



# Highly conductive, stretchable and biocompatible Ag–Au core–sheath nanowire composite for wearable and implantable bioelectronics

## Citation

Choi, Suji, Sang Ihn Han, Dongjun Jung, Hye Jin Hwang, Chaehong Lim, Soochan Bae, Ok Kyu Park et al. "Highly conductive, stretchable and biocompatible Ag–Au core–sheath nanowire composite for wearable and implantable bioelectronics." *Nature Nanotechnology* 13, no. 11 (2018): 1048-1056. DOI: 10.1038/s41565-018-0226-8

## Published Version

doi:10.1038/s41565-018-0226-8

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1 **Highly conductive, stretchable, and biocompatible Ag-Au**  
2 **core-sheath nanowire composite for wearable and**  
3 **implantable bioelectronics**

4  
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22

23 **Abstract**

24

25 Wearable and implantable devices require conductive, stretchable, and biocompatible  
26 materials. However, obtaining composites that simultaneously fulfil these requirements is  
27 challenging due to a trade-off between conductivity and stretchability. Here we report on Ag-  
28 Au nanocomposites composed of ultralong gold-coated silver nanowires in an elastomeric  
29 block-copolymer matrix. Owing to the high aspect ratio and percolation network of the Ag-  
30 Au nanowires, the nanocomposites exhibit an optimized conductivity of 41,850 S/cm (max:  
31 72,600 S/cm). Phase separation in the Ag-Au nanocomposite during the solvent drying  
32 process generates a microstructure that yields an optimized stretchability of 266% (max:  
33 840%). The thick gold sheath deposited on the silver nanowire surface prevents oxidation and  
34 silver ion leaching, making the composite biocompatible and highly conductive. Using the  
35 nanocomposite, we successfully fabricate wearable and implantable soft bioelectronic devices  
36 that can be conformally integrated with human skin and swine heart for continuous  
37 electrophysiological recording, and electrical and thermal stimulation.

38

39 Conductive and stretchable nanocomposites based on the percolation network of  
40 conductive nanomaterials in elastomeric media<sup>1-3</sup> offer a viable alternative to rigid and brittle  
41 conventional metallic materials such as gold<sup>4,5</sup> and indium tin oxide<sup>6</sup>. These nanocomposites  
42 have been applied in e-skin<sup>7,8</sup>, wearable bioelectronics<sup>9,10</sup>, and implantable biomedical  
43 devices<sup>11,12</sup>. Ultralong one-dimensional metal nanowires are favourable filler materials for  
44 these conductive nanocomposites because their high aspect ratio lowers the percolation  
45 threshold of filler materials, resulting in high conductivity<sup>13</sup>. Silver (Ag) nanowires are  
46 particularly popular because they are highly conductive and can be easily produced on a large  
47 scale<sup>13,14</sup>. However, direct exposure of human tissues to Ag ions that leach out from Ag  
48 nanowires can have potential adverse health effects<sup>15</sup>. Due to the high oxidation tendency of  
49 Ag, Ag nanowires are highly corrosive in biological environments, limiting their applications  
50 in bioelectronics<sup>16</sup>. Although gold nanowires have advantages over Ag nanowires in terms of  
51 biocompatibility and oxidation tendency, their conductivity is lower than Ag nanowires, and  
52 producing long and thick gold nanowires in large quantity is very challenging<sup>17,18</sup>.

53 Here, we present the highly conductive, biocompatible, and soft Ag-Au nanocomposites  
54 consisting of ultralong gold-coated Ag nanowires dispersed in poly(styrene-butadiene-styrene)  
55 (SBS) elastomer. The high aspect ratio of Ag nanowires confers high conductivity while the  
56 inert gold shell ensures that the nanowires are biocompatible and resistant to oxidation. The  
57 phase separation during the low temperature drying process induces microstructures in the  
58 nanocomposite, which increases the softness of the material. Cytotoxicity test and  
59 histological analysis confirm that the Au sheath effectively improves biocompatibility by  
60 preventing Ag ion leaching and protecting Ag nanowires from oxidation. Using the highly  
61 conductive, biocompatible, and soft nanocomposites, we successfully fabricated wearable and  
62 implantable bioelectronic devices for biosensing and stimulation on the human skin and

63 swine heart.

64

### 65 **Fabrication and characterization of the Ag-Au nanocomposite**

66 The fabrication of the microstructured Ag-Au nanocomposite requires a mixture of Ag-Au  
67 nanowires decorated with hexylamine ligands, SBS elastomer, and an additional hexylamine  
68 in toluene (Fig. 1a). To obtain Ag-Au nanowires, we firstly synthesized ultralong Ag  
69 nanowires (~100  $\mu\text{m}$ ) using the previous method with slight modifications (Supplementary  
70 Fig. 1a)<sup>19,20</sup>. For galvanic-free deposition of Au on the Ag nanowires, we used sodium sulfite  
71 to selectively bind Au cations and consequently lower the reduction potential of Au ( $E^{\circ} =$   
72 0.111 V vs. standard hydrogen electrode; Supplementary Fig. 1b)<sup>21</sup>. Because the resulting  
73 gold(I) sulfite complex is relatively benign to the Ag surface, ligand-assisted oxidative  
74 etching does not occur, instead Au coating is boosted. The galvanic replacement reaction is  
75 also prevented by keeping the reaction solution at pH 9 (Supplementary Fig. 2)<sup>22</sup>. After the  
76 gold coating, the surface of Ag-Au nanowires is modified with hexylamine using the  
77 previously-reported ligand exchange procedure (Supplementary Fig. 1c)<sup>23</sup>.

78 To obtain the microstructured Ag-Au nanocomposite, hexylamine-decorated Ag-Au  
79 nanowires, a SBS solution, and additional hexylamine in toluene are combined and casted on  
80 a glass mold under ambient conditions (Fig. 1b). During the dry-casting and solvent-drying  
81 process, the initially homogeneous solution (Fig. 1c left) is separated into two phases, a  
82 hexylamine-rich region containing Ag-Au nanowires and a toluene-rich region containing  
83 SBS (Fig. 1c middle). Subsequent solvent evaporation results in a microstructured Ag-Au  
84 nanocomposite composed of a Ag-Au nanowire-rich region and a SBS-rich region (Fig. 1c  
85 right). When the microstructured Ag-Au nanocomposite is stretched, the Ag-Au nanowire  
86 rich region maintains the stable electrical conduction and the SBS-rich region forms an

87 elastic microstructured strut (Fig. 1d). Despite the high concentration of the nanowire filler  
88 added to the nanocomposite for improved conductivity (Supplementary Fig. 3a), the cushy  
89 microstructure ensures softness and stretchability (Fig. 1e, Supplementary Fig. 3b).  
90 Stretchability can be further improved by heat rolling-press (Fig. 1f, Supplementary Fig. 3c,  
91 Supplementary Movie 1).

92 We confirmed the Ag-Au nanowire core-sheath structure using various electron  
93 microscopy and spectroscopy methods. Scanning electron microscopy (SEM) image in Fig.  
94 2a shows the nanowires are long (~100  $\mu\text{m}$ ) and interconnected each other. A backscattered  
95 electron image in the inset illustrates the Ag nanowire core and Au sheath (highlighted in  
96 yellow) of the Ag-Au nanowire (before surface modification). High-resolution transmission  
97 electron microscopy (HRTEM) image of the Ag-Au nanowire shows a clear boundary  
98 between the heavy atomic shell (Au) and the light core (Ag) (Fig. 2b). The lattice parameter  
99 of the outer shell confirms the crystalline structure of Au in the [111] direction (Fig. 2b inset).  
100 Mapping the spatial distribution of Ag and Au using high-angle annular dark field scanning  
101 transmission electron microscopy (HAADF-STEM) and energy-dispersive X-ray  
102 spectroscopy (EDS) further confirmed the core-sheath structure of the Ag-Au nanowires (Fig.  
103 2c). The smooth morphology indicates that Ag etching by galvanic replacement reaction does  
104 not occur. The atomic intensity profile in a line scan of the Ag-Au nanowire (Fig. 2d top)  
105 shows that the mean diameter of the nanowire and thickness of the Au shell are 140 nm and  
106 35 nm, respectively (Fig. 2d bottom).

107 Because oxidation and/or corrosion can increase contact resistance between nanowires, and  
108 Ag nanowires are vulnerable to these processes when exposed to biofluids such as sweat<sup>24</sup>,  
109 interstitial fluid<sup>25</sup>, and blood<sup>11</sup>, we examined the oxidation resistance of our Ag-Au nanowire  
110 using hydrogen peroxide as the oxidant. TEM images show that the Ag nanowire is heavily

111 oxidized and corroded, while the Ag-Au nanowire with the protective Au shell remains intact  
112 (Fig. 2e). The resistance against oxidation is further confirmed by UV-Vis spectra, which  
113 show a significantly diminished extinction spectrum for Ag nanowires that have undergone  
114 oxidation and an unchanged spectrum for Ag-Au nanowires (Fig. 2f). Similar protective  
115 effect by the Au shell could be obtained when tested with the Ag-Au nanowires kept in H<sub>2</sub>O  
116 for 6 months, indicating that the Au shell remains intact for long period of time under the  
117 aqueous solution (Supplementary Fig. 4a).

