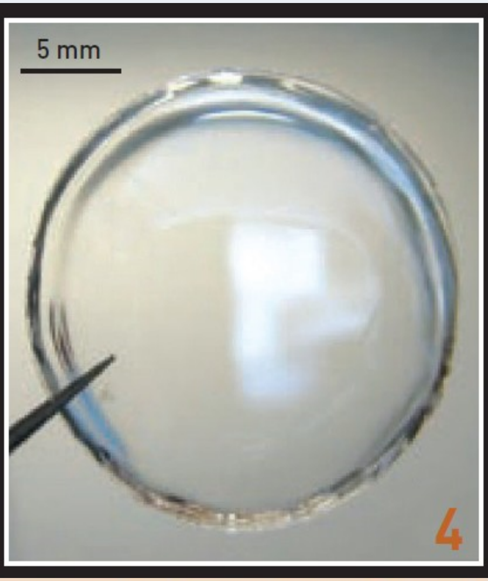


FIG. 3. Fabrication of a silk-silk waveguide. (a) B. mori sil (n¼1.559 at 500 nm) film was sandwiched between two A assamensis silk (n¼1.524 at 500 nm) films, and the stack wa hot-pressed to form a waveguide. (b) Optical setup for the observation of light guidance in the silk-silk waveguide. (c Microscopic image showing light guidance in the core layer o the slab waveguide. (d) Spectra in the core and in the cladding of the silk-silk waveguide, measured with hyperspectral camera.

✓ Silk : A Different Kind of "Fiber Optics“[4]

- 실크 필름은 가시광선영역에서 매우 투명하며 5nm정도의 rms를 가질 정도로 균일함.
- 이러한 특징이 있어 diffraction gratings와 phase masks, white-light holograms, photonic crystal lattice로 활용이 가능하고 새로운 device, sensor등의 응용이 치료법을 가능케 함.
- 실크 필름은 silk fibroin 용액을 기판 위에 붇고 말리는 식으로 만들 수 있으며, 기판의 굴곡에 맞춰 형성하므로 다양한 모양의 optic device를 만들 수 있음.
- 특정 패턴의 silk film 산업적으로 대량 생산하기 위한 방법은 silk film으로 만든 틀을 이용하여 patterning이 된 silk film을 생산하는 것임.
- Nano scale patterning에서는 electron beam을 이용하여 실리콘기판을 틀로 만들 수 있으며, 대략 10nm크기까지 가능함.
- 실크 필름은 매우 투명하고 biological system을 안정화 시키므로 blood sensors로 활용가능하며, photonic-crystal, microfluidic sensors, implantable optics의 개발도 가능함.



From silkworm to silk film

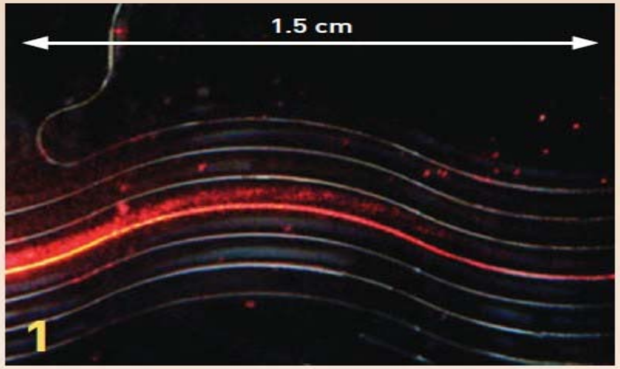
1. Silkworms use the raw material in mulberry leaves to create silk fiber to spin their cocoons.

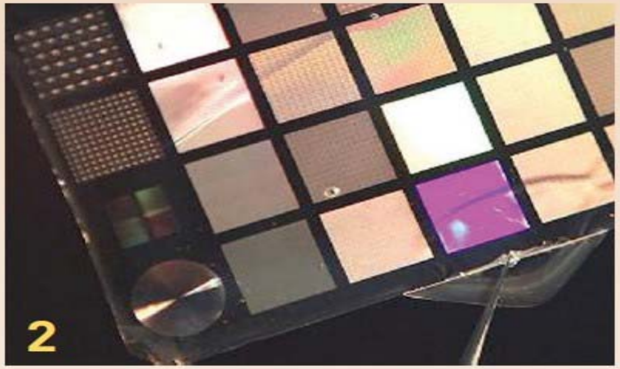
2. For use in optical devices, cocoons are cooked (left) to isolate silk fibroin fibers (right).

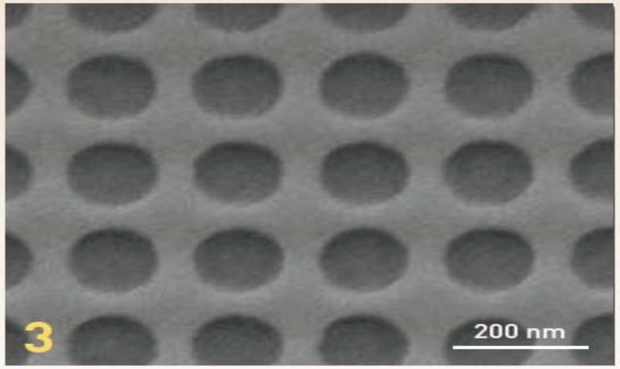
3. These tough fibers are dissolved to obtain liquid silk

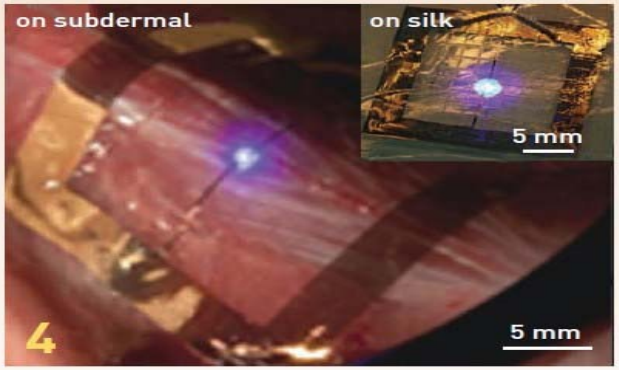
4. The silk solution can then be formed into multiple material formats, including clear free-standing films (shown), nanoparticles, sponges, adhesives and gels, blocks and fibers.

Adapted from F.G. Omenetto and D.L. Kaplan, Nat. Photonics **2**, 641 (2008), © 2008 Macmillan Publishers Ltd.









Multiple scales, multiple uses

Examples of silk devices at various scales and with differing optical applications include:

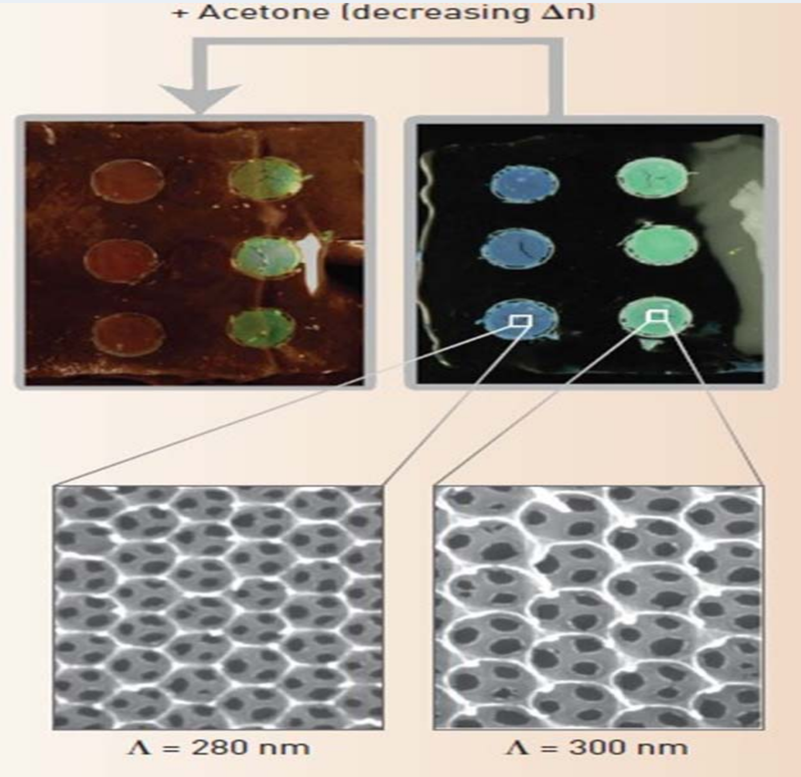
1. Printed silk waveguides.

