Bio-Machines and Bio-Manufacturing
生物机器和生物制造

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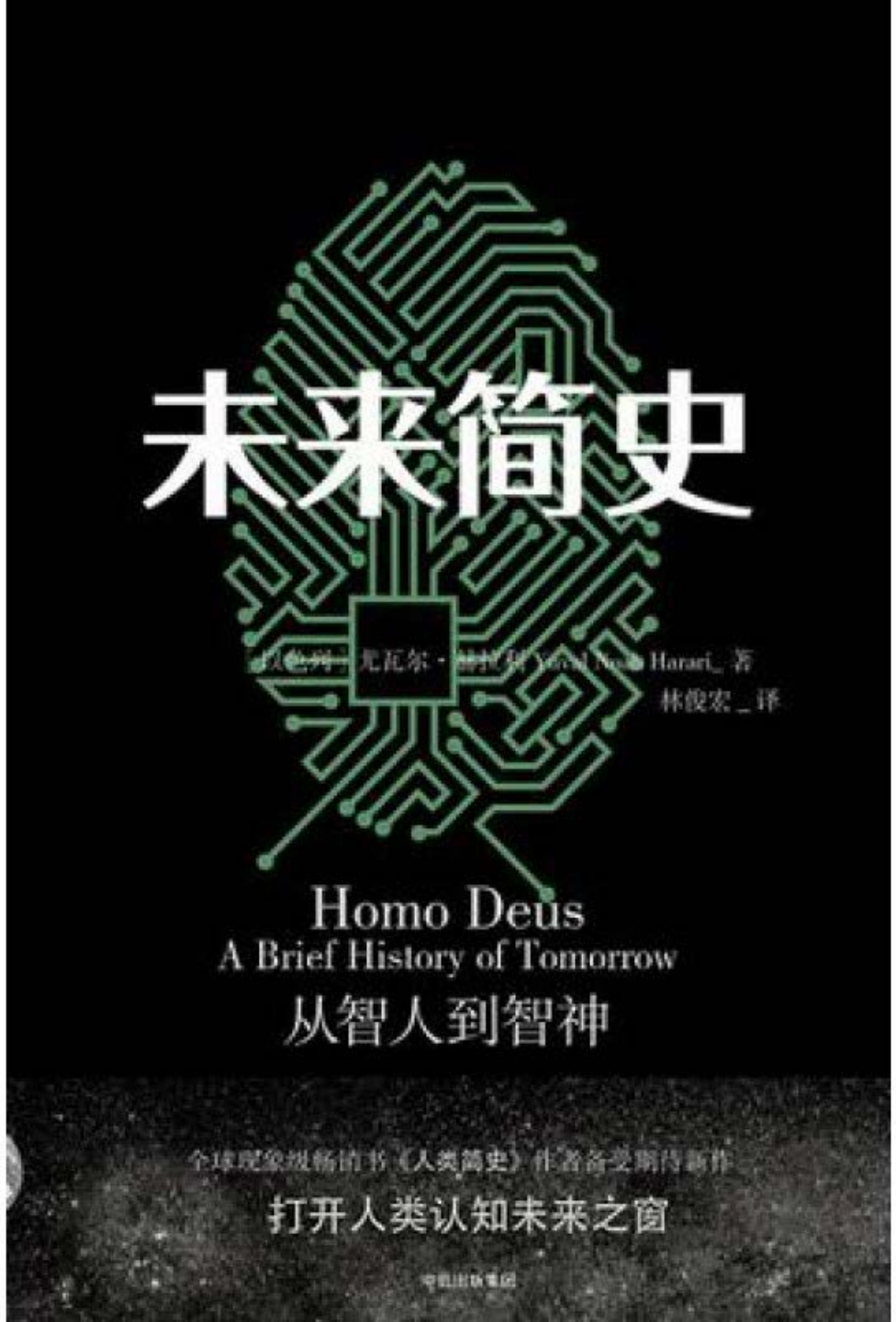
Oct 26 2017, Shanghai