118 We characterized the conductivity of the Ag-Au nanocomposite (prepared at a 60:40  
119 weight ratio of nanowire:SBS; Fig. 2g). Nanocomposites with longer nanowires (~100  $\mu$ m)  
120 have a higher conductivity (~41,850 S/cm) than those with shorter nanowires (25  $\mu$ m) (Fig.  
121 2g). The high aspect ratio of the ultralong nanowires significantly reduces their percolation  
122 threshold in the nanocomposite compared to zero-dimensional nanoparticles<sup>1</sup> or two-  
123 dimensional nanoplates<sup>9</sup>. The percolation threshold of the Ag-Au nanocomposite ( $V_c =$   
124 0.0037; critical volume fraction at a percolation threshold; Supplementary Fig. 5a) is obtained  
125 by experiments, which is higher than theoretical percolation threshold ( $V_{c,ideal} = 0.0009$ )  
126 based on the assumption of ideal distribution of nanowires. This is due to the phase  
127 separation effect (Supplementary Fig. 5b)<sup>26</sup>. We also confirmed that the percolation threshold  
128 increases in proportional to the applied strain (Supplementary Fig. 5a)<sup>27</sup>. Conductivity can be  
129 increased up to around 72,600 S/cm by increasing the content of Ag-Au nanowires in the  
130 composite (75:25 weight ratio of nanowires:SBS; Fig. 2h). However, at such a high nanowire  
131 content, stretchability decreases. The conductivity of ~41,850 S/cm is obtained at the 60:40  
132 weight ratio of nanowires:SBS, which is the mixing ratio for co-optimization of conductivity  
133 and stretchability. In air and physiological solutions, the conductivity of Ag-Au  
134 nanocomposite did not deteriorate, while that of the Ag nanocomposite (made of Ag

135 nanowires and SBS) continuously decreased over 3 weeks (Supplementary Fig. 4b and c).  
136 For the further confirmation of stability of the Ag-Au nanocomposite, we treated  
137 ultraviolet/ozone (UV/O<sub>3</sub>) (40 mW/cm<sup>2</sup>, 2 hours; ozone as an oxidant) to the nanocomposites.  
138 The conductivity of Ag-Au nanocomposite remained unchanged, whereas the conductivity of  
139 control Ag nanocomposites deteriorated significantly due to oxidation (Fig. 2i). SEM images  
140 confirm severe oxidation of the Ag nanocomposite by UV/O<sub>3</sub> (Fig. 2j top) and the inertness  
141 of the Ag-Au nanocomposite (Fig. 2j bottom).

142

### 143 **Phase separation effects on the nanocomposite properties**

144 Phase separation determined by solvent drying temperature and hexylamine concentration  
145 has a pronounced effect on the conductivity, softness, and stretchability of the Ag-Au  
146 nanocomposite. We found that the room temperature solvent drying process leads to a thinner  
147 nanocomposite film with a higher density of the percolated nanowire network, and a more  
148 conductive nanocomposite than higher temperature processes (Supplementary Fig. 6a and 6b).  
149 Room temperature drying facilitates the separation of Ag-Au nanowires into hexylamine-rich  
150 regions and promotes the stabilization of SBS in toluene-rich regions (Supplementary Fig.  
151 6c). This phase separation results in the formation of microstructures and regions showing  
152 different elasticity (Fig. 3a left, Supplementary Fig. 6d). Upon stretching, a porous  
153 microstructure is observed (Fig. 3a right, Supplementary Fig. 7). This cushion-like  
154 microstructure lowers Young's modulus and increases softness (Fig. 3b). Computer  
155 simulation shows that local stress is distributed in the elastic SBS-rich region under stretching,  
156 while the mesh-like Ag-Au nanowire-rich region maintains the original percolation network  
157 (Supplementary Fig. 8; see Supplementary Materials and Methods 1.5 for simulation details).  
158 For experimental confirmation, we prepared the double-layered Ag-Au nanocomposite



159 encapsulated in elastic substrates (VHB film), and the resistance was measured under  
160 stretching. Consequently, the microstructured Ag-Au nanocomposite (0.36:0.24:0.4; weight  
161 fraction of Ag-Au nanowires:SBS:hexylamine) fabricated at room temperature shows a  
162 conductivity of 41,850 S/cm (at 0% strain) and a stretchability of ~266%, both of which are  
163 higher than the composites obtained through the high temperature processes (Fig. 3c).

164 Another key factor that affects phase separation is the amount of hexylamine. Without  
165 hexylamine (*i.e.*, 0 wt% hexylamine), phase separation is limited and no microstructure is  
166 formed (Fig. 3d), leading to low stretchability. However, higher weight fraction of  
167 hexylamine tends to promote phase separation, and therefore, boosts softness (Fig. 3e) and  
168 stretchability (Fig. 3f). When the weight fraction of hexylamine is increased up to 0.4 at the  
169 fixed weight ratio of 60:40 for Ag-Au nanowires:SBS, Young's modulus decreases  
170 significantly while softness and stretchability increases. Based on our experimental results  
171 (22 conditions;  $n = 3$ ) using different weight fractions of Ag-Au nanowires, SBS, and  
172 hexylamine for nanocomposites made under room temperature, we made maps of  
173 conductivity and stretchability (Fig. 3g and 3h). The optimum composition to maximize  
174 stretchability, while maintaining a high conductivity of 41,850 S/cm is 0.36:0.24:0.4 weight  
175 fraction of Ag-Au nanowires:SBS:hexylamine (mapped as red dotted lines in Fig. 3h).

176 In order to improve stretchability, we increased toughness of the Ag-Au nanocomposite  
177 using the heat rolling-press process (Supplementary Fig. 9a, see Methods for details of the  
178 heat rolling-press process)<sup>28</sup>. The elastic SBS-rich microstructured struts were cross-linked to  
179 each other, and therefore toughness of the Ag-Au nanocomposite increased (Supplementary  
180 Fig. 9b). However, the heat rolling-press did not affect the microstructure of the  
181 nanocomposite formed by the phase separation (Supplementary Fig. 9c). The stretchability of  
182 the Ag-Au nanocomposite (fixed weight ratio of 60:40 for Ag-Au nanowires:SBS) can be

183 increased up to ~840%, when the weight fraction of hexylamine is increased up to 0.3 and the  
184 heat rolling-press is applied (Fig. 3i). At the early stage of stretching (*e.g.*, applied strain of  
185 100% or lower), the applied strain is mostly dissipated in the soft SBS rich regions, and  
186 therefore electrical conduction in the Ag-Au nanowire rich region is stabilized  
187 (Supplementary Fig. 9d and e). As the strain is applied further (*e.g.*, applied strain of 300% or  
188 higher), the induced strain in the hard Ag-Au nanowire rich region results in formation of  
189 local cracks. But connected electrical pathways via adjacent Ag-Au nanowire rich regions  
190 (Supplementary Fig. 9f) as well as Ag-Au nanowires aligned in the stretching direction  
191 between the isolated Ag-Au nanowire rich regions (Supplementary Fig. 9g and its inset)<sup>29</sup>  
192 stably preserve the percolation network. Meanwhile, when the strain above the critical limit  
193 (*e.g.*, applied strain of 840% or higher) is applied, massive charging in SEM occurs, which  
194 implies that the percolation of nanowires and electrical pathways through Ag-Au nanowire  
195 rich regions become disconnected (Supplementary Fig. 9h). When the weight fraction of  
196 hexylamine is 0.3, the roll-pressed Ag-Au nanocomposites exhibit stretchability of 840%,  
197 520%, 300%, and 180% with the initial conductivity of 30,000 S/cm, 38,800 S/cm, 50,600  
198 S/cm, and 69,400 S/cm for 60:40, 65:35, 70:30, and 75:25 Ag-Au nanowire:SBS weight  
199 ratios, respectively (Fig. 3j and inset). Electrical and mechanical stability of the Ag-Au  
200 nanocomposite after the cyclic stretching test was shown in Supplementary Fig. 10. Even  
201 after the Ag-Au nanocomposite with the Ag-Au nanowires:SBS:hexylamine weight fraction  
202 of 0.36:0.24:0.4 was stretched with the 10%, 20%, and 30% applied strain repetitively over  
203 3,000 times, there was no significant change in the performance.

204

### 205 **Biocompatibility of Ag-Au nanowire composite**

206 For bioelectronic applications, biocompatibility is crucial and preventing direct exposure

207 of Ag nanowires to tissues is important. We examined the effect of the Au sheath on the  
208 biocompatibility *in vitro* and *in vivo*. To test the leaching of Ag ions, Ag nanowires, Ag-Au  
209 nanowires, and Ag-Au nanocomposite were incubated in Dulbecco modified eagle medium  
210 (DMEM) for 3 days and the dissolution of Ag ions was analysed using inductively coupled  
211 plasma mass spectrometry (ICP-MS). DMEM extract for Ag nanowires has 5,349 ppb Ag  
212 ions. Very low concentration of Ag ions (311 ppb) was detected in the DMEM extract for Ag-  
213 Au nanowires and only trace levels (65 ppb) were detected for the Ag-Au nanocomposite,  
214 indicating that the Au sheath effectively inhibits the dissolution of Ag ions (Fig. 4a). The  
215 detected Au ion concentration was negligibly low (0.847 ppb; Supplementary Fig. 11). Heart  
216 myoblast (H9C2; Fig. 4b) and human skin fibroblast (CCD-986sk; Supplementary Fig. 12)  
217 cells exposed to DMEM extract from Ag nanowires showed damaged actin skeleton and  
218 DNA while those exposed to extract from Ag-Au nanowires and Ag-Au nanocomposite  
219 remained healthy. Furthermore, H9C2, CCD-986sk, and mouse connective tissue (L929) cells  
220 exposed to DMEM extracts from Ag nanowires exhibit significantly decreased viability (Fig.  
221 4c). These results confirm that the Au sheath effectively protects the Ag nanowires from  
222 leaching potentially lethal Ag ions.