2. A silk card containing diffractive optical elements (microlens arrays, phase masks, diffraction gratings).

3. An electron micrograph of a 2-D photonic lattice.

4. An InGaN thin-film LED on a silk substrate, which conforms to animal skin and is wirelessly powered—an example of biological integration of silk-hybrid photonics.

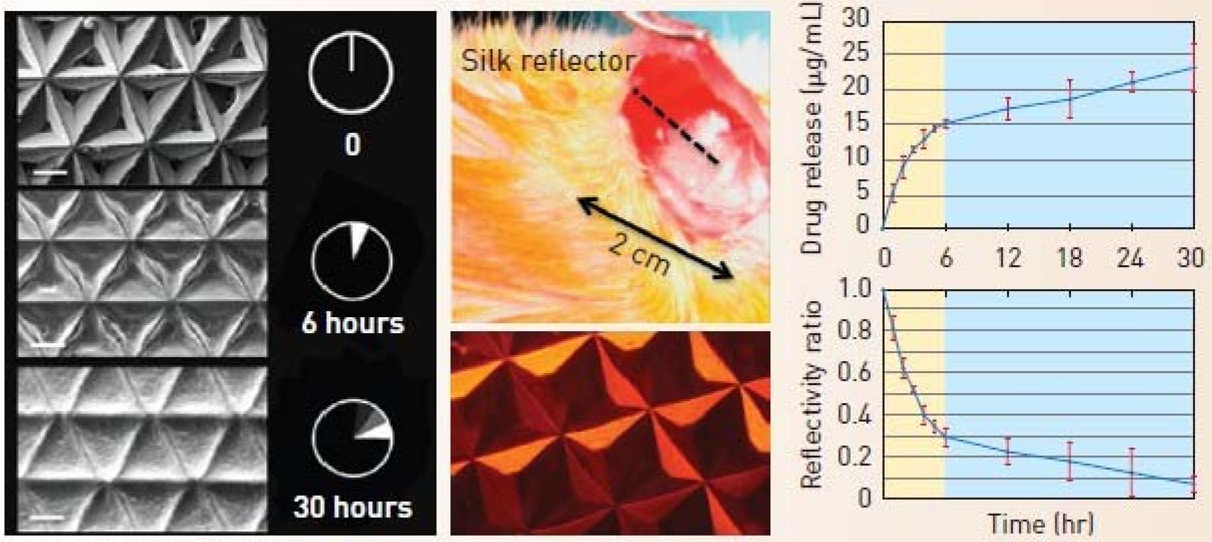
Clockwise from top left: S.T. Parker et al., Adv. Mater. **21**, 2411 (2009), © 2009 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim; F. Omenetto; J.J. Amsden et al., Opt. Express **17**, 21271 (2009); R.H. Kim et al., Small **8**, 2812 (2012), © 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.



- **Inverse opals**

(Top) Free-standing silk film with nanopatterned 3-D inverse opals, displaying iridescence according to the lattice constant (L) of the devices. (Center) The devices change color when infiltrated with a fluid, thus changing the index contrast of the photonic crystal lattice. (Bottom) Electron microscope image of the different silk inverse opals.

Kim et al., Nat. Photonics 6, 818 (2012),



Implantable silk mirrors

(Left) Electron microscope image of silk microprism arrays degrading in the presence of enzymes. (Center) Silk microprism array loaded with the chemotherapeutic doxorubicin. When these silk devices are loaded with drugs in this manner, the drug is released and correspondingly the microprisms change their geometry, allowing for correlation of the reflectivity from the silk device and the amount of drug delivered (right).

Hu et al., Proc. Natl. Acad. Sci. USA **109**, 19584 (2012).

✓ Deformable and conformal silk hydrogel inverse opal[5]

- 실리콘 기판위에 submicrometer poly(methyl methacrylate)(PMMA) 구를 올려 놓고, 실크 피브로인과 stilbene 수용액을 부은 다음 EUV를 이용하여 굳히고 아세톤으로 PMMA 구를 녹이면, silk hydrogel inverse opal(SHIO)이 만들어짐.

- SHIO는 광 결정이며, SHIO가 주변 유체에 따라, 내부 구조의 팽창이 이루어져 pseudophotonic band gap (pseudo-PBG)이 변화하고, 반사하는 색이 변화함.

- SHIO는 x, y축 방향으로 잡아 당기거나 (stretched), 표면에 수직으로 균일한 압력을 가할 시, SHIO의 두께가 변화하고 pseudo-PBG가 영향을 받아 가장 많이 반사시키는 빛의 파장이 감소하게 됨. 이를 이용하여 deformation정도에 따라 pseudo-PBG를 조정할 수 있음.

- SHIO를 사용하여 인공 휘판 (artificial tapetum lucidum)를 제작할 수 있음. 휘판은 밝기가 낮은 곳에서 망막에 빛을 반사시켜 어두운 곳에서의 시력을 증진시킬 수 있음.

- 또한, SHIO는 높은 내구성, 변형성, 생체적합성을 가져 생체 내의 큰 변형과 습한 환경을 견뎌내므로 바이오 센서나 의안과 같은 인고 눈 삽입물(artificial ocular prostheses)로 활용 가능함.