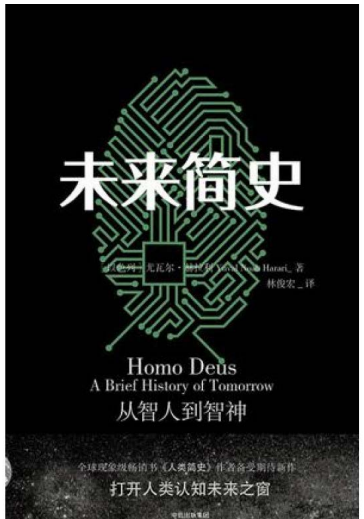


Yuval Noah Harari

Converging Technologies will Give Human
人机科技融合可以带给人类

- Immortality 永生
- Happiness 快乐
- Divinity 神性

- Genetics
- Organ regeneration
- Synthetic biology
- Nano-medicine
- … …



- AI
- IoT
- Robotics
- Electronics
- Nano-materials
- … …

Google

IBM

facebook

DARPA

NIH

National Institutes of Health

NEURALINK

NSF

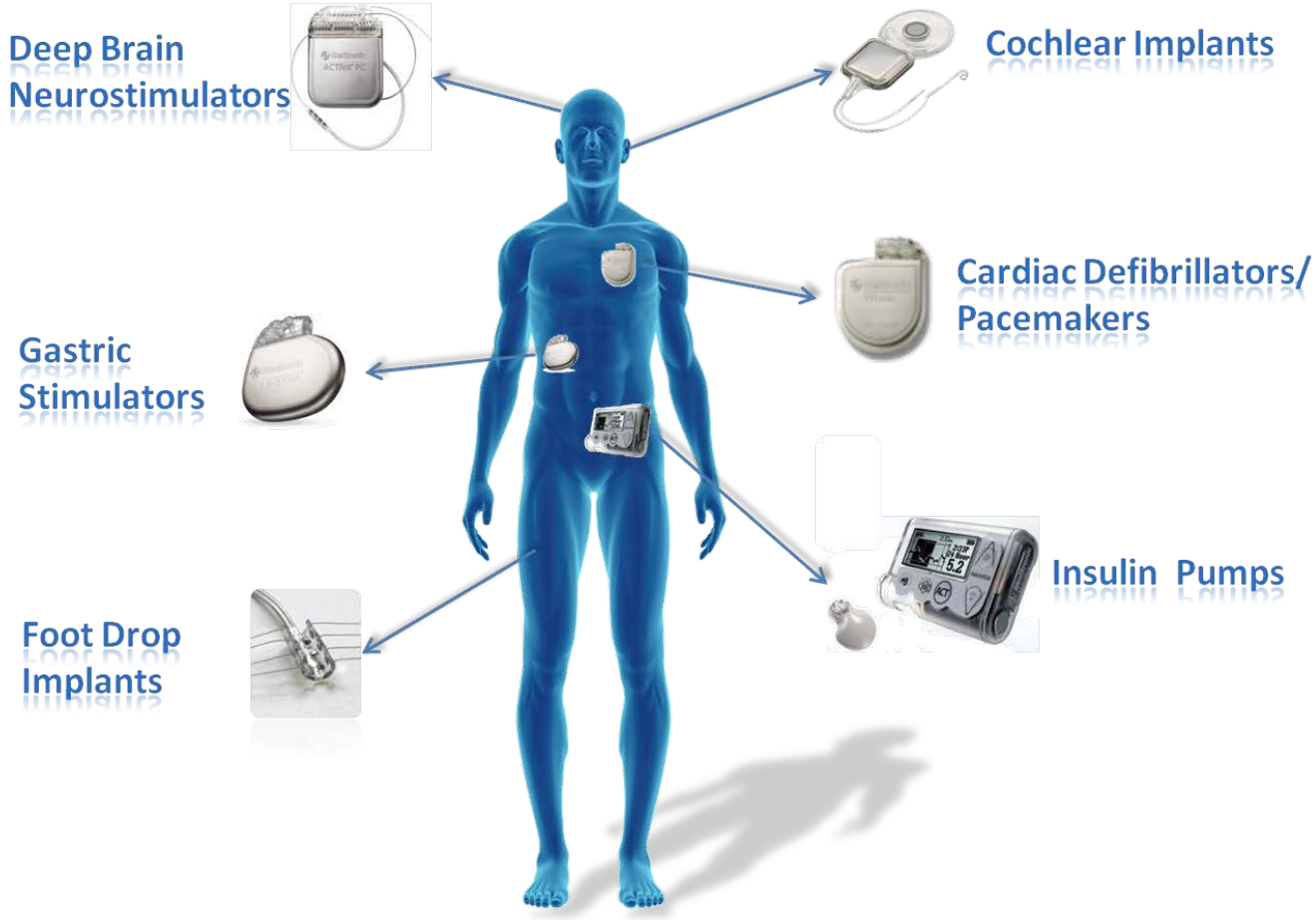
U.S.ARMY

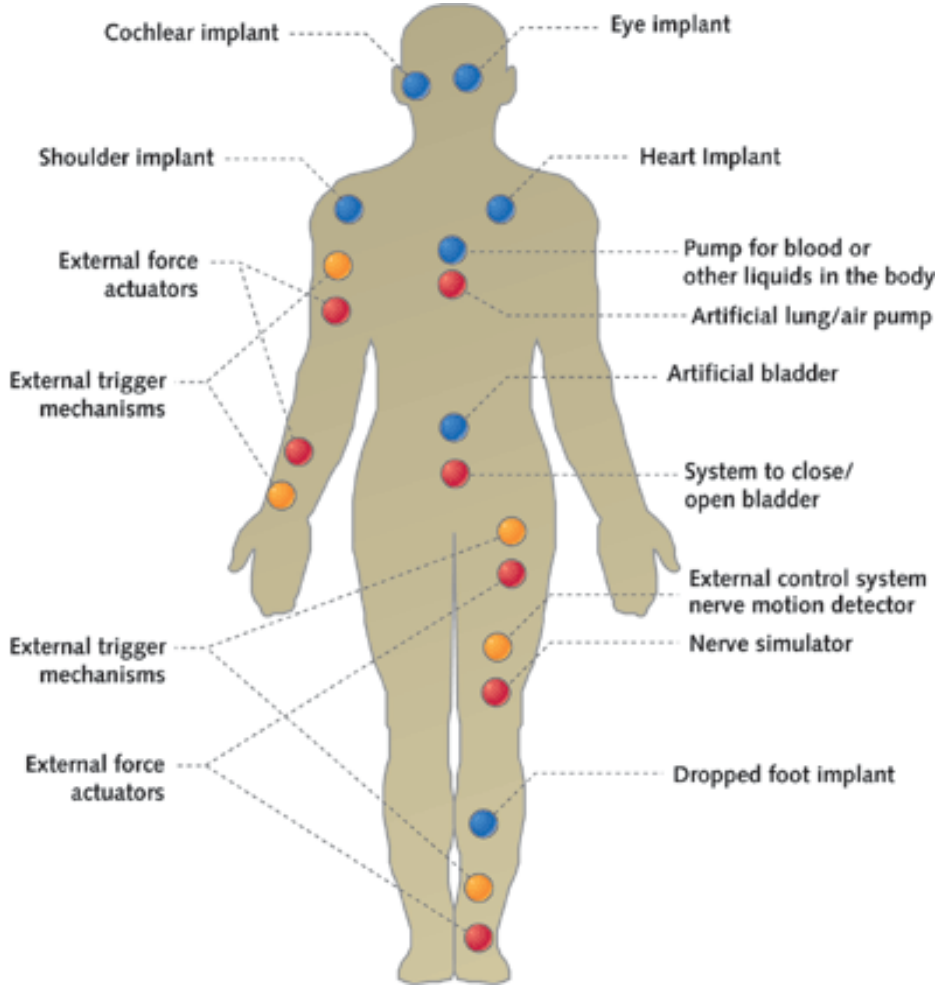
Humans must merge with machines or become irrelevant in AI age -- **Elon Musk**

人机融合或被人工智能时代淘汰

Short-Term: Medical Implants

医疗植入器械





Annual Medical Implants Market is expected to exceed **$116 billion** by 2022.

（医疗植入器械5年内将成为年千亿美元产业)

Short-Term: Wearable Devices 可穿戴仪器

Wearable Technology Market worth **$51.60 Billion** by 2022

（可穿戴仪器5年内将成为年500亿美元产业)