223 We further implanted the Ag nanocomposite and Ag-Au nanocomposite on the rat's heart  
224 for 3 weeks and measured the biodistribution of Ag ions in the liver, spleen, lung, and kidney  
225 using ICP-MS (Fig. 4d). The Au sheath effectively reduces accumulation of Ag ions in all the  
226 organs. Histology analysis (Masson's trichrome staining, Hematoxylin and Eosin staining) of  
227 the cardiac muscle after 3 weeks of implantation reveals significantly lower fibrotic reaction  
228 and inflammatory responses in the Ag-Au nanocomposite than those in the Ag nanocomposite  
229 (Fig. 4e, Supplementary Fig. 13a). The data were further analysed by measuring the  
230 percentage of fibrotic area over whole area using image-J image analysis software (NIH) and

231 quantitatively confirmed less fibrotic reaction in the Ag-Au nanocomposite compare to the  
232 Ag nanocomposite (Supplementary Fig. 13b).

233

#### 234 **Ag-Au nanocomposite for wearable bioelectronics**

235 Due to the high stretchability and conductivity, we used the Ag-Au nanocomposite to  
236 develop wearable bioelectronics for measuring electrophysiological signals and applying  
237 electrical/thermal stimulations on the human skin. The Ag-Au nanocomposite and SBS are  
238 patterned by using polydimethylsilane (PDMS) molds and assembled (Supplementary Fig.  
239 14a) into a multifunctional wearable electronic patch consisting of recording electrodes to  
240 measure electrophysiological signals, bipolar stimulation electrodes, and a heating element to  
241 apply electrical and thermal stimulations (Fig. 5a). Because the device is soft and stretchable  
242 (Fig. 5b), it can follow the contour of flexible joints such as the wrist (Fig. 5c). The  
243 conformal contact minimizes the gap between the electrode and skin, and thus high quality  
244 signals can be obtained<sup>30</sup>. Furthermore, the low resistance of the Ag-Au nanocomposite  
245 electrodes is helpful to reduce the impedance of the device on the skin (Fig. 5d) and are  
246 therefore capable of obtaining electrocardiogram (ECG; from the right forearm with ankle  
247 ground) and electromyogram (EMG; from the right forearm) from the human skin with a high  
248 signal-to-noise ratio (Fig. 5e).

249 While electrophysiological signals (*e.g.*, ECG, EMG) provide information on muscle  
250 and/or cardiac dysfunction, electrical stimulation is useful for pain relief<sup>31</sup>, rehabilitation<sup>32</sup>,  
251 and prosthetic motor control<sup>33,34</sup>. Therefore, in addition to recording electrophysiological  
252 signals, the wearable bioelectronics can be used to concurrently administer therapies through  
253 the skin. We applied constant-current monophasic square pulses (Supplementary Fig. 14b) to  
254 the skin through the wearable device. Due to lower impedances, the stimulation electrodes

255 made of the Ag-Au nanocomposite have lower threshold current than commercial electrodes,  
256 allowing stimulation with high power efficiency (Supplementary Fig. 14c)<sup>35</sup>. The Ag-Au  
257 nanocomposite wearable device can simultaneously record EMG signals and deliver  
258 electrical stimulations (Fig. 5f). It is well-known that thermal stimulations in conjunction  
259 with electrical stimulations can bring synergetic therapeutic effect<sup>14,32</sup>. The stretchable  
260 heating element at the centre of the wearable device is used for joule heating. Figure 5g  
261 shows the temperature-time profiles with various input voltages. Since the heater shows little  
262 resistance change under stretching, heating performance is stable under deformation (Fig. 5h).  
263 The softness of the patch ensures firm contact with the skin, allowing reliable heat transfer  
264 even when the wrist is flexed or extended (Fig. 5i).

265

#### 266 **Implantable cardiac bioelectronics using Ag-Au nanocomposite**

267 The Ag-Au nanocomposite is highly conductive, biocompatible, and soft, making them  
268 suitable for implantable devices. Various soft cardiac devices (*e.g.*, mesh<sup>11</sup>, film<sup>36</sup>, and  
269 sleeve<sup>37</sup>, etc.) have been reported previously on the rat heart model. However, due to intrinsic  
270 differences between rodents and human such as the heart rate, cardiac action potential, and  
271 pathophysiologic effects of cardiac diseases, studies using large animal models such as the  
272 swine model, which accurately approximates the human physiology, are needed<sup>38</sup>.  
273 Meanwhile, the large area soft cardiac mesh for recording and stimulating at multiple  
274 locations of the swine heart has not been reported yet. Using the Ag-Au nanocomposite, we  
275 fabricated a customized large-area cardiac mesh, whose design is based on the detailed shape  
276 of the swine heart obtained using magnetic resonance imaging (Fig. 6a). The mesh is  
277 designed to cover the entire surface of the ventricles, and it contains multi-channel electrodes  
278 for recording and stimulation (Fig. 6b and c).

279 We simplified the shape of the cardiac silhouette into a conical frustum (Fig. 6b top),  
280 which is subsequently unfolded to form a two-dimensional fan shape (Fig. 6c). The cardiac  
281 mesh is designed based on this fan shape, which consists of 7 welded repetitive segments,  
282 each containing six pairs of electrodes. Each segment is made up of 5 layers: two electrode  
283 layers made of the Ag-Au nanocomposite and three insulation layers made of SBS (Fig. 6b  
284 bottom and Supplementary Fig. 15a). This multi-layer format enables the multi-channel  
285 electrodes to cover from apex to base of the ventricles.

286 We show that resistance change under mechanical strain is negligible, and the 30% cyclic  
287 stretching (considering maximum heart movement<sup>11</sup>) does not change the performance of the  
288 cardiac mesh, indicating the implanted mesh is stable during repetitive heart movements  
289 (Supplementary Fig. 15b and c). Furthermore, because the modulus of each segment of the  
290 cardiac mesh is much lower than the swine myocardium (Supplementary Fig. 15d)<sup>39</sup>, the  
291 mesh does not interfere with the heart's pumping activity<sup>11,37</sup>.

292 We implanted the cardiac mesh on the swine heart to record myocardial electrophysiology  
293 and stimulate the ventricles *in vivo* (Fig. 6d). Figure 6e shows intracardiac electrograms  
294 recorded by the multi-channel cardiac mesh that wraps around the ventricles in a healthy  
295 swine model. The left anterior descending coronary artery (LAD) was occluded with a  
296 balloon catheter to induce acute ischemia mimicking a heart attack in the clinical setting. On  
297 the voltage map constructed from the multi-channel mesh recording data, high voltage  
298 change in local intracardiac electrograms was observed during ischemia at the anterior wall  
299 of the mid-apex left ventricle (Fig. 6f). The surface electrocardiogram and intracardiac  
300 electrogram were continuously recorded by limb-leads and the cardiac mesh, respectively.  
301 Reliable recording was performed at baseline and during myocardial ischemia, which  
302 exhibited clearly differentiated patterns (Fig. 6g). In Fig. 6h, continuous electrical stimulation

303 (*i.e.*, pacing) at different sites produced different QRS configurations in surface ECG with the  
304 pacing output of  $< 1$  mA at 2 ms, suggesting adequate compartmentalization of individual  
305 electrodes in the cardiac mesh without current leakage or uneven current flow.

306

## 307 **Conclusions**

308 In conclusion, we report a new class of highly conductive, biocompatible, and soft  
309 nanocomposite using ultralong Ag-Au nanowires and SBS elastomer. Epitaxial deposition of  
310 the Au sheath on ultralong Ag nanowires without the galvanic replacement reaction  
311 effectively improves biocompatibility by preventing Ag ion leaching and Ag oxidation. High  
312 conductivity is attained using ultralong nanowires that formed a high density percolated  
313 network in the composite. The ambient solvent drying process during the composite  
314 formation along with an optimized content of hexylamine promotes phase separation and  
315 formation of a cushy microstructure, generating the soft and highly stretchable  
316 nanocomposite. The additional heat rolling-press treatment increases stretchability of the Ag-  
317 Au nanocomposite by increasing toughness. When fabricated into a wearable skin-like device  
318 and implantable cardiac mesh, the highly conductive Ag-Au nanocomposite follows the  
319 contours of a curvilinear human wrist and a pulsating swine heart, allowing  
320 electrophysiological signals including surface EMG, surface ECG, and intracardiac  
321 electrogram to be monitored, and thermal and electrical stimulations to be administered  
322 effectively. These advanced nanocomposite technologies are poised to create new  
323 possibilities for next-generation soft bioelectronics.

324

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419

#### 420 **Acknowledgement**

421 This work was supported by IBS-R006-D1 and IBS-R006-A1. The authors thank the staff of  
422 the National Center for Inter-university Research Facilities (NCIRF) and Research Institute of

423 Advanced Materials (RIAM) in Seoul National University. We all sincerely thank Dr. Mark  
424 Josephson for his material and intellectual support of the animal research.