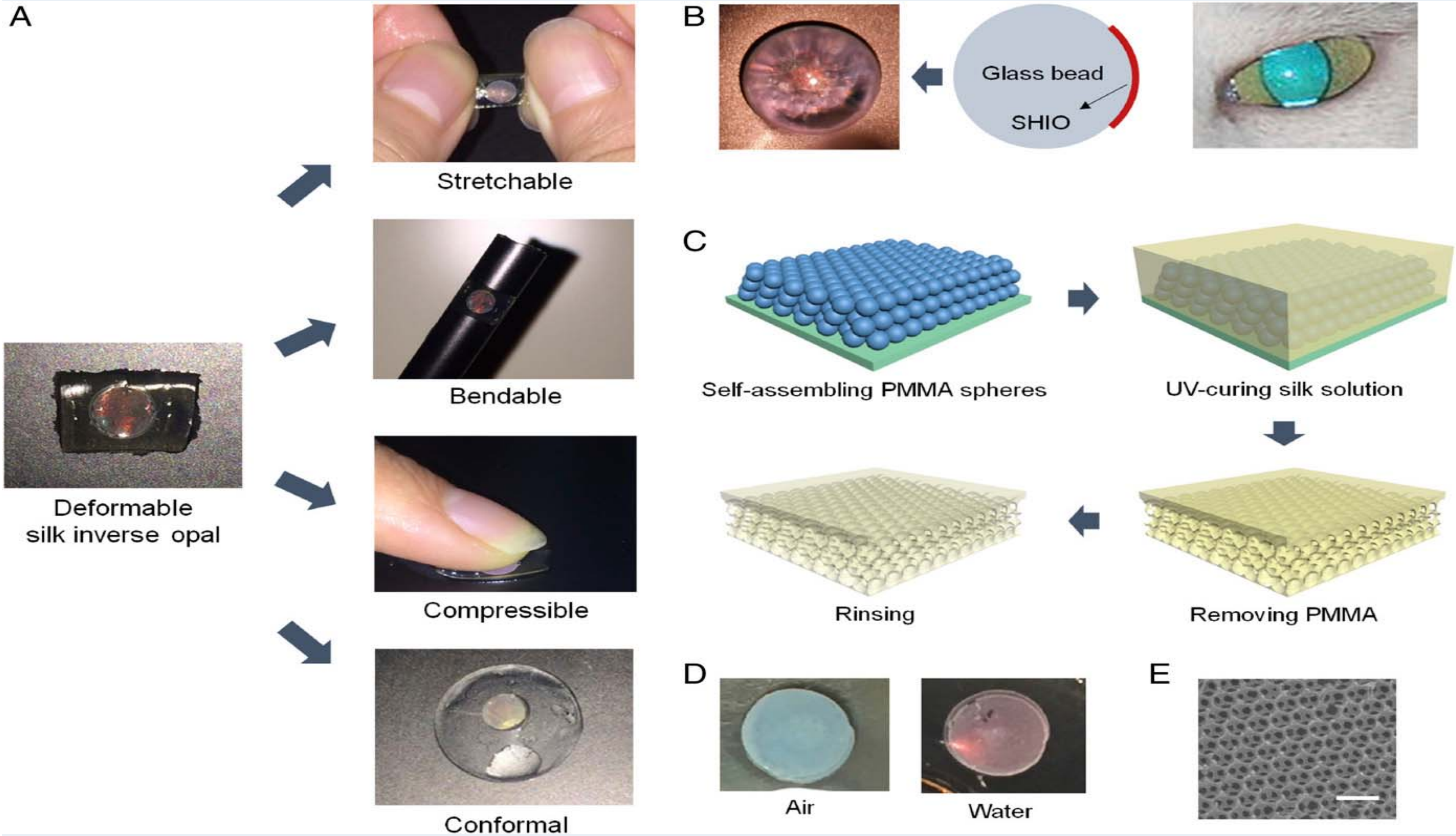


Fig. 1. Deformable SHIO. (A) Conceptual images showing deformations (stretchable, bendable, compressive, and conformal) of SHIOs. All SHIOs exhibited red opalescence corresponding to their pseudo-PBG. (B) Photograph showing brilliant opalescence of the SHIO attached under a glass bead. Analogous phenomena can be found in nocturnal animals with superior night vision. (C) Fabrication steps for the deformable SHIO. A PMMA opal is generated on a silicon substrate. A silk fibroin solution mixed with the stilbene chromophore infiltrates the PMMA opal and then is cured by UVC light from a low-pressure UV lamp. The remaining PMMA spheres are dissolved in acetone. The generated SHIO is immersed in water to wash out the remaining stilbene. (D) Photograph taken under white-light illumination in air (Left) and water (Right), showing clear changes in opalescence. (E) SEM image of the SHIO. (Scale bar, 500 nm.)

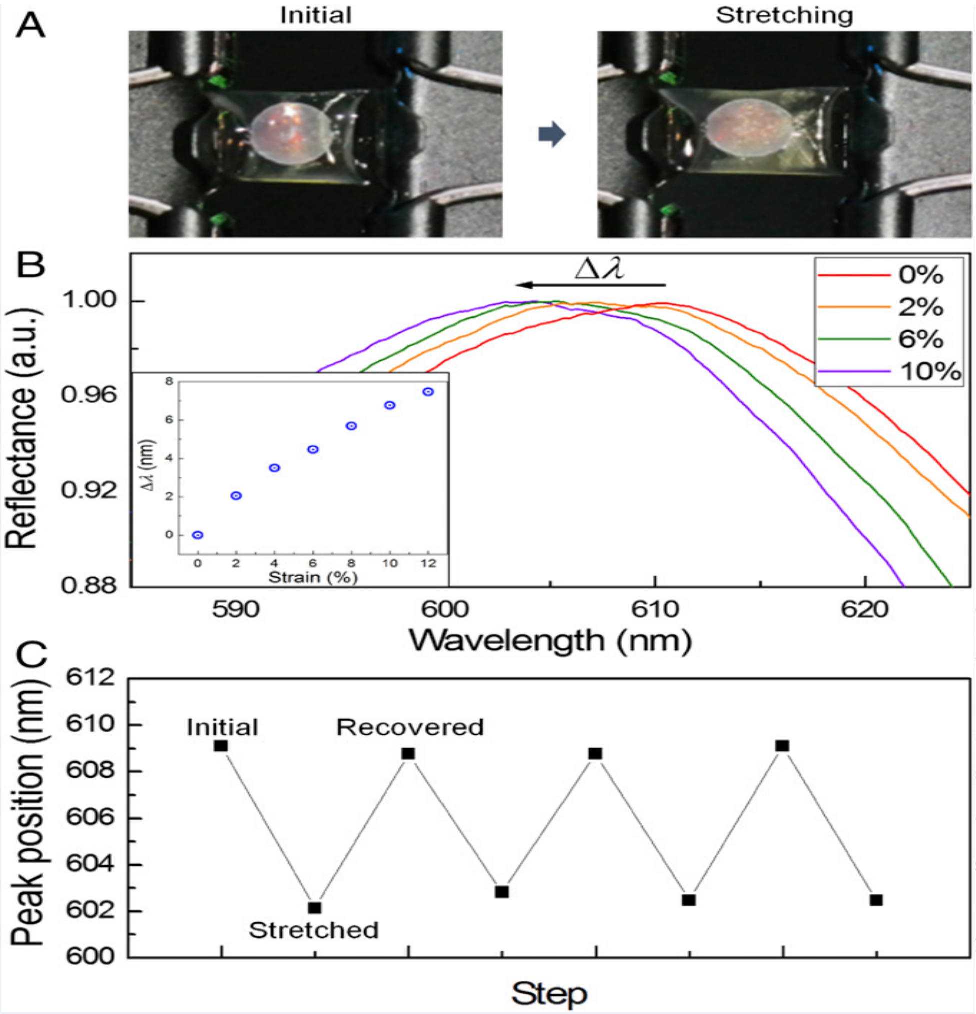


Fig. 3. Optical response of the SHIO film to stretching. (A) Photographic images taken under the application of tension to the SHIO. (B) Reflection spectra showing the blue shift in the pseudo-PBG owing to stretching. Elongation of the SHIO sheet induces contraction of the interplanar space in the vertical direction, thereby blue-shifting the reflection peak. (Inset) Plot of the wavelength shifts of the reflection peak as a function of strain. (C) The stretching–recovering cycling of the peak wavelength position when the SHIO is subjected to 10% strain. There is no deterioration in reflection properties for up to three cycles.

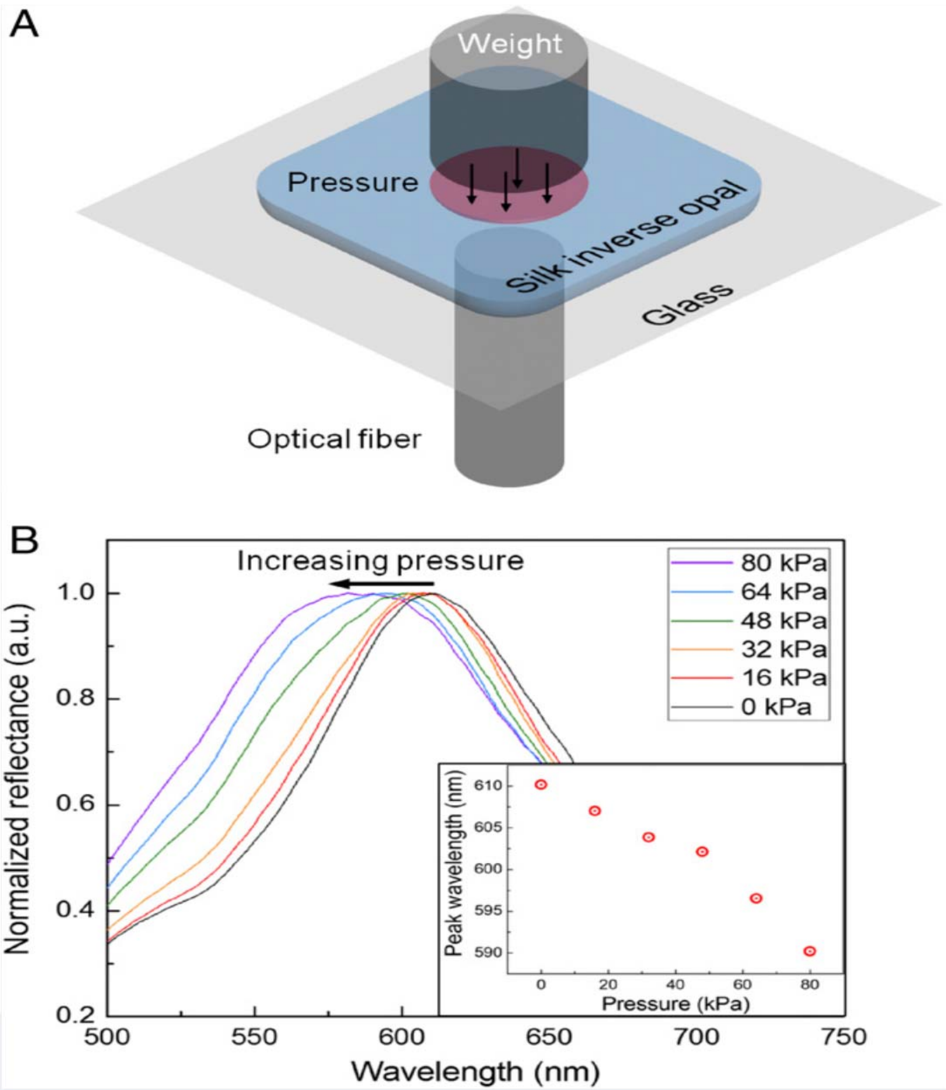


Fig. 4. Optical response of the SHIO on compression. (A Schematic diagram showing how the optical response of the SHIO under pressure is measured. To induce compression weights of the same diameter as the SHIO were loaded ontc the SHIO. (B) Relationship between peak positions anc compressive pressures. The plot shows the blue shift of the reflection peak with increasing pressure due to reduction o the interplanar space. (Inset) Plot of peak wavelength as function of pressure.