Grand Challenges in Materials, Mechanics & Manufacturing
材料，机械，制造领域的重大挑战

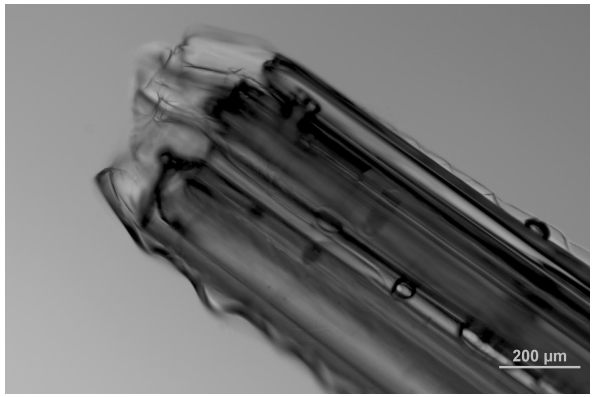
Soft, Wet, Living
柔软,含水,生命

Merge?
怎么融合？

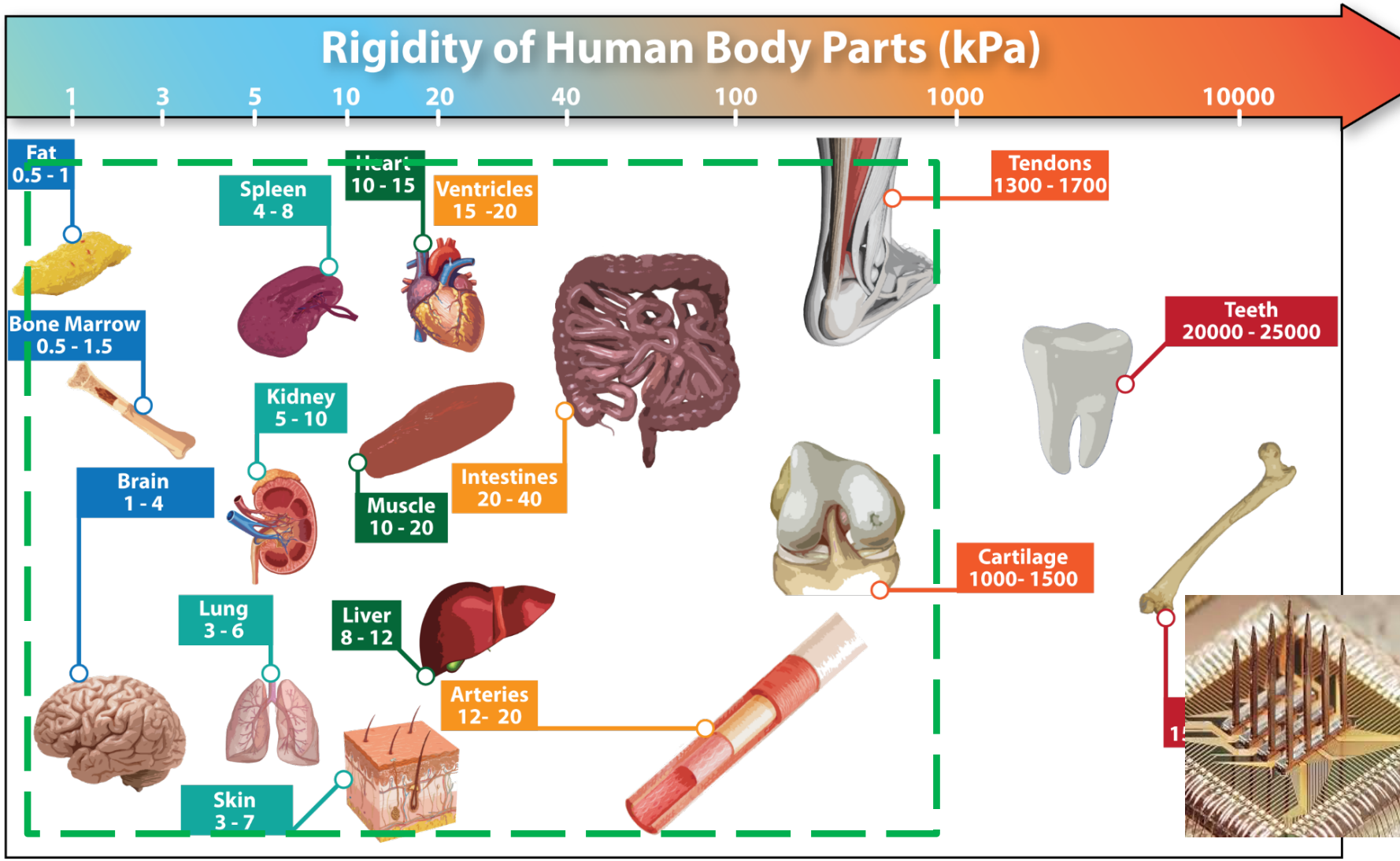
Hard, Dry, Non-living
坚硬,干燥,无生命

Major Components of Human Body are Soft Materials
人体主要是由软材料组成的

- **Soft:** 1kPa~10MPa;
- **Wet:** 70~90% water
- **Living:** growth, sensing, responding, self-healing
- **Robust:** under millions of cycles of loads.



Hydrogel Neural Probe with Anikeeva
超软水凝胶神经探头



Merging Human Body and Machines
人机融合

Soft, Wet, Living
柔软,含水,生命

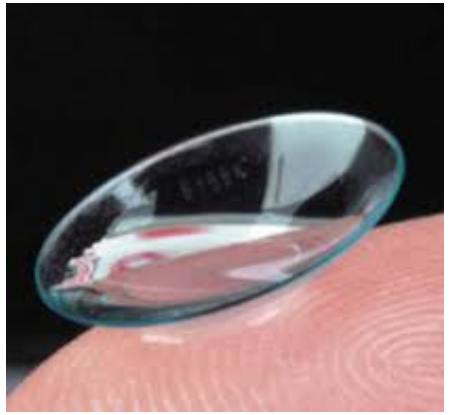
Soft living machines
柔软活性机器

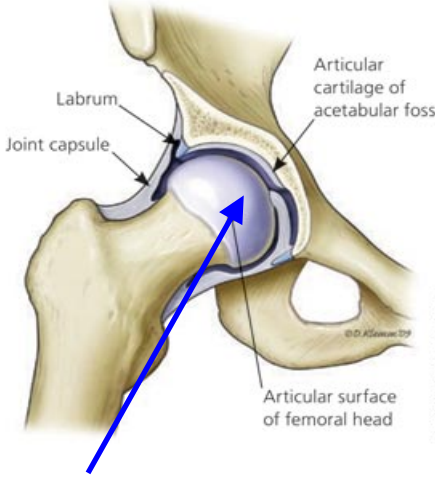
Hard, Dry, Non-living
坚硬,干燥,无生命

Soft Living Machines
柔软活性机器

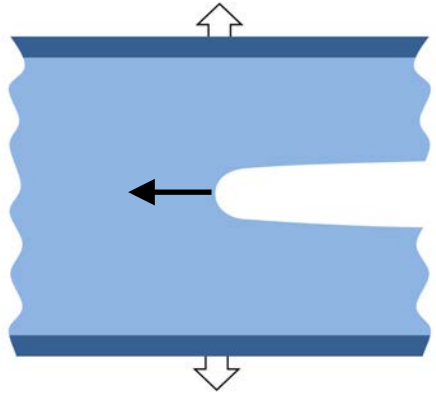
- **Robust soft materials (tough, strong, anti-fatigue)**
  坚韧的软材料
- **Robust interfaces (with metals, silicon, elastomers et al)**
  坚韧的界面
- **Personalized manufacture (3D/4D Printing)**
  个性化制造

Design of soft materials with high toughness?
如何设计坚韧的软材料？



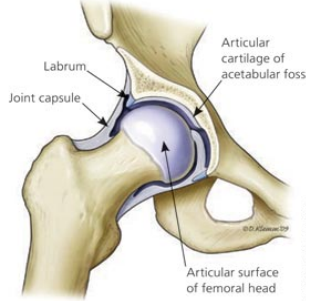


Fracture toughness: ~1 Jm^{-2}; ~10 Jm^{-2} ~100 Jm^{-2} >1000Jm^{-2}



Fracture toughness: Mechanical energy required to propagate a crack by a unit area. (Unit Jm^{-2})

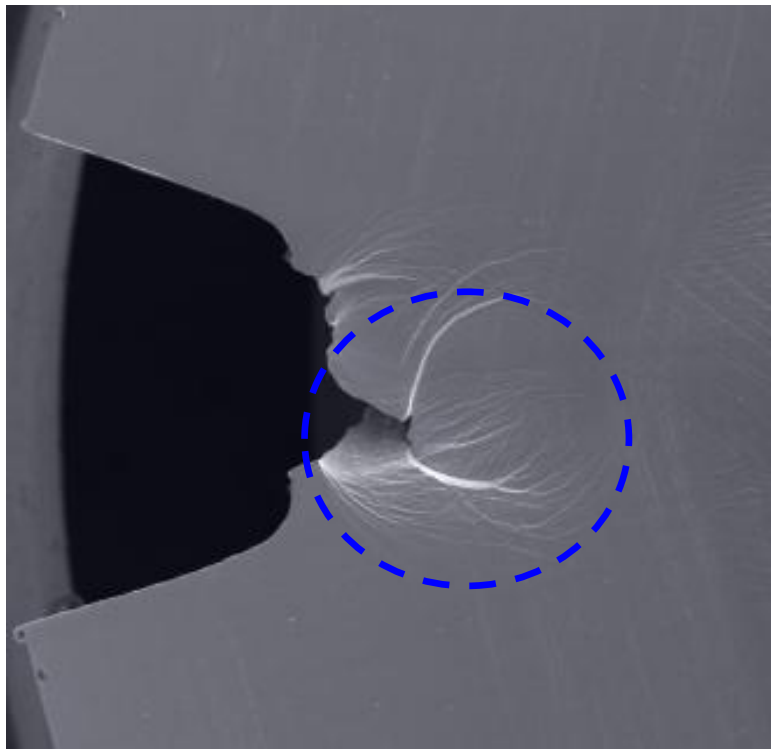
Conventional hydrogel
Fracture toughness ~1 Jm^{-2}
传统水凝胶很脆弱



Cartilage
Fracture toughness ~1,000 Jm^{-2}
软骨很坚韧

Glass 玻璃

Metal 金属



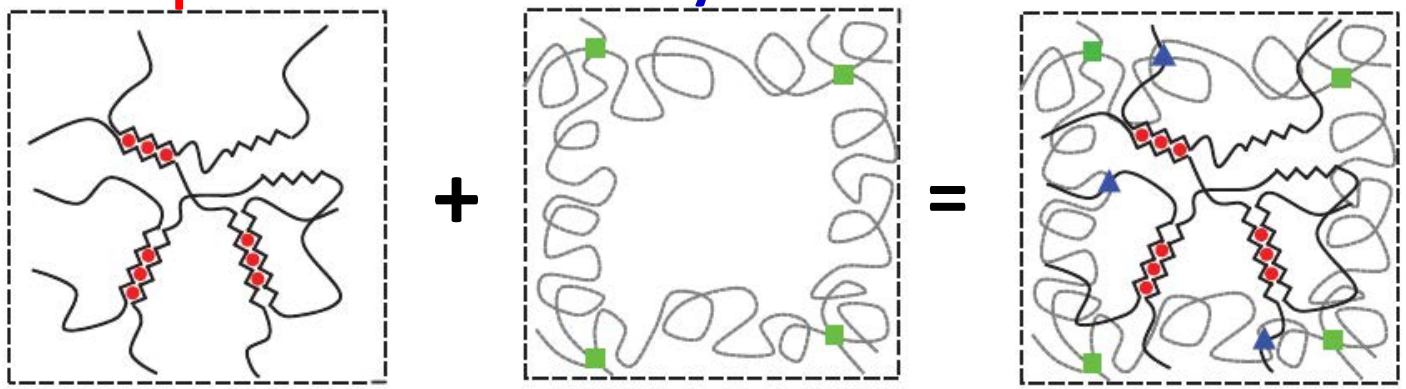
Fracture toughness
= Surface energy

Zhao, Soft Matter, **10**, 672 (2014)
Zhao, PNAS, **114**, 8138 (2017)