425

426 **Author contributions**

427 S.C., S.I.H., D.J., H.J.H., T.H., and D.-H.K. designed the experiments. S.C., S.I.H., D.J., C.L.,  
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429 H.J.H., C.L., S.B., O.K.P., C.M.T., S.Y.B., S.W.L., K.P., P.M.K., and R.N. performed *in vivo*  
430 animal experiments and data analysis. S.I.H., S.W.L., and K.P. performed *in vitro*  
431 experiments and analysis. J.W.Y., J.H.R., and W.B.L. performed computer simulation. S.C.,  
432 S.I.H., D.J., H.J.H., S.B., T.H., and D.-H.K. wrote the paper.

433

434 **Additional information**

435 Supplementary information is available in the online version of the paper. Reprints and  
436 permission information is available online at [www.nature.com/reprints](http://www.nature.com/reprints). Correspondence and  
437 requests for materials should be addressed to T.H. and D.-H. K.

438

439 **Competing financial interests**

440 The authors declare no competing financial interests.

441

442

443 **Figure legends**

444

445 **Figure 1. Fabrication of microstructured Ag-Au nanocomposite.** **a**, Ag-Au nanocomposite  
446 is made by combining a mixture of Ag-Au nanowires decorated with hexylamine ligands,  
447 SBS elastomer, and an additional hexylamine in toluene. **b**, Illustration of the solvent drying  
448 process under ambient conditions. **c**, Schematic showing that the initial solution (left) is  
449 separated into a Ag-Au nanowire-rich phase and a SBS-rich phase during dry-casting  
450 (middle). Subsequent solvent evaporation (right) forms the microstructured Ag-Au nanowire  
451 nanocomposite. (red dot: hexylamine, yellow wire: Ag-Au nanowire, green wire: SBS) **d**,  
452 Schematic illustration of the microstructured Ag-Au nanocomposite before and after the  
453 stretching. **e,f**, Optical camera image of the Ag-Au nanocomposite before (**e**; inset shows  
454 before stretching) and after (**f**) the heat rolling-pressed Ag-Au nanocomposite sandwiched  
455 between the elastomeric substrates (VHB film). All scale bars, 10 mm.

456

457 **Figure 2. Characterization and oxidation resistance of Ag-Au nanowire.** **a**, SEM image  
458 and inset back-scattered electron (BSE) image of Ag-Au nanowires (before surface  
459 modification; Au sheath is in yellow). Scale bars, 5  $\mu\text{m}$  and 200 nm (inset). **b**, HRTEM image  
460 of the Ag-Au nanowire. Dash line indicates the boundary between Ag core and Au sheath.  
461 Inset: an electron diffraction pattern at the Ag-Au boundary showing the crystalline structure  
462 of Au in the [111] direction. Scale bar, 5 nm. **c**, EDS elemental mapping of Ag and Au in the  
463 bare Ag-Au nanowire, and their merged image confirm the core-sheath structure. Scale bar,  
464 100 nm. **d**, EDS cross-section line scan of the Ag-Au nanowire shows the mean diameter of  
465 nanowire is 140 nm and thickness of Au shell is 35 nm. **e**, TEM image of the Ag nanowire  
466 (top) and the Ag-Au nanowire (bottom) treated with 1.5 M of  $\text{H}_2\text{O}_2$ . Ag-Au nanowire is  
467 protected against oxidation. Scale bars, 100 nm (top) and 200 nm (bottom). **f**, UV-Vis spectra  
468 of Ag nanowires (left) and Ag-Au nanowires (right) after  $\text{H}_2\text{O}_2$  treatment confirm protection  
469 of Ag-Au nanowires against oxidation. **g**, Graph shows that nanocomposites with longer Ag-  
470 Au nanowires have higher conductivity than those with shorter nanowires. **h**, Graph shows  
471 that the nanocomposites with higher Ag-Au nanowire content are more conductive than those  
472 with lower Ag-Au nanowire content. Maximum conductivity is 72,700 S/cm at the weight  
473 ratio of nanowire:SBS of 75:25 and co-optimized conductivity and stretchability was  
474 achieved at the weight ratio of nanowire:SBS of 60:40 where the conductivity is 41,850 S/cm  
475 with highest stretchability. **i**, At the same weight ratio of nanowire:SBS of 80:20, conductivity  
476 of Ag-Au nanocomposite remains unchanged whereas that of Ag nanocomposite shows a  
477 decrease. All error bars represent s.e.m. **j**, SEM image of Ag nanocomposite (top) and Ag-Au  
478 nanocomposite (bottom) after 2 hours UV/ $\text{O}_3$  treatment. Oxidation is prevented in Ag-Au  
479 nanowires. All scale bars, 1  $\mu\text{m}$ .

480

481 **Figure 3. Effect of phase separation on electrical and mechanical properties.** **a**, SEM  
482 images of the Ag-Au nanocomposite with hexylamine before (left) and after (right) stretching.  
483 Room temperature drying process promotes phase separation and formation of

484 microstructures with unequal elasticity between the phase separated regions, allowing  
485 materials to be stretched. All scale bars, 100  $\mu\text{m}$ . **b**, Stress-strain curve of the Ag-Au  
486 nanocomposite with hexylamine for three different solvent drying temperatures. Room  
487 temperature (25  $^{\circ}\text{C}$ ) drying lowers Young's modulus and forms a softer composite. **c**,  
488 Conductivity change of the Ag-Au nanocomposite under tensile strain for three different  
489 drying temperatures. Nanocomposite obtained through room temperature drying is highly  
490 conductive and stretchable. **d**, SEM images of the Ag-Au nanocomposite without hexylamine  
491 before (left) and after (right) stretching. No microstructures are seen. All scale bars, 100  $\mu\text{m}$ .  
492 **e,f**, Changes of Young's modulus (**e**) and stretchability (**f**) of the Ag-Au nanocomposite film  
493 according to the fraction of hexylamine. Weight ratio of Ag-Au nanowire:SBS is 60:40. All  
494 error bars represent s.e.m. **g,h**, Map showing stretchability (**g**) and conductivity (**h**) of the  
495 nanocomposite at different weight fractions of Ag-Au nanowires, SBS, and hexylamine. The  
496 point (0.36:0.24:0.4 weight fraction of Ag-Au nanowires:SBS:hexylamine) indicated by three  
497 red dotted lines represents the optimum composition for the highest stretchability. Colour  
498 bars in **g,f** indicate conductivity (S/cm) and stretchability (%), respectively. **i**, Graphs  
499 showing conductivity (left) and stretchability (right) of the Ag-Au nanocomposite at different  
500 weight fractions of hexylamine after the heat rolling-press. The Ag-Au nanocomposite can be  
501 stretched up to  $\sim 840\%$  when the weight fraction of hexylamine is 0.3. All weight fraction  
502 means (each component weight) / (sum of Ag-Au nanowires, SBS, and hexylamine weight).  
503 All error bars represent s.e.m. **j**, Graph showing conductivity change of the Ag-Au  
504 nanocomposites under tensile strain for the different weight ratios of Ag-Au nanowire and  
505 SBS at a fixed weight fraction of hexylamine of 0.3. Inset graph shows the initial  
506 conductivity and the conductivity change up to 100% applied strain.  
507

508 **Figure 4. Biocompatibility of Ag-Au nanocomposite *in vitro* and *in vivo*.** **a**, ICP-MS  
509 analysis of Ag ions released from Ag nanowires, Ag-Au nanowires, and the Ag-Au  
510 nanocomposite after incubating each in DMEM for 3 days. Low levels of Ag ions for Ag-Au  
511 nanowires and Ag-Au nanocomposite show that the Au sheath effectively protects Ag  
512 nanowires from dissolution. Data are analysed using one-way ANOVA with the Tukey's post  
513 hoc test and are expressed as averages  $\pm$  s.e.m. ( $n = 3$ ). Significance is set at \*\*\*\* $P < 0.0001$   
514 versus the Ag nanowires. **b**, Confocal microscope image of H9C2 cells after exposure to  
515 original DMEM (control) or DMEM extracts of Ag nanowires, Ag-Au nanowires, and the  
516 Ag-Au nanocomposite for 24 hrs. Cells exposed to Ag nanowire extracts exhibit damaged  
517 (arrows) actin cytoskeleton (red) and DNA (blue). Scale bar, 50  $\mu\text{m}$ . **c**, MTT assay shows  
518 H9C2, CCD-986sk, and L929 cells exposed to DMEM extracts of Ag nanowires have  
519 significantly decreased viability compared to those exposed to original DMEM (control) or  
520 extracts of Ag-Au nanowires and Ag-Au nanocomposite. Data are analysed using one-way  
521 ANOVA with the Tukey's post hoc test and are expressed as averages  $\pm$  s.e.m. ( $n = 3$ ).  
522 Significance is set at \*\*\*\* $P < 0.0001$  versus the control. **d**, ICP-MS analysis of Ag ions  
523 accumulated in liver, spleen, lung, and kidney after sham surgery (control) or implantation of  
524 the Ag nanocomposite and the Ag-Au nanocomposite for 3 weeks. Au sheath effectively

525 reduces Ag ion accumulation in all organs. Data are analysed using one-way ANOVA with  
526 the Tukey's post hoc test and are expressed as averages  $\pm$  s.e.m. (n = 3). Significance is set at  
527 \*P < 0.05 versus the control. **e**, Masson's trichrome staining (left) and hematoxylin & eosin  
528 staining (right) of cardiac muscles after 3 weeks implantation of the Ag-Au nanocomposite  
529 shows less fibrotic reaction and inflammatory response than those implanted with Ag  
530 nanocomposite. Arrows in the first and the third panels indicate fibrosis and inflammatory  
531 cells, respectively (n = 5). Scale bars, 250  $\mu$ m.