✓ Silk Fibroin for Flexible Electronic Devices[6]

- 기존에 연구하고 있는 실리콘 기반 electronic devices는 기계적인 유연성이 없어서 활용도가 높지 않다는 단점을 가지고 있어 이러한 문제를 해결하기 위하여 부드럽고 유연하며 바이오 인터페이스가 좋은 소재로 만들어진 flexible electronic devices는 인체 삽입형 디바이스나 센서를 만드는데 응용성이 높아 많은 연구자들이 보고하고 있음.

- 우수한 기계적, 전기적, 광학적 특성을 가지고 있으며 생체 적합성이 좋고, 환경 친화적이며 저렴한 비용으로 제공되는 바이오 폴리머인 실크 피브로인은 flexible electronic devices의 소재로 큰 장점을 가지고 있음.

- 실크 기반 전자 장치(silk-based electronic devices)의 개발은 인간-기계 인터페이스, 컴퓨팅 기술, 바이오 메디컬 진단, 바이오 통합 전자 장치등의 미래의 바이오 응용성을 제시함.

Figure 1. Schematic of silk fibroin-based electronic devices. Silk fibroin can serve as both active and passive components for a variety of applications.

A brief timeline of the silk “electronic road”

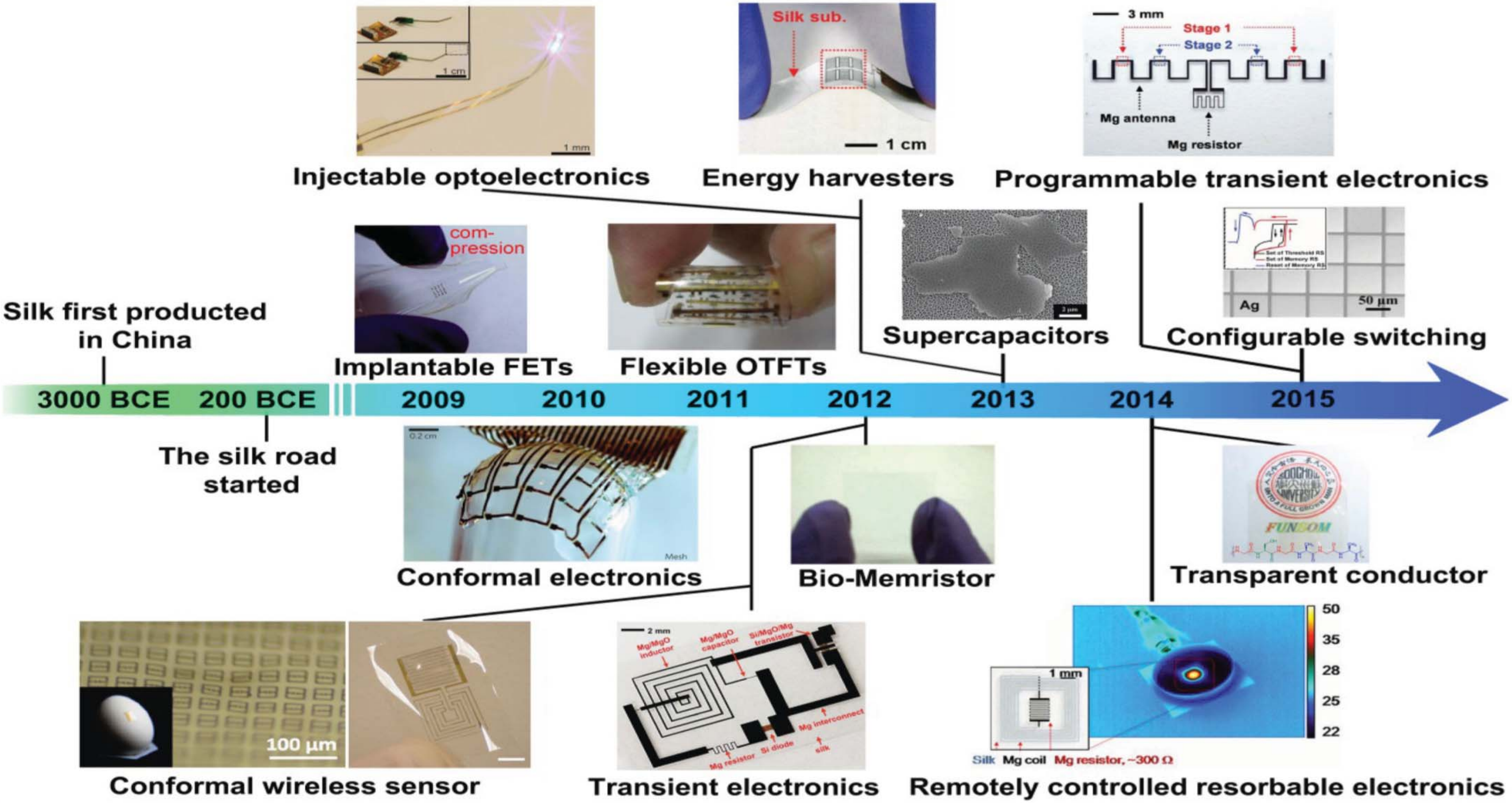


Figure 3. A brief timeline of the silk “electronic road”. Images reproduced with permission: “Implantable FETs”. Copyright 2009, American Institute of Physics. “Conformal electronics”. Copyright 2010, Nature Publishing Group. “Flexible OTFTs”. Copyright 2011, Wiley. “Bio-Memristor”. Copyright 2012, Wiley-VCH. “Transient electronics”. Copyright 2012, American Association for the Advancement of Science. “Conformal wireless sensor”. Right image. Copyright 2012, Nature Publishing Group. Left image. Copyright 2012, Wiley-VCH. “Supercapacitors”. Copyright 2013, Wiley-VCH. “Injectable optoelectronics”. Copyright 2013, American Association for the Advancement of Science. “Energy harvesters”. Copyright 2013, Wiley-VCH. “Transparent conductor”. Copyright 2014, American Chemical Society. “Remotely controlled resorbable electronics”. Copyright 2014, National Academy of Sciences USA. “Configurable switching”. Copyright 2015, Wiley-VCH. “Programmable transient electronics”. Copyright 2015, Wiley.