Fracture toughness
= Surface energy +
Dissipation in a zone

Tough Soft Materials: Build dissipation into stretchy network.
坚韧软材料:在可拉伸网络里建立能量耗散

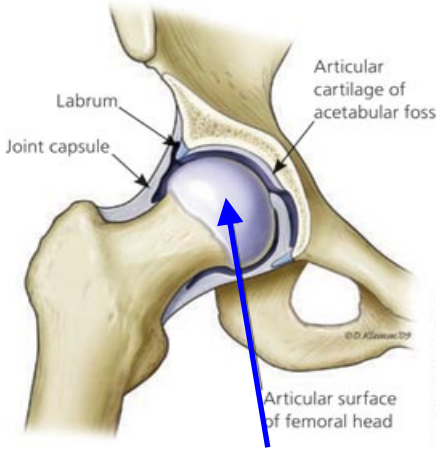
Dissipation + **Stretchy network** =



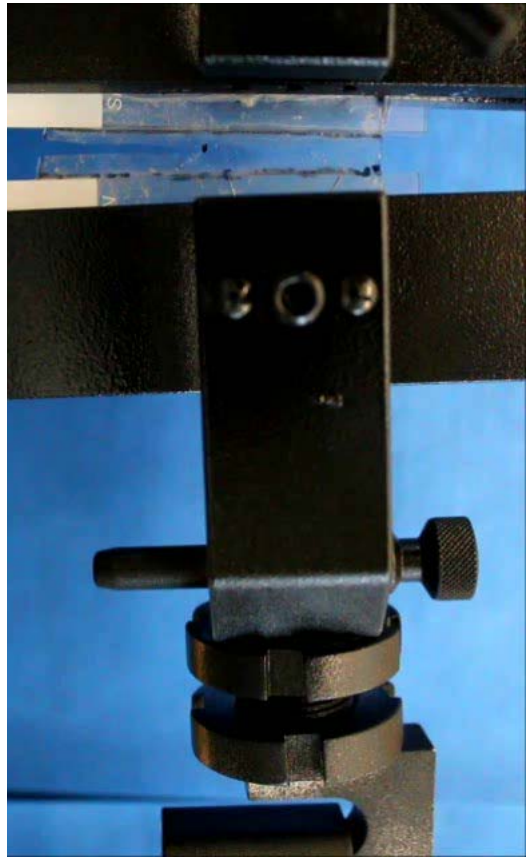
Reversible crosslink:
Alginate+Ca^{2+}

Long-chain network:
PAAm

- **~90% water**
- **Fracture energy 9000 Jm^{-2}**
- **Stretchability 21 times**



>1000Jm^{-2}

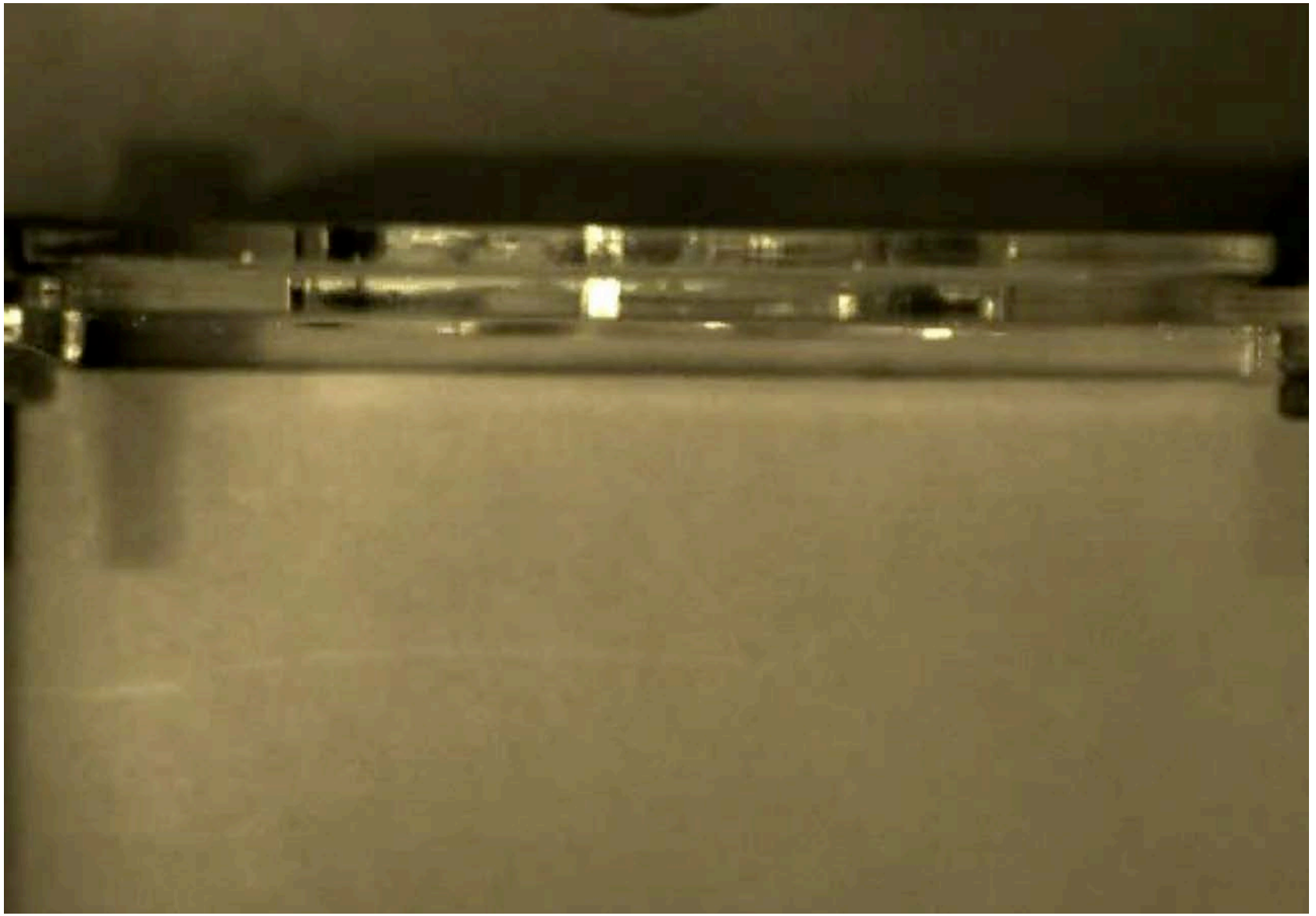


Patent at Harvard and MIT
在Harvard和MIT的专利

Sun et al, Nature, **489**, 133 (2012)