532

533 **Figure 5. Wearable skin-like bioelectronics using the Ag-Au nanocomposite.** **a**, Optical  
534 camera image of a multifunctional wearable electronic patch consisting of bipolar stimulation  
535 electrodes, electrophysiological signal recording electrodes, and a heating element. Scale bar,  
536 1 cm. **b,c**, Optical camera images show the wearable device can be stretched 10%, 50%, and  
537 100% (**b**), making them suitable for flexible joints such as the wrist (**c**). Scale bars, 1 cm and  
538 2 cm for **b** and **c** respectively **d**, Impedance of the Ag-Au nanocomposite electrode at the  
539 skin/electrode interface is lower than Ag/AgCl gel electrodes. **e**, Electrocardiogram (ECG)  
540 and electromyogram (EMG) measurements obtained through the wearable device on the skin.  
541 **f**, EMG signals measured during electrical stimulation. **g**, Temperature profiles of the heating  
542 element in the wearable device with applied voltages of 1, 2, and 3 V show reliable heating  
543 performance. **h**, Resistance (left axis) and temperature (right axis) change of the heating  
544 element under applied strain in longitudinal direction. Inset shows an optical camera image of  
545 multifunctional wearable electronic patch stretched in longitudinal direction. **i**, Infrared (IR)  
546 camera images show reliable heating performance of the wearable device on a wrist. Colour  
547 bar indicates temperature ( $^{\circ}$ C).

548

549 **Figure 6. Ag-Au nanocomposite-based implantable cardiac mesh for monitoring and**  
550 **stimulating the swine heart *in vivo*.** **a**, 3D cardiac MRI image of a swine heart (red). **b,c**,  
551 Schematic illustrating the design process for the cardiac mesh. The shape of the heart is  
552 simplified as a cone frustum (**b**), which is unfolded into a two-dimensional fan shape (**c**)  
553 consisting of 7 repetitive segments welded together. Lower inset in **b** shows the cardiac mesh  
554 consists of 2 electrode layers (Ag-Au nanocomposite) and three insulation layers (SBS). **c,d**,  
555 Optical camera image of a cardiac mesh (**c**) and implanted cardiac mesh on a swine heart (**d**).  
556 RV = right ventricle, LV = left ventricle, LAD = left anterior descending coronary artery.  
557 Scale bar, 5 cm. **e**, Representative intracardiac electrograms in a healthy swine model (n = 2)  
558 recorded by the cardiac mesh, displayed on a 3D reconstructed image of the heart (Red = LV  
559 anterior, Orange = LV lateral, Green = LV posterior, and Blue = RV, signals were recorded  
560 from 34 electrodes while the other electrodes were connected to the stimulator). **f**, Voltage  
561 map is constructed from local intracardiac electrograms recorded by the cardiac mesh during  
562 acute ischemia and the anterior wall of the left ventricle shows high voltage change. Acute  
563 ischemia is induced by occluding the left anterior descending coronary artery (LAD) using a  
564 balloon catheter. **g**, Surface ECG and intracardiac electrograms recorded from healthy and  
565 injured regions of the ischemic heart. Arrow indicates ST elevation due to ischemic change.

566 Following prolonged myocardial ischemia of one hour, ventricular tachycardia occurred. **h**,  
567 Representative surface ECG presents different QRS configurations depending on the pacing  
568 sites ( $n = 1$ ). Electrode positions are numbered in **e**.  
569

570

## 571 **Methods**

### 572 **Synthesis of Ag-Au nanowires**

573 Growth solution (gold-sulfite complex) is prepared by mixing 1.4 ml of 0.25 M hydrogen  
574 tetrachloroaurate(III) hydrate ( $\text{HAuCl}_4 \cdot \text{H}_2\text{O}$ , Strem Chemical Inc., USA), 8.4 ml of 0.2 M  
575 sodium hydroxide (NaOH, Sigma Aldrich), 105 ml of 0.01 M sodium sulfite ( $\text{Na}_2\text{SO}_3$ , Sigma  
576 Aldrich), and 165 ml of  $\text{H}_2\text{O}$ , and left undisturbed for 12 hrs. A separate solution is prepared  
577 by mixing 320 ml of  $\text{H}_2\text{O}$ , 20 ml of Ag nanowires (5 mg/ml), 70 ml of 5 wt% poly-  
578 vinylpyrrolidone (PVP,  $M_w$  40,000, Sigma Aldrich), 14 ml of 0.5 M sodium hydroxide (NaOH,  
579 Sigma Aldrich), 14 ml of 0.5 M L-ascorbic acid (L-AA, Sigma Aldrich), and 3.5 ml of 0.1 M  
580  $\text{Na}_2\text{SO}_3$ . Subsequently, the prepared growth solution was added into the Ag nanowire solution  
581 to initiate the reaction and left undisturbed for 2 hrs at the room temperature. Finally, the  
582 resulting Ag-Au nanowires were washed multiple times with ethanol and redispersed in  
583 dimethylformamide (DMF, Samchun Chemical). For characterization, the SEM image and  
584 cross-sectional backscattered electron image of Ag-Au nanowires were obtained by Focused  
585 Ion Beam SEM (FIB-SEM, AURIGA, Carl Zeiss, Germany). HRTEM images and energy-  
586 dispersive X-ray spectroscopy (EDS) data were obtained by Cs corrected transmission  
587 electron microscope (Cs-TEM, JEM-ARM200F, JEOL, Japan).

588

### 589 **Preparation of the Ag-Au nanocomposite**

590 The nanocomposite solution is prepared by mixing the SBS polymer solution (10 wt% in



591 toluene), Ag-Au nanowires (30 mg/ml in toluene), and hexylamine with the desired amounts.  
592 All weight fraction means (each component weight) / (sum of Ag-Au nanowires, SBS, and  
593 hexylamine weight). The solution is dried in a glass mold under desired temperatures. After  
594 drying the solution, the Ag-Au nanocomposite is heated under 140 °C for 5 mins on a  
595 hotplate to completely evaporate the remaining solvent. Microscopy images were taken by  
596 the field emission scanning electron microscope (FE-SEM, JSM-6701F, JEOL, Japan) and  
597 the time of flight secondary ion mass spectrometer (TOF-SIMS, TOF.SIMS-5, ION-TOF,  
598 Germany).

599

#### 600 **Cell viability test**

601 H9C2, CCD-986sk, and L929 are seeded in the 96-well plate with 10,000 cells per well  
602 and cultured for 24 hrs. Subsequently, the original DMEM is replaced by extract of samples  
603 (control; original DMEM, Ag nanowire, Ag-Au nanowire, and Ag-Au nanocomposite  
604 incubated at 37 °C in DMEM for 10 days) and incubated for another 24 hrs. 20 µl (5 mg/ml)  
605 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) was added to each  
606 well and incubated at 37 °C for 4 hrs. Finally, the medium is removed and 200 µl  
607 dimethylsulfoxide is added to each well. The absorbance was measured at 540 nm using a 96-  
608 well plate reader (Victor X4, Perkin-Elmer, USA).

609

#### 610 **Cell morphology analysis**

611 H9C2 and CCD-986sk were seeded in the 35 mm glass bottom dish with ~70% confluency  
612 and cultured for 24 hrs. Subsequently, the original DMEM was replaced by extract of samples  
613 and incubated for another 24 hrs. The cells were fixed with 4 % paraformaldehyde in 1x PBS  
614 for 15-20 min and permeabilized with 0.1 % Triton X-100 in 1x PBS for 5 mins. After

615 washing thoroughly with the PBS buffer, cells were incubated with TRITC-conjugated  
616 Phalloidin (1:100; Millipore, Billerica, MA, USA) for 50 mins. After washing thoroughly  
617 with the PBS buffer, the cells were incubated with DAPI (1:1000; Millipore, Billerica, MA,  
618 USA) for 5mins. The morphology of cells was visualized by the confocal microscopy (LSM  
619 780, Carl Zeiss, Oberkochen, Germany).

## 620 **Histology Analysis**

621 1 cm size serpentine-shape ribbon samples of the Ag nanowire/SBS nanocomposite and the  
622 Ag-Au nanowires/SBS nanocomposite were sutured in the rat heart (n = 5). The rats were  
623 sacrificed in 3 weeks after the implantation. Harvested organs were fixed with 4%  
624 paraformaldehyde in the PBS for 2 days and embedded in paraffin. Each paraffin was  
625 sectioned (2  $\mu$ m) and stained with hematoxylin and eosin (H&E) by following the standard  
626 protocol. To visualize collagen fibre deposition in tissues, trichrome staining was performed  
627 by using Masson Trichrome Staining Kit (Sigma Aldrich) The histology analysis was made at  
628 the region where the suture scar was not present.