- **Silk fibroin substrate based Implantable flexible electronics**

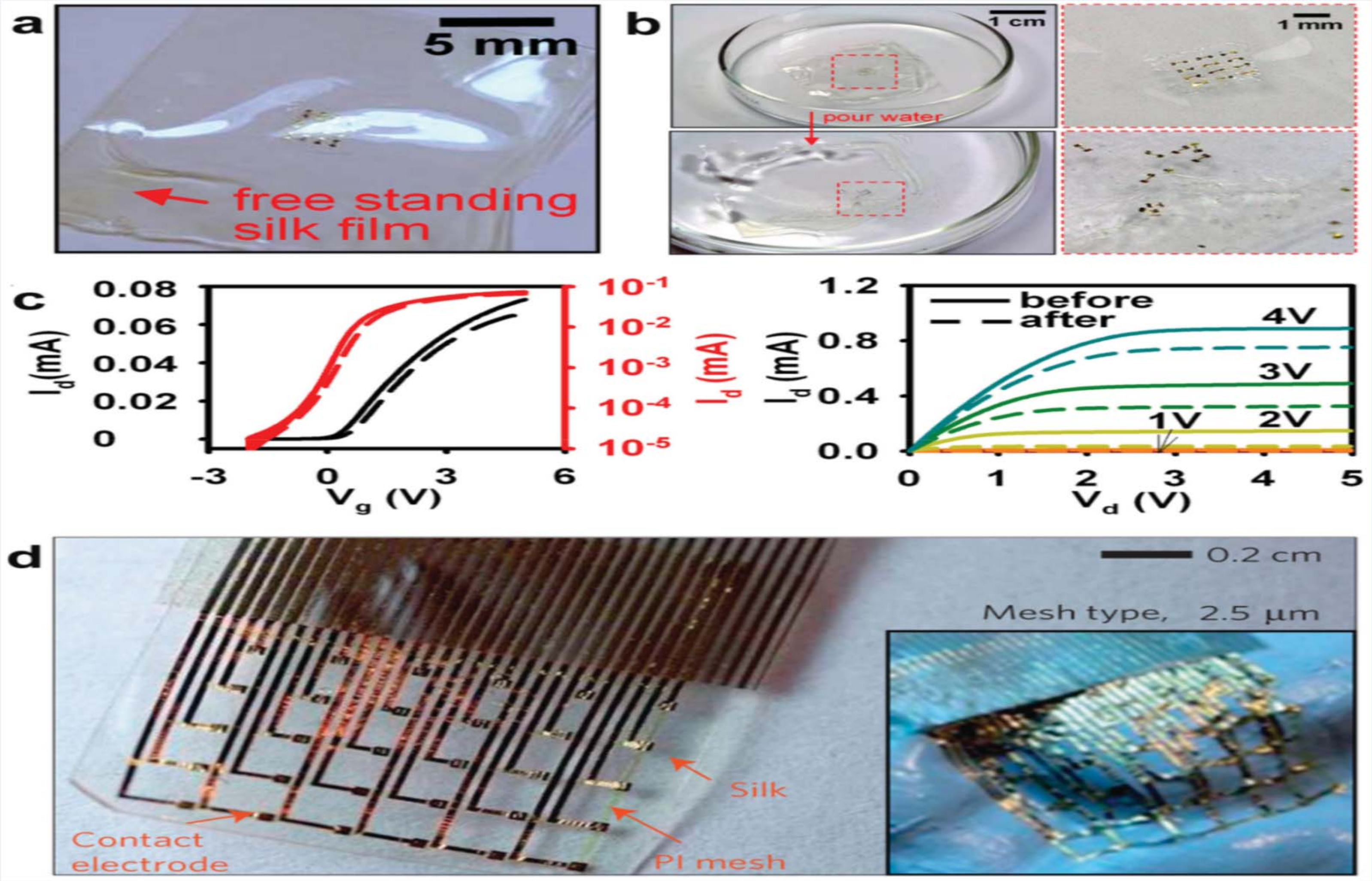


Figure 4. Implantable flexible electronics based on silk fibroin substrates. a) Ultrathin silicon-based transistors on silk-fibroin fi lm. b) Dissolution of the silk-fibroin substrate in water. c) Transfer curves and current–voltage curves of the transistors before and after the dissolution of the silk substrate. (I_d, drain current; V_g, gate voltage; V_d, drain voltage). a–c) Reproduced with permission. Copyright 2009, American Institute of Physics. d) Implantable electrode arrays on silk-fibroin substrate. The dissolution of the silk substrates renders a conformal contact between the electrode arrays and the brain model. d) Reproduced with permission. Copyright 2010, Nature Publishing Group.

• Silk fibroin based wireless sensor

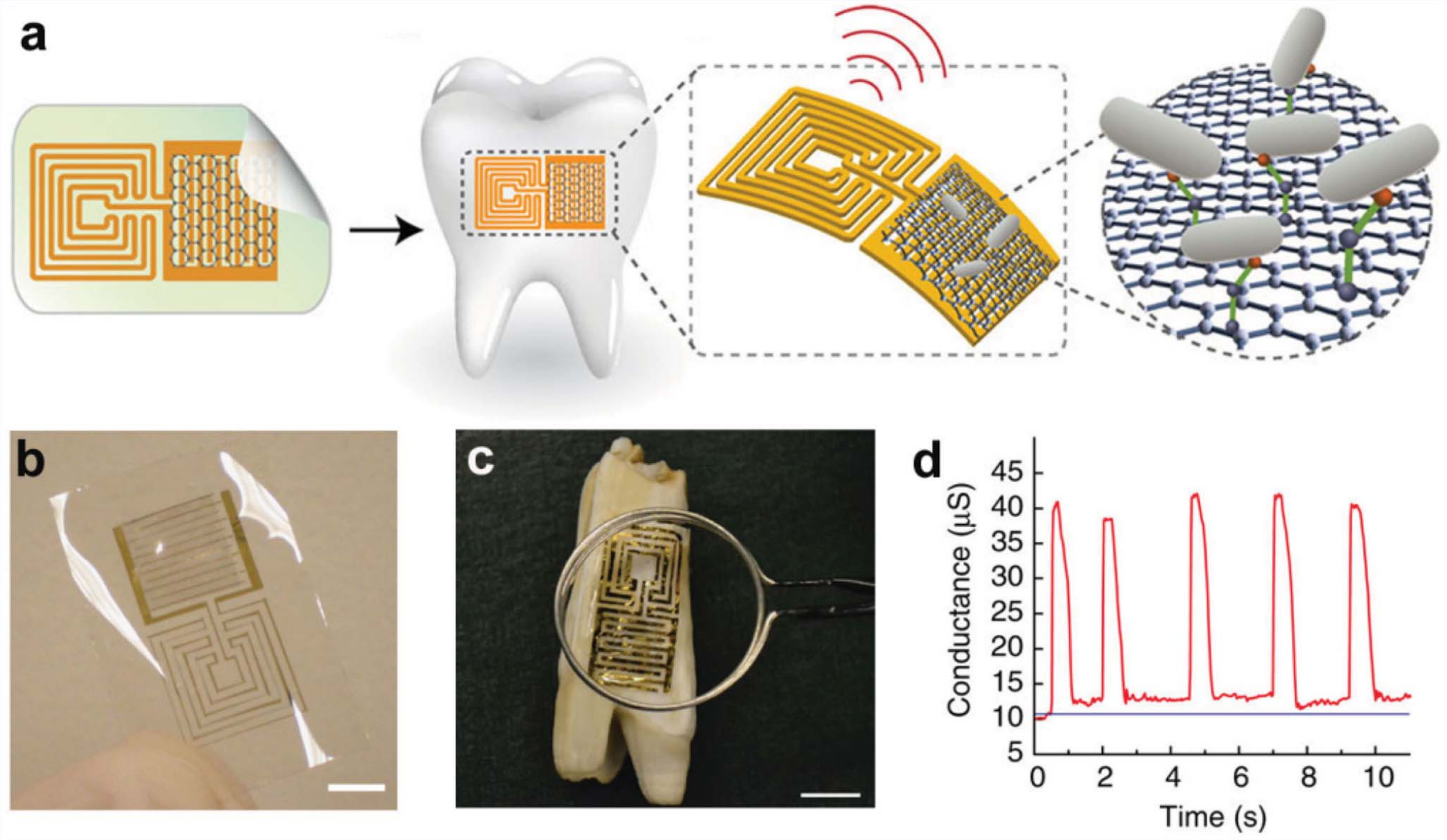


Figure 5. Biotransferable graphene wireless sensor based on silk fibroin. a) Schematic illustration of the transfer and sensing processes. Graphene films and wireless coils are generated on silk-fibroin film and transferred onto a tooth for bacteria detection. a) A photo of the sensor on silk-fibroin film. Scale bar: 5 mm. c) A photo of the graphene wireless sensor on a tooth after the dissolution of the silk substrate. Scale bar: 1 cm. d) Conductance change of the sensor toward pulses of exhaled breath (red) and baseline (blue). a–d) Reproduced with permission. Copyright 2012, Nature Publishing Group.

Silk fibroin substrate based Transient electronics with silk substrates.