in collaboration with Prof. Suo, Vlassak and Mooney

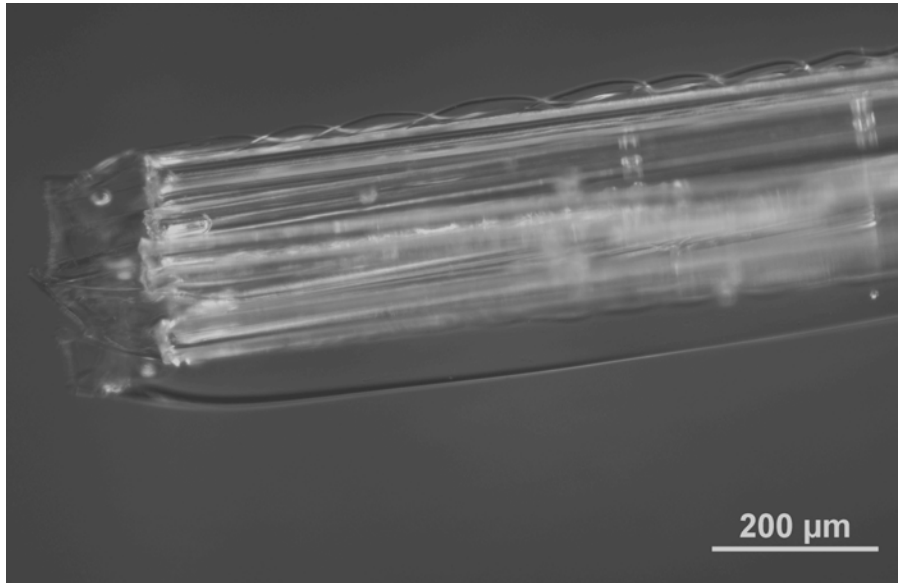
Hydrogel film with 90% water and 1mm thickness



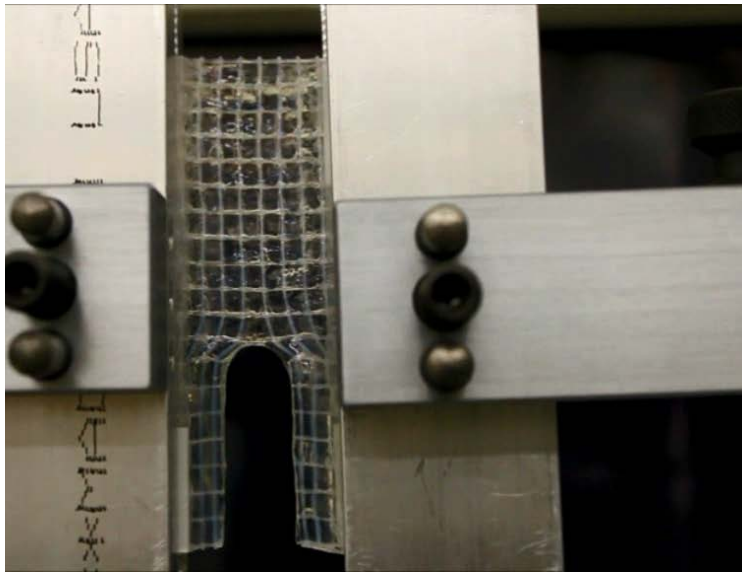
- 1毫米厚
- 含水90%以上
- “防弹”软材料

Impact of a ball of 64 g at 6m/s

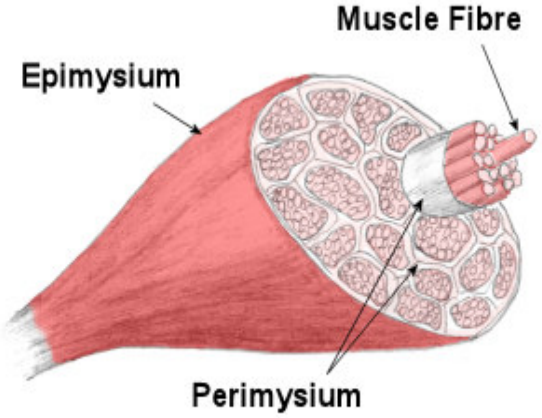
Robust Soft Materials -- A Wide Range of Rigidity
不同硬度适配不同人体部位

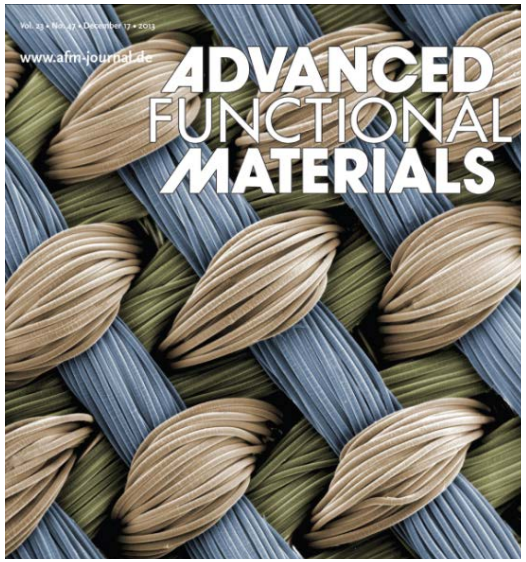


1~5 kPa;
1,000 Jm^{-2}

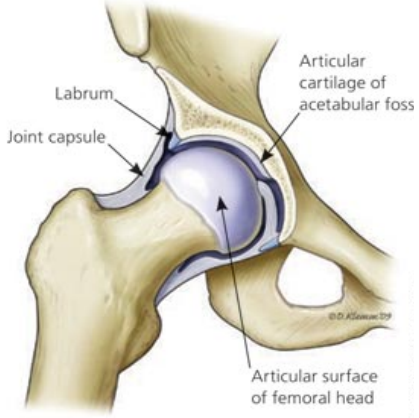


10~100 kPa;
1~10 kJm^{-2}





1~10 MPa
10~50 kJm^{-2}

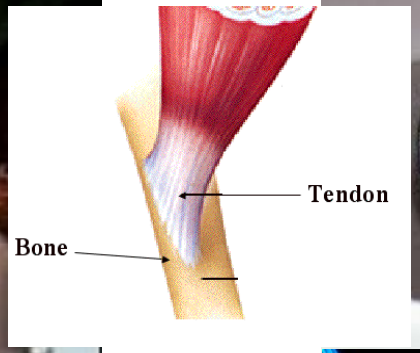


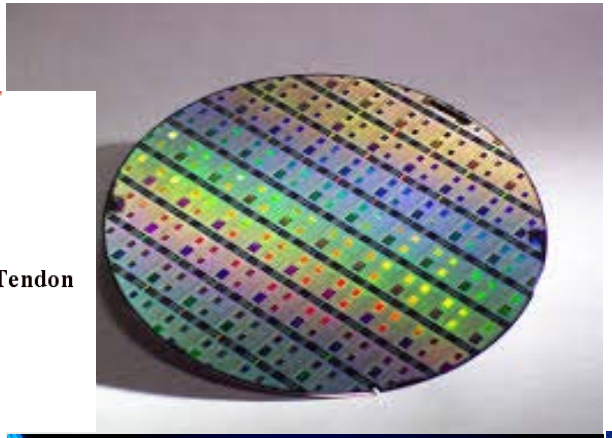
Patent at MIT 在MIT的专利

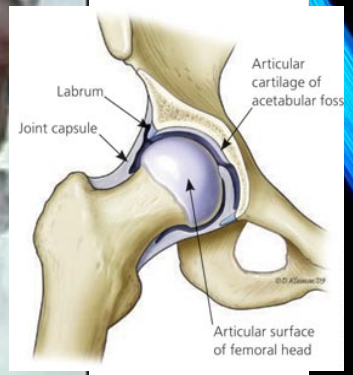
Soft Living Machines
柔软活性机器

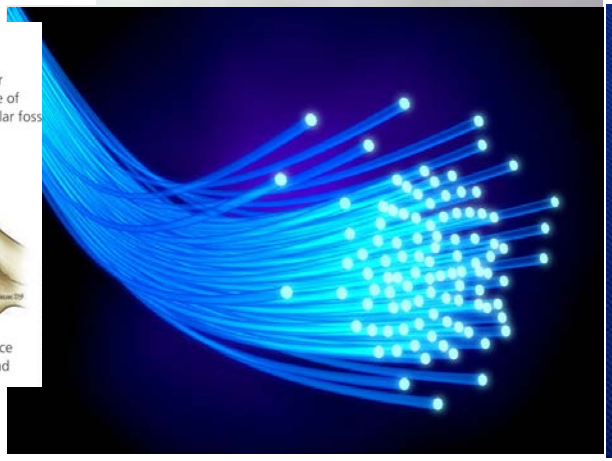
- **Robust interfaces (with metals, silicon, elastomers et al)**
  坚韧的界面