629

## 630 **Measurement of electrical performance of Ag-Au nanocomposite**

631 The electrical performance was measured using double-layered Ag-Au nanocomposite (15  
632 mm  $\times$  3 mm) which was laminated by the heat rolling-press. Conductivity is calculated by the  
633 equation<sup>40</sup>,

$$634 \quad \sigma = 1 / \rho_0 \quad (1)$$

$$635 \quad \rho_0 = \text{film thickness} \times \text{sheet resistance} \quad (2)$$

636 , where  $\sigma$  is conductivity and  $\rho_0$  is resistivity. The sheet resistance was measured with a  
637 custom-made 4-point probe (probe: LS system, Korea; instrument: Keithley 2400, Tektronix,  
638 USA), and the thickness was measured by using SEM. For the stretching test, each end of the

639 nanocomposite was connected to a copper wire using the Ag paste and stretched after the  
640 encapsulation with VHB films (VHB<sup>TM</sup> Tape 4910 Clear, 3M, USA). Stretchability and  
641 conductivity under strain were measured using two-point-resistance and four-point resistance  
642 change, respectively (Keithley 2400, Tektronix, USA). The cyclic performance test was  
643 carried out by measuring the two-point resistance while 30% tensile strain was applied  
644 repetitively. The resistance was measured using a digital multimeter (NI USB-4065, National  
645 Instruments, USA) after releasing the applied strain.

646

#### 647 **Heat rolling-press of Ag-Au nanocomposite**

648 Two layers of nanocomposite were put in between ketone films and heat rolling-press was  
649 applied using a heat roll press (ETK16-486-1, Wellcos Corporation, Korea). Temperature of  
650 the rollers was set at 105 °C. For soft nanocomposite, heat rolling-press was performed until  
651 the average thickness was unchanged compared to thickness of the original nanocomposite,  
652 while for highly stretchable nanocomposite, the heat rolling-press is performed until the  
653 average thickness decrease by 15% compared to thickness of the original nanocomposite.  
654 After the process, double-layered nanocomposite was detached from the ketone film.  
655 Conductivity and stretchability were measured in the same method as above.

656

#### 657 **Wearable skin-like bioelectronics using the Ag-Au nanocomposite**

658 The wearable skin-like device was attached to the forearm using Tegaderm (3M, USA),  
659 and an Ag/AgCl electrode was placed on the ankle and elbow for ground. The ECG and  
660 EMG signals were measured using a data acquisition equipment (DAQ; National Instruments)  
661 with the LabVIEW software (encoded with 60 Hz notch filter). The signals were acquired  
662 with the sampling rate of 1000 Hz. 3 Hz high-pass filter, 300 Hz low-pass filter, and 59-61

663 band block filter were applied on the raw data to remove motion artefacts and non-  
664 physiological noises. Electrical stimulation was applied through stimulation electrodes. While  
665 applying the electrical stimulation, stimulation pulses were measured using EMG electrodes  
666 adjacent to the stimulation electrodes. Thermal stimulation was conducted by joule heating.  
667 Voltage was applied on the heating element of the wearable skin-like device by the voltage  
668 supplier (Agilent, USA). Infrared (IR) camera (Thermovision A320, FLIR system, Sweden)  
669 was used for temperature measurement. The impedance at the skin/electrode interface was  
670 measured using a pair of Ag/AgCl gel electrodes (2223H Ag/AgCl electrode, 3M, USA) and  
671 a pair of Ag-Au nanocomposite films. The Ag-Au nanocomposite was prepared with the size  
672 of 1 cm square and attached using the Tegaderm dressing film. The distance between the  
673 electrodes was 5 cm. The impedance measurement was conducted using an electrochemical  
674 analyser (CHI-660E, CH instruments, Inc., USA). The measurement frequency was scanned  
675 from 1 Hz to 90000 Hz. All human experiments were conducted under approval by the  
676 Institutional Review Board of the Seoul National University (approval number SNU 17-12-  
677 006).

678

#### 679 **Fabrication of the cardiac mesh**

680 Metal molds with each layer pattern were fabricated. PDMS replicated molds were  
681 prepared using the previously-reported fabrication procedure of PDMS mold<sup>13,18</sup>. Prepared  
682 nanocomposite solution and SBS solution were patterned on the PDMS mold for electrode  
683 layers and encapsulation layers, respectively. Then, the solution is dried under the ambient  
684 condition, and the patterned Ag-Au nanocomposite is prepared after solvent is fully  
685 evaporated. Each layer is transferred in sequence using PDMS stamp coated with 1:40  
686 (weight ratio of curing agent to prepolymer) ratio of PDMS. For each transfer, the layers were

687 welded under heat of 140 °C for 20 min. The multi-channel electrodes of the cardiac mesh  
688 were connected to a customized flexible printed circuit board using Ag paste, which are, in  
689 turn, connected to a ZIF connector on a customized printed circuit board to record signals  
690 from each channel and control stimulation sites.

691

### 692 ***In vivo* swine experiment**

693 The research protocol was approved by the Institutional Animal Care and Use Committee  
694 and conformed to the Position of the American Heart Association on Research Animal Use.  
695 The research was performed at the Beth Israel Deaconess Medical Center, Experimental  
696 Electrophysiology Laboratory in Boston, MA. Sedation was initiated with 1.4 mg/kg  
697 intramuscular injection of Telazol (tiletamine/zolazepam hydrochloride). Endotracheal  
698 intubation was then performed, and general anaesthesia was maintained with isoflurane  
699 inhalation (1.5% – 2.5%). Ventilation was maintained between 10 and 16 breaths/min and  
700 hemodynamic assessment including heart rate, oxygen saturation, and blood pressure were  
701 continuously monitored. After median sternotomy to expose the hearts, the 3D cardiac sock  
702 mesh was implanted. Myocardial ischemia was induced by ligation of the mid-left anterior  
703 descending artery.

704

### 705 **Statistical analyses**

706 Statistical analyses were carried out using the Origin 9.0 software. The one-way ANOVA  
707 analysis with the Tukey's post hoc test was used for the Ag ion releasing, cell viability, and  
708 biodistribution studies (Fig. 4a, Fig. 4c, and Fig. 4d, respectively). The Shapiro-Wilk test ( $\alpha =$   
709 0.05;  $n \geq 3$  replicates per group) showed that there was no significant deviation from

710 normality. The Levene's test ( $\alpha = 0.05$ ) was performed to all data sets with  $n \geq 3$  replicates  
711 to test homogeneity of variances. The sample size was selected to ensure adequate power of  
712 90 % for the Ag ion releasing and cell viability studies (Fig. 4a, Fig. 4c, respectively) and 75 %  
713 for the biodistribution studies (Fig. 4d). For analysis of percentage of fibrotic area  
714 (Supplementary Fig. 13b), the p value was calculated by the Mann-Whitney U-test. The  
715 investigators were not blinded to experiments and analyses, and no randomization method  
716 was used.