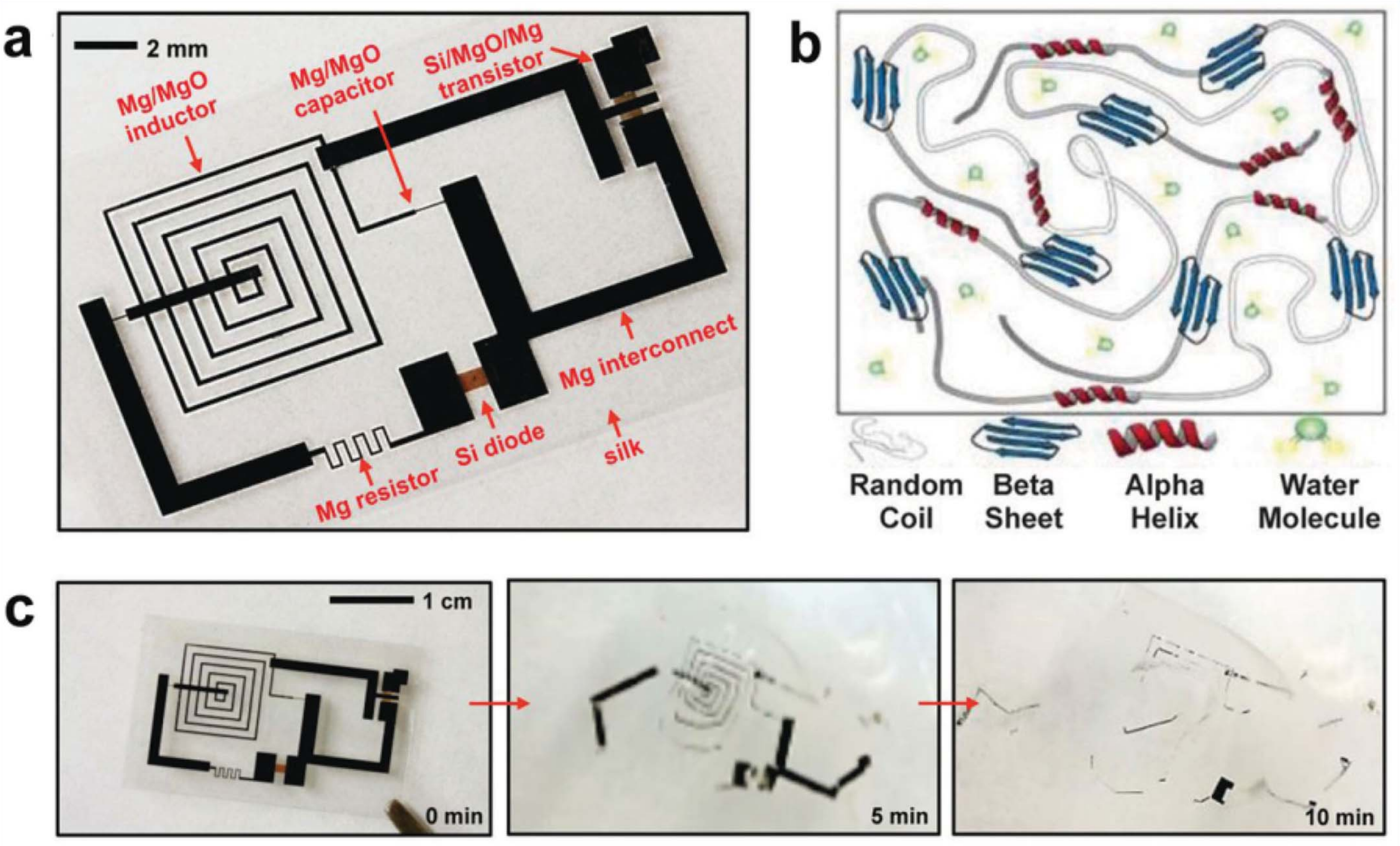


Figure 6. Transient electronics with silk substrates. a) Image of a transient circuit on a silk-fibroin substrate. b) Disintegration of silk fibroin with water. c) Dissolution of the transient circuit in deionized (DI) water. a–c) Reproduced with permission. Copyright 2012, American Association for the Advancement of Science.

Silk-based resorbable wireless heating devices

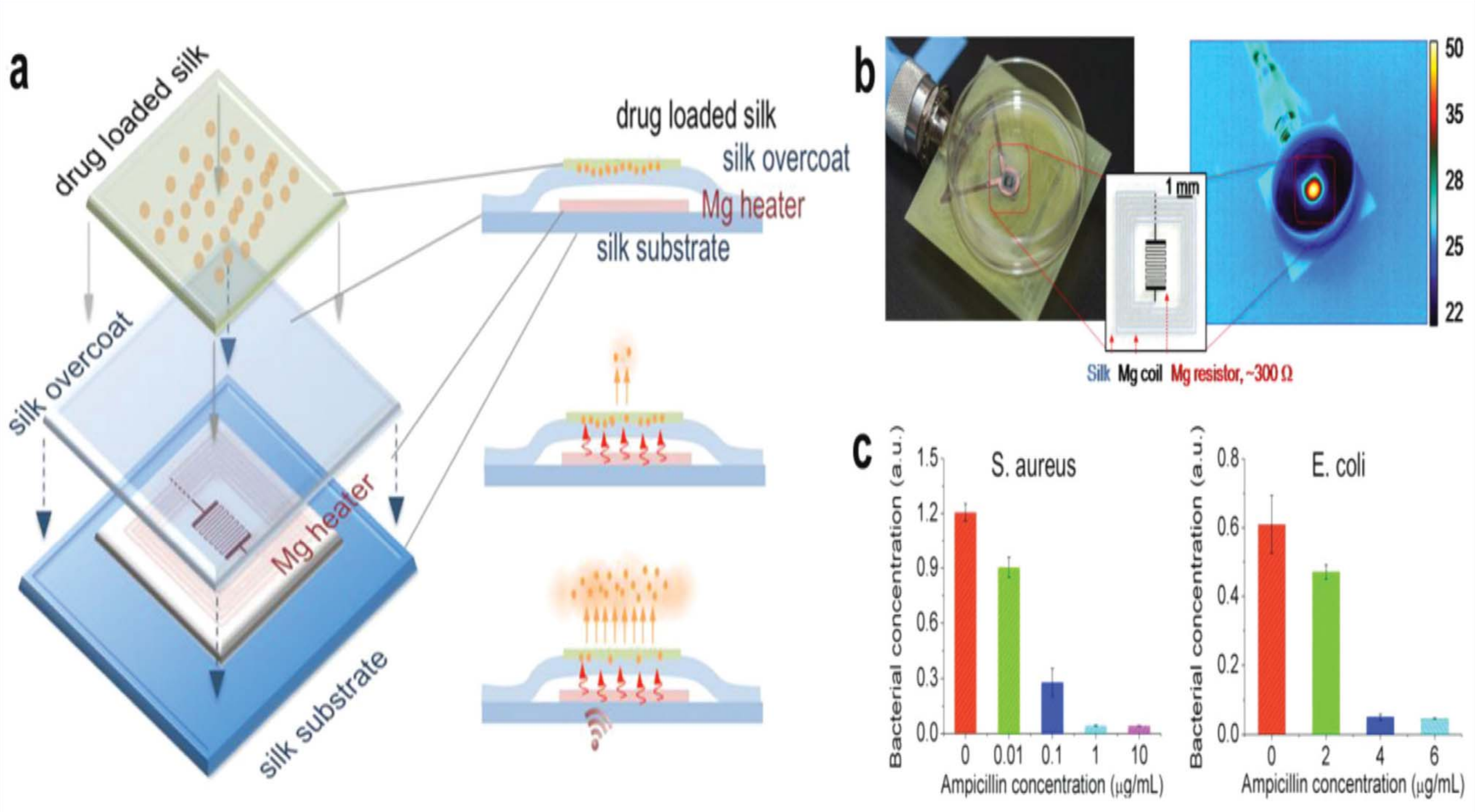


Figure 7. Silk-based resorbable wireless heating devices for therapy and drug release. a) Schematic of the wireless heating device integrated with drug loaded silk. The heating device comprises a resistor and a wireless coil encapsulated in silk fibroin. b) Wireless powering of the heating device to a desired temperature. c) Drug molecules loaded in the silk film can be triggered to release under heat treatment for bacterial inhibition. a–c) Reproduced with permission. Copyright 2014, National Academy of Sciences USA.