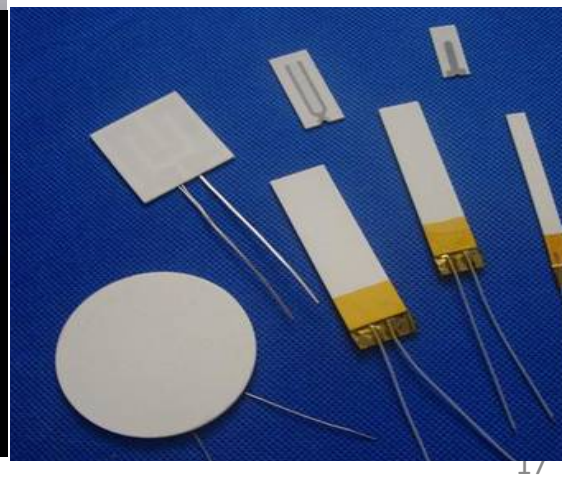
Robust Interfaces
坚韧的界面









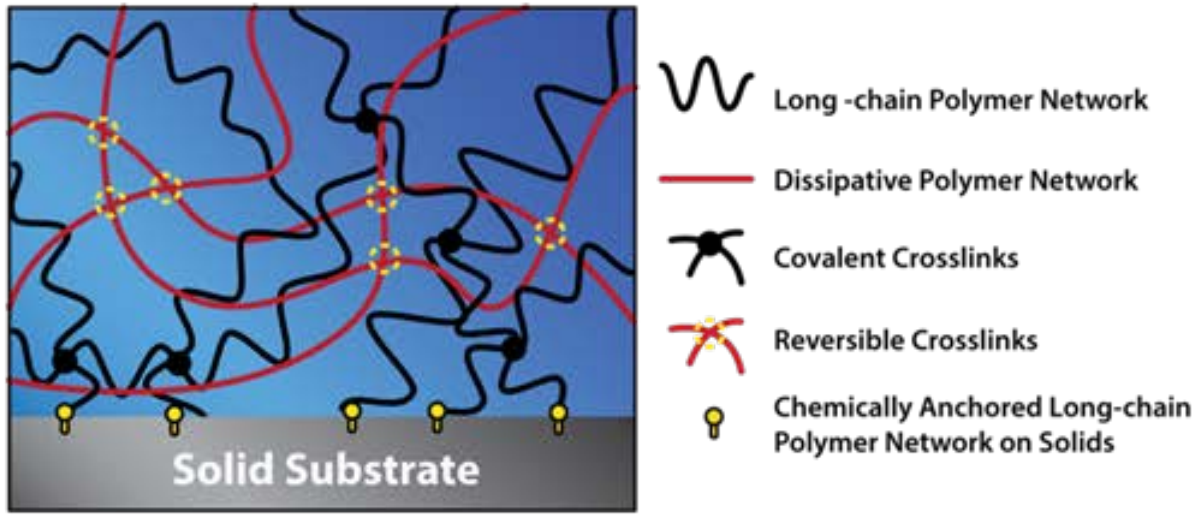


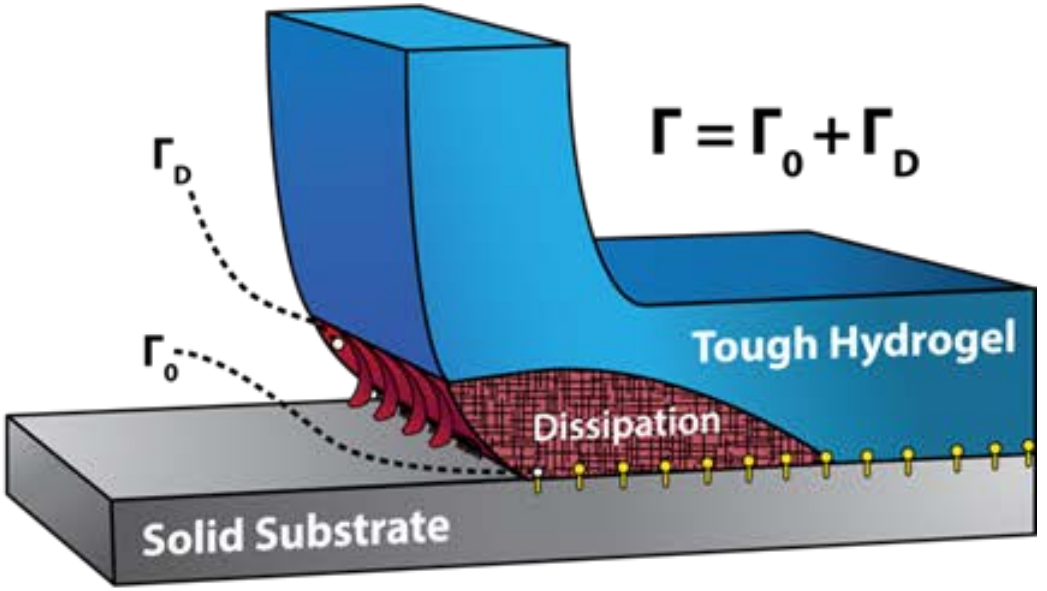
90% water; ~kPa

Diverse engineering solids; MPa~GPa

Tough Soft Materials: Build dissipation into stretchy network.
坚韧软材料:在可拉伸网络里建立能量耗散

Tough Interface: Anchor stretchy network on solid surface.
坚韧界面：固定可拉伸网络在固体表面



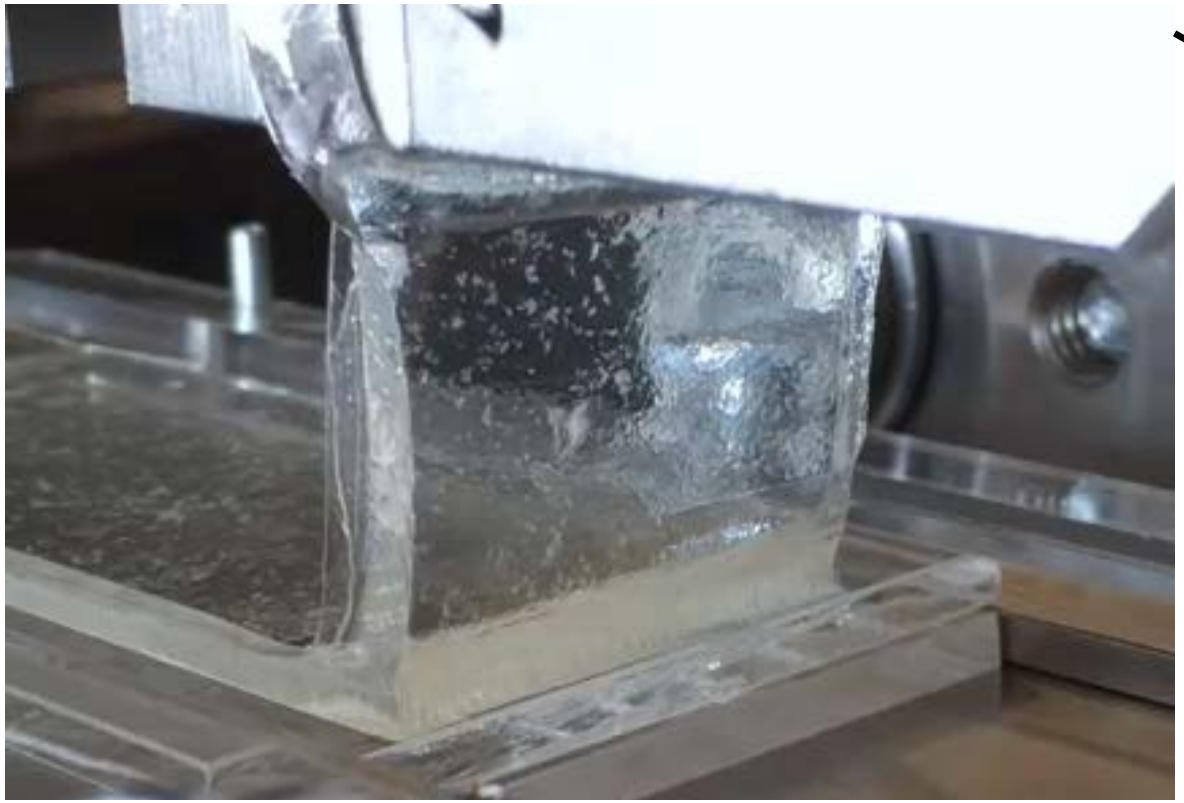


Yuk et al, Nature Materials, **15**, 190 (2016)