717

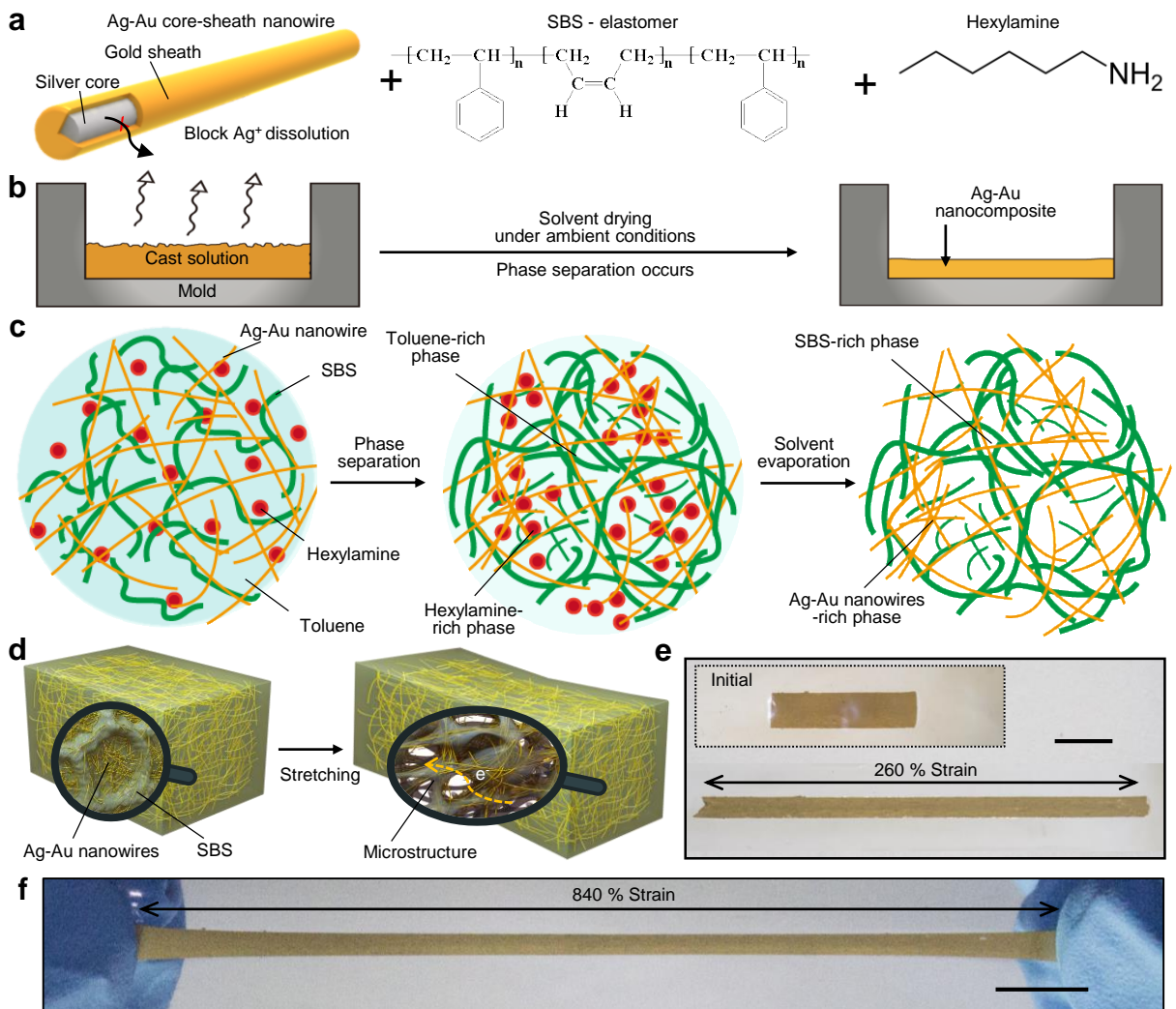
#### 718 **Data availability**

719 The data that support the plots within this paper and other findings of this study are available  
720 from the corresponding author upon reasonable request

721

#### 722 **Reference for Methods**

723 40. Smits F. M. Measurement of Sheet Resistivities with the Four-Point Probe. Bell Syst.  
724 Tech. J. 37, 711-718 (1958).



**Figure 1**

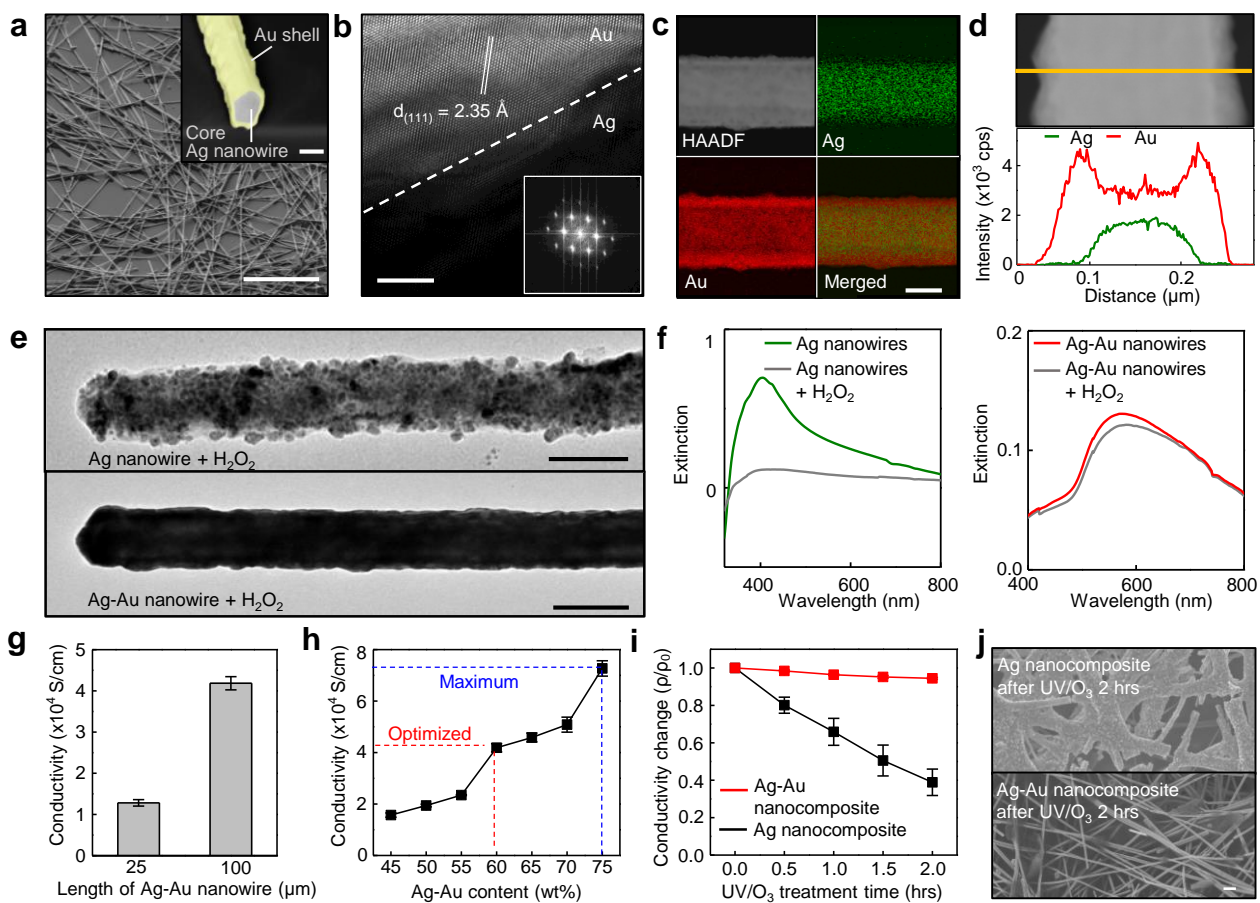
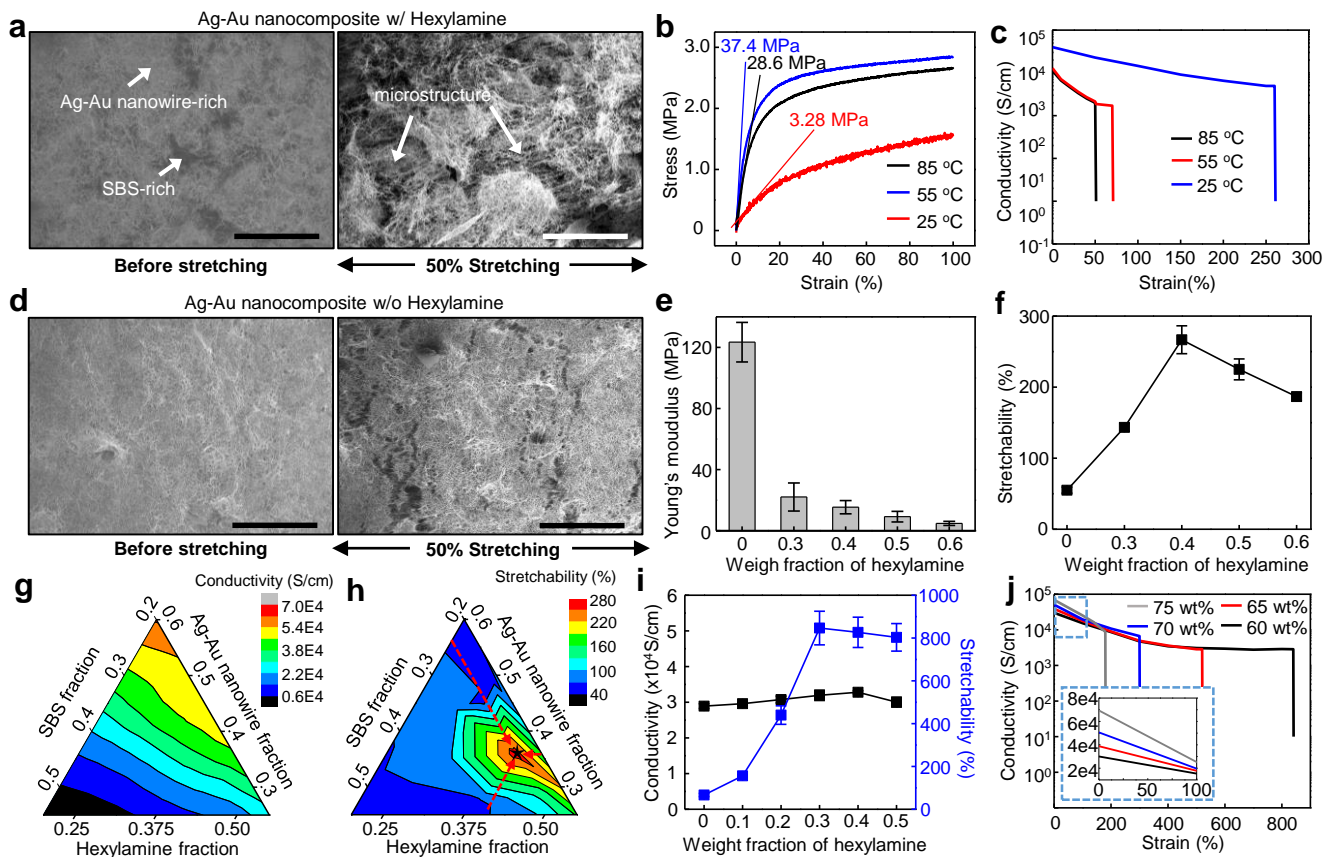
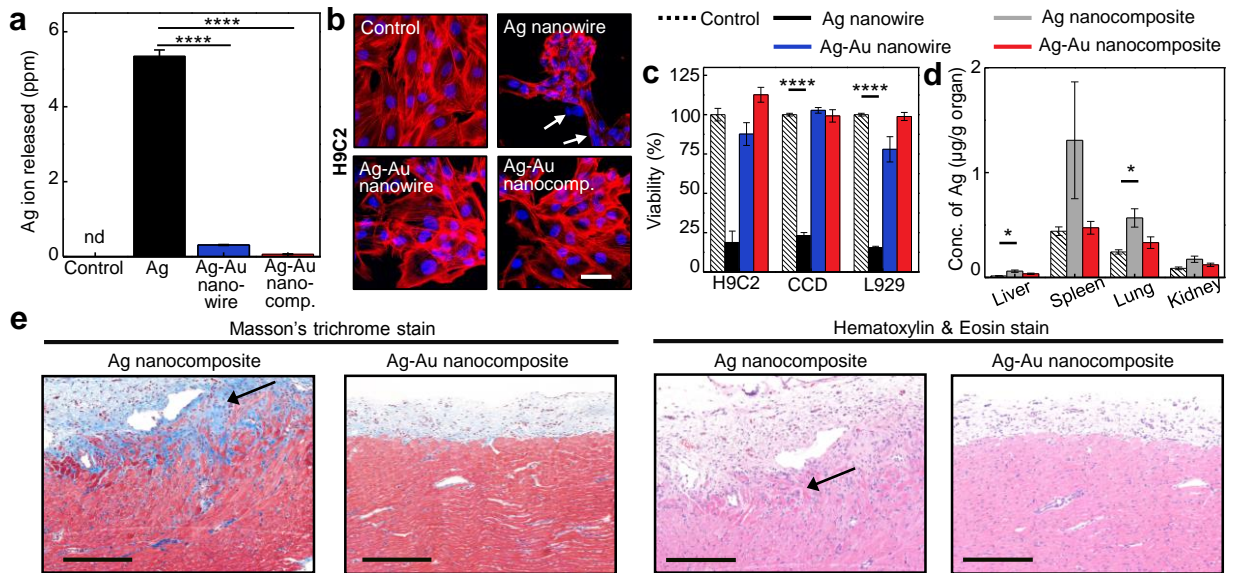