- **Silk fibroin based supercapacitors**

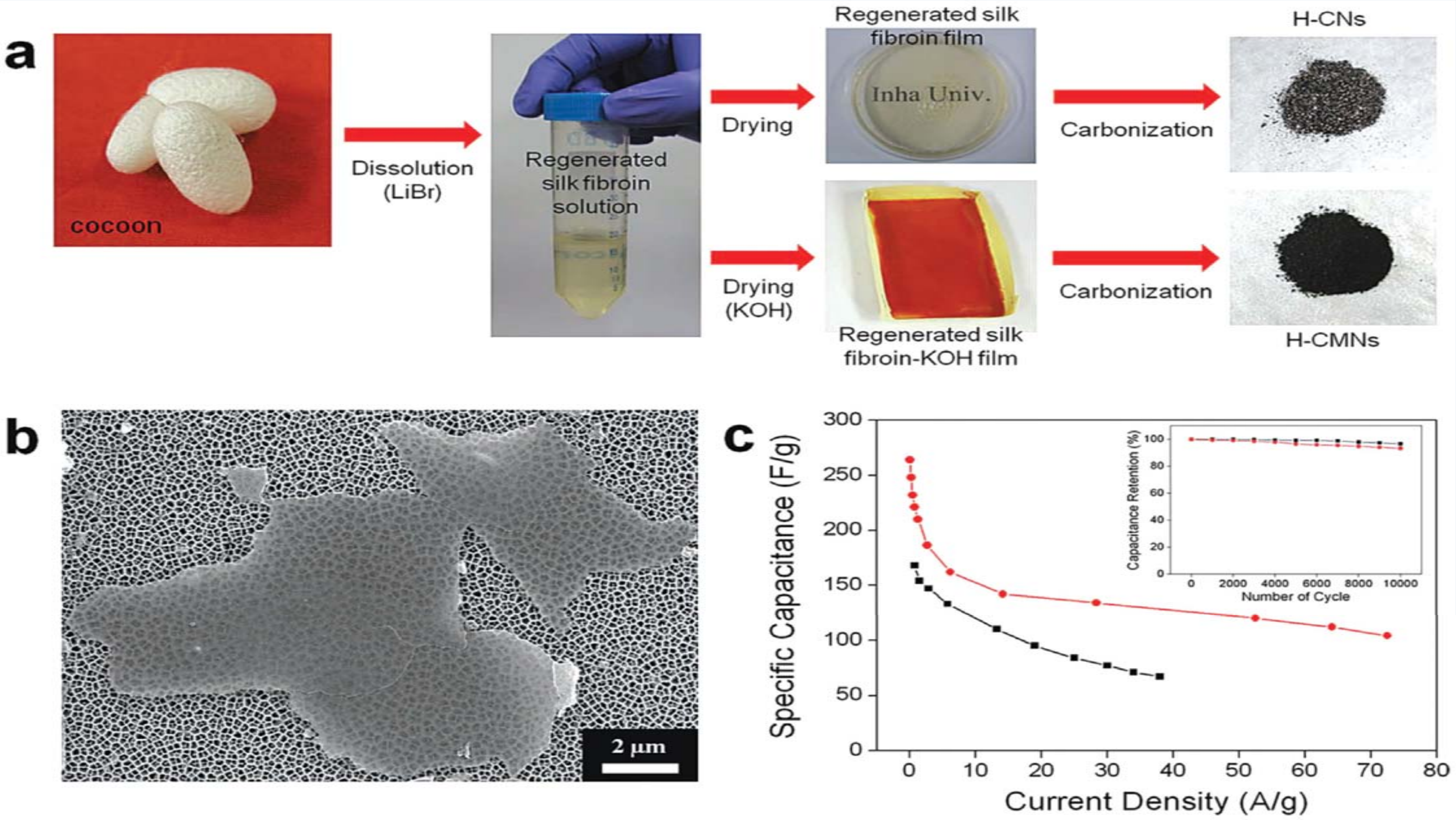


Figure 8. Regenerated-silk-fibroin-based supercapacitors. a) Schematic illustration of the fabrication process of the carbon nanoplates from silk fibroin. b) Scanning electron microscopy (SEM) image of the carbon nanoplate on alumina template membranes. c) Specific capacitance and capacitance retention performance (inset) of the supercapacitors under different current densities in organic (black curves) and aqueous electrolytes (red curves). (a–c) Reproduced with permission. Copyright 2013, Wiley-VCH.

- **Silk fibroin based Flexible organic field-effect transistors**

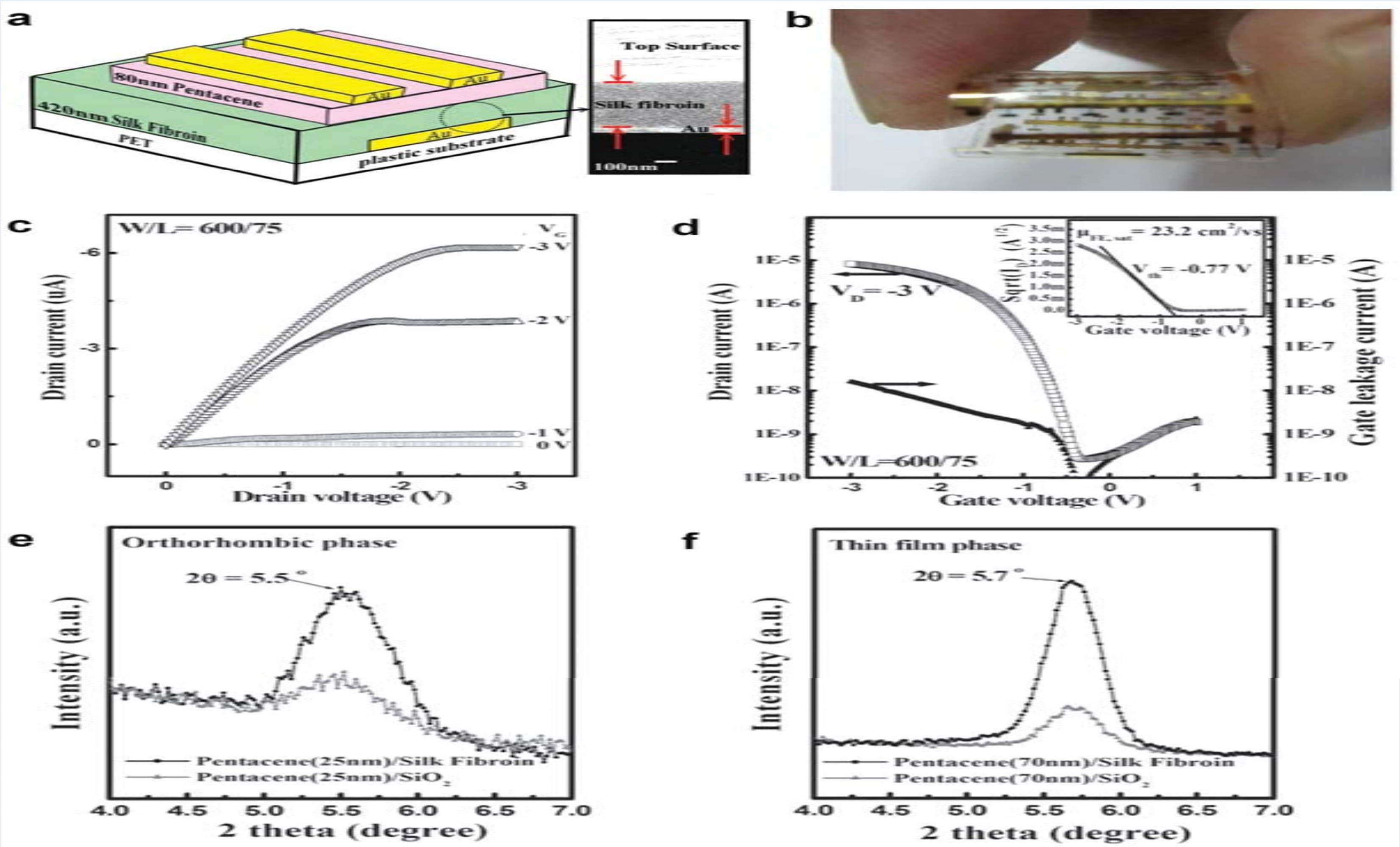


Figure 9. Flexible organic field-effect transistors using silk fibroin as the gate dielectric. a) Schematic of the transistor structure and cross-sectional SEM image of silk-fibroin film with a thickness of 420 nm on a Au gate electrode. b) A photo of the OFETs on a flexible PET substrate. c) Output characteristics of the transistors. d) Transfer and gate-leakage-current curves of the devices. e) GIXRD spectra of the (001) peak of a pentacene orthorhombic phase deposited on fibroin and SiO_2 substrates. f) GIXRD spectra of the (001) peak of a pentacene thin-film phase deposited on fibroin and SiO_2 substrates. a–f) Reproduced with permission. Copyright 2011, Wiley-VCH.