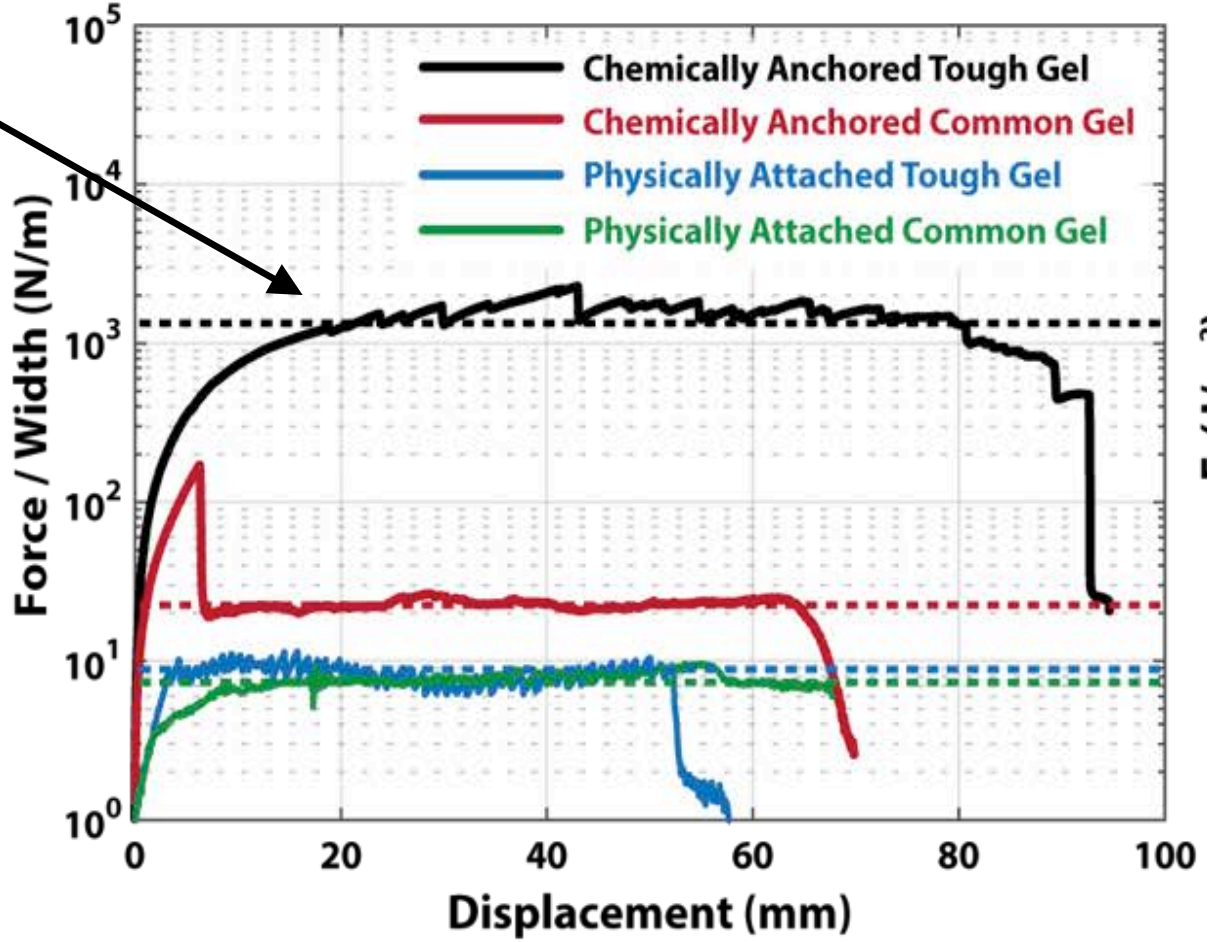
Yuk et al, Nature Communications **7**, 12028 (2016)

Patent at MIT
在MIT的专利

Hydrogels with 90% water adhered on Si, SiO_2, glass, ceramics, Ti, Al, Fe, Elastomers et al