Figure 2

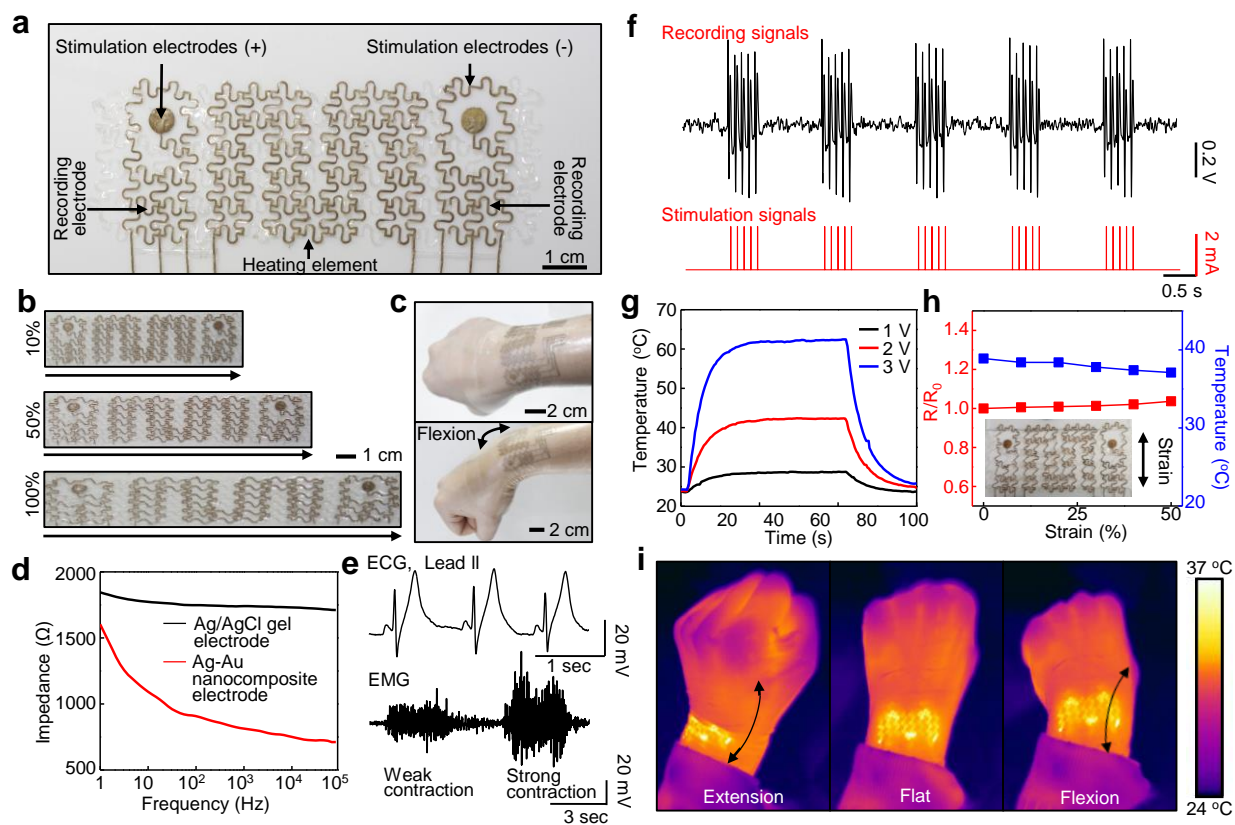




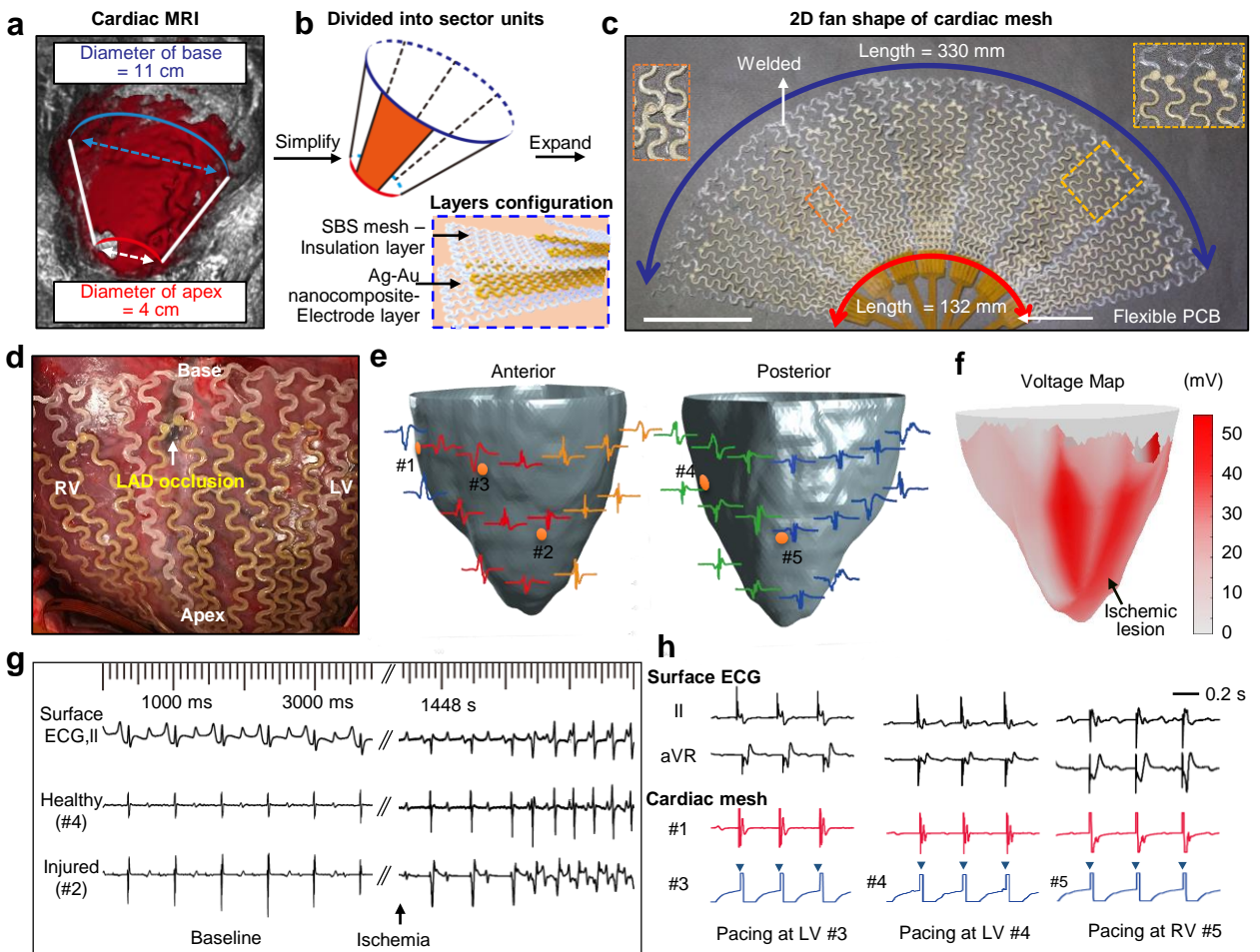
**Figure 3**



**Figure 4**



**Figure 5**



**Figure 6**