- **Silk fibroin based resistive switching device**

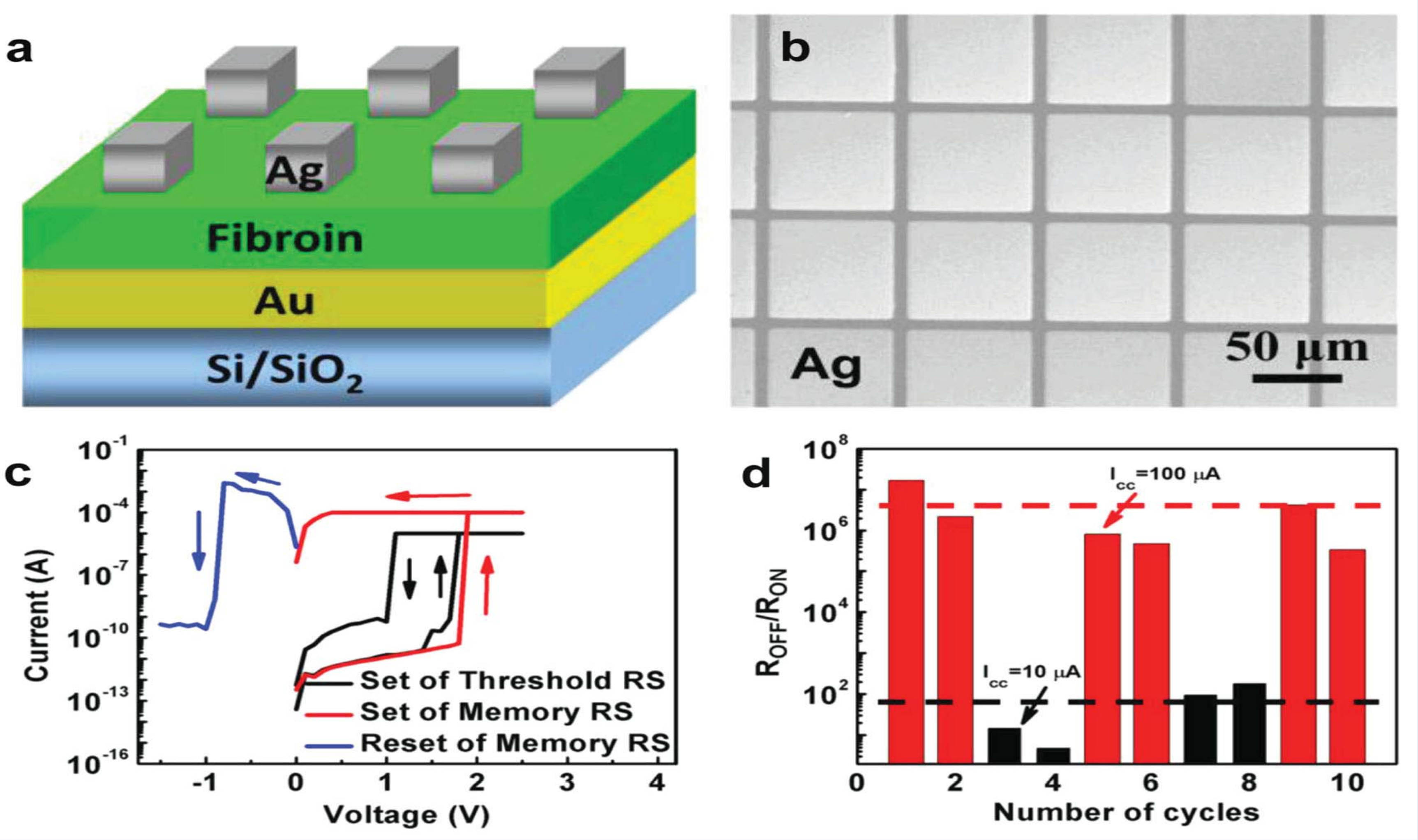


Figure 10. Silk-fibroin-based resistive switching device with both memory and threshold characteristics. a) Schematic of the device with a layered Ag/fibroin/Au configuration. b) An SEM image of fibroin resistive-switching device arrays. c) Resistive-switching behaviors of a Ag/fibroin/Au device. The threshold and memory resistive-switching processes can be achieved by applying different compliance currents. d) Different resistive-switching behaviors of the device in a series of cycles. a–d) Reproduced with permission. Copyright 2015, Wiley-VCH.

- **Silk fibroin based Food sensor**

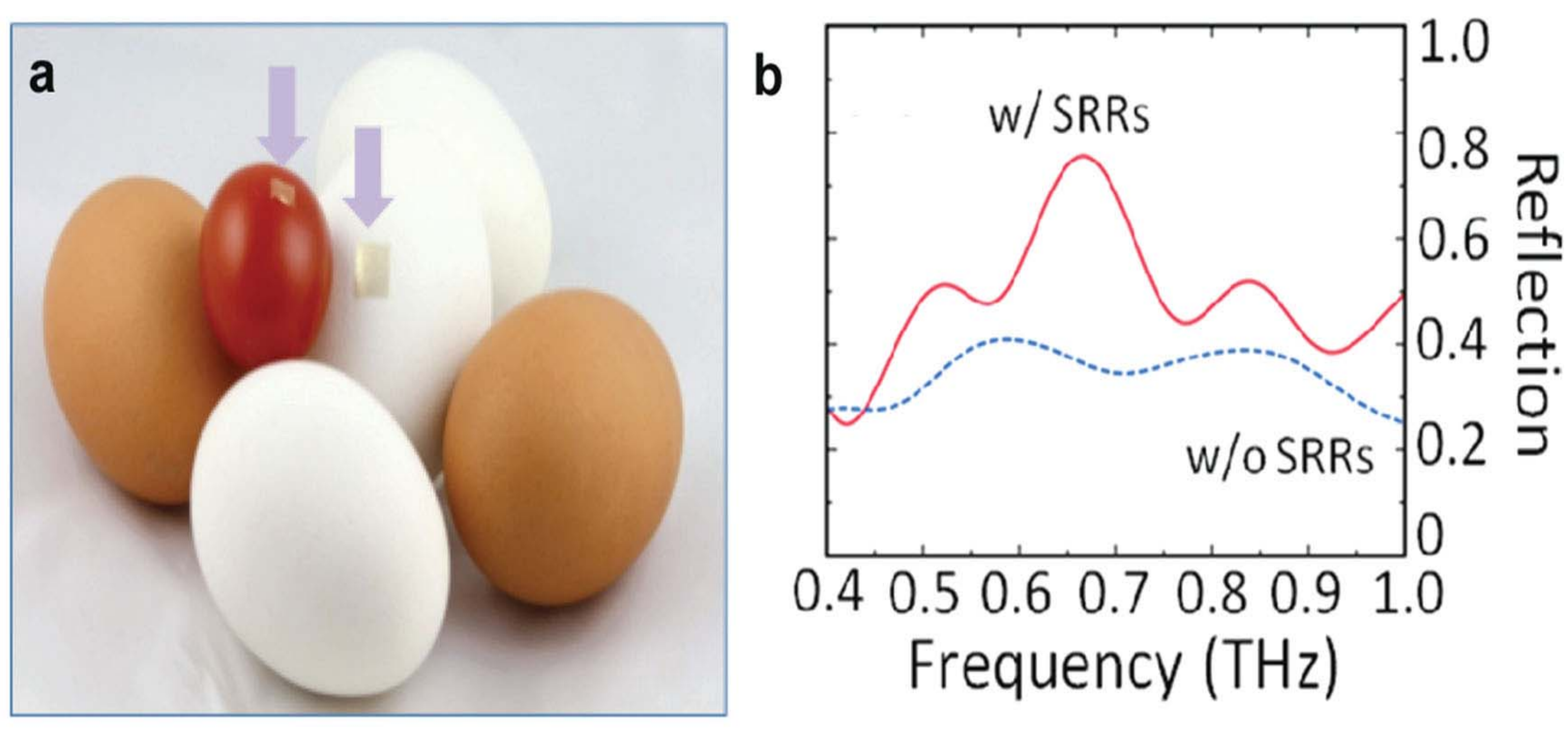


Figure 11. Silk-fibroin-based conformal wireless food sensor. a) Photo of the sensor wrapped on arbitrary food surfaces. b) Reflection spectra of eggs with (red) and without (blue) the food sensor. a, b) Reproduced with permission. Copyright 2012, Wiley-VCH.

3. 결론

- ✓ 4차 산업의 차세대 소재인 실크 피브로인은 인체 내 삽입형 소자나 인체 부착형 소자를 이용한 헬스 케어 플랫폼 구현에 따른 연구 보고가 활발히 진행되고 있으며 새로운 부가 가치가 창출될 것이라 기대됨.[2]

- ✓ 최근에는 인체삽입형 기술의 보다 진보된 형태로서 실크와 같은 생체분해성 기판을 이용함으로써 부드러운 생체조직에 기계적인 변형 및 저항을 줄이면서, 물리적으로 장기 표면에 적절하게 붙일 수 있는 기술이 개발되고 있음.[7]

- ✓ 뇌 수술을 위한 진단기구, 인간-컴퓨터 제어 시스템을 위한 인터페이스, 피부를 기반으로 한 생리현상 모니터링, 심장 질환 치료를 목적으로 풍선 카테터(balloon catheter)에 적용한 연구 등을 보고되고 있음.[7]

- ✓ 또한, 고성능 유연 디바이스(Flexible Electronic Devices)는 신체 내부 장기와 피부에 적용되어 다양한 기능을 확인하였고 실제 환자의 건강상태를 모니터링하는데 있어 매우 중요하여 바이오 메디컬 소자로서의 응용성 및 향후 산업화가 기대됨.[7]

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