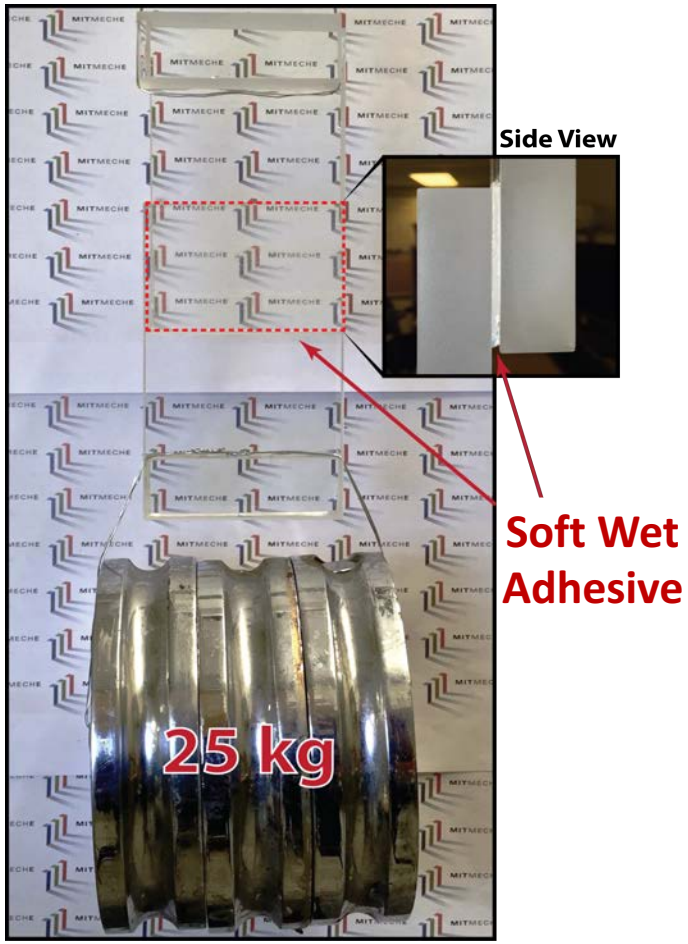


Detachment and Finger Instability



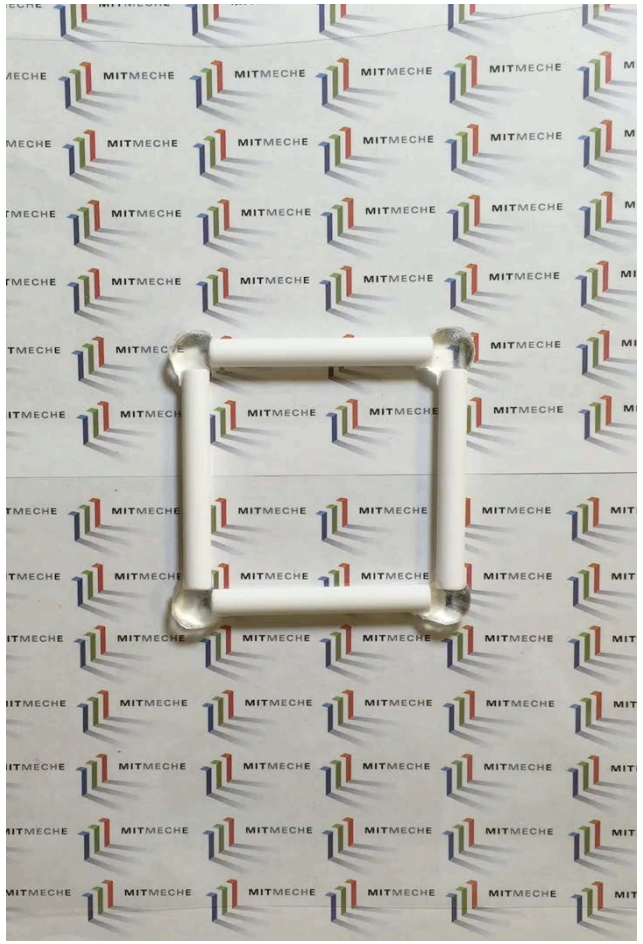
Yuk et al, Nature Materials, **15**, 190 (2016)

Hydrogel-Engineering Material Hybrids



With glass

With silicon



With ceramics

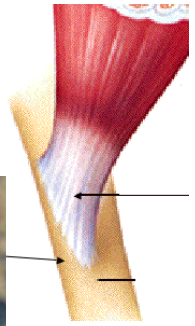
With elastomer

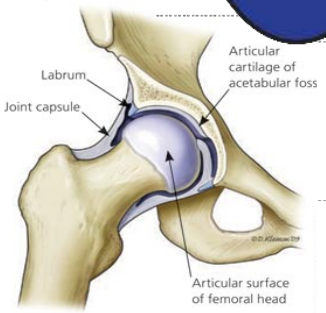
Patent at MIT

Nature Materials, **15**, 190 (2016);
Nature Communications **7**, 12028 (2016)

Our approach on Si, SiO_2, glass, ceramics, Ti, Al, Fe, PDMS, polyurethane, Ecoflex, latex, acrylic et al

Anchor stretchy network + Bulk dissipatio





Tissue Adhesives (HISTOACRYL blue & Tisseel)

DOPA-modified Hydrogels

Nanoparticle Gel Adhesion

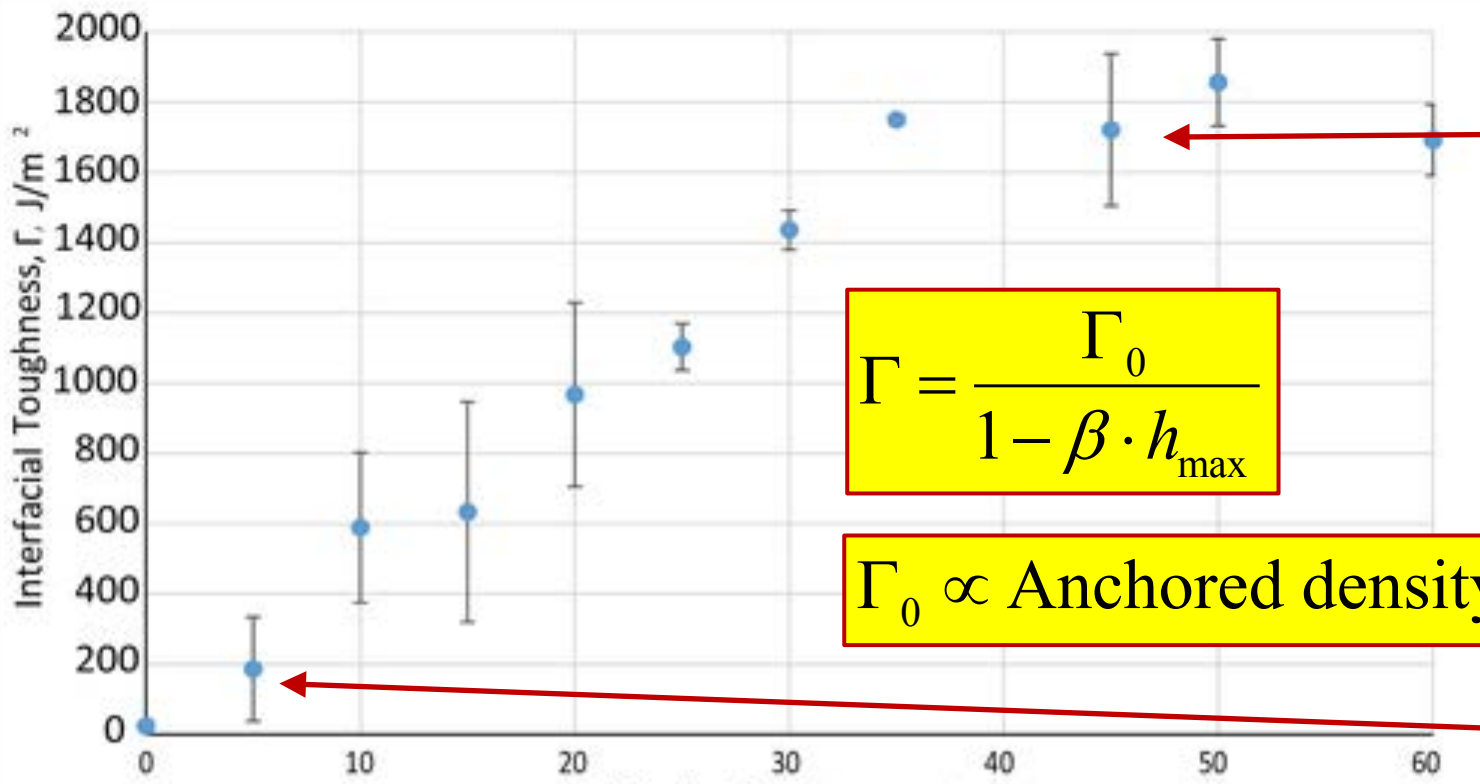
Interfacial Toughness (J/m^2)

1750
1500
1250
1000
750
500
250
0

0 20 40 60 80 100

Water Contents (wt%)

Tunable Adhesion from 1 to 1000 Jm-2
可调节的粘性

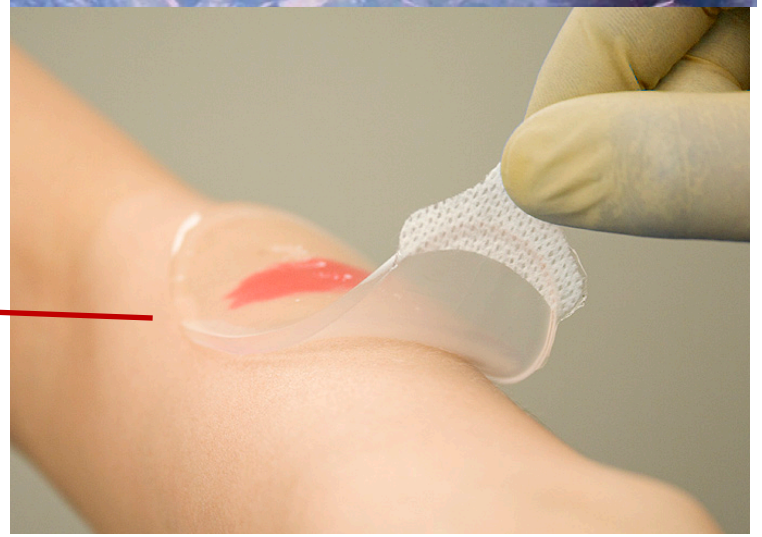


$$\Gamma = \frac{\Gamma_0}{1 - \beta \cdot h_{max}}$$

$\Gamma_0 \propto$ Anchored density

Functional group coverage (%)

Zhang et al, AMS, 33, 543 (2017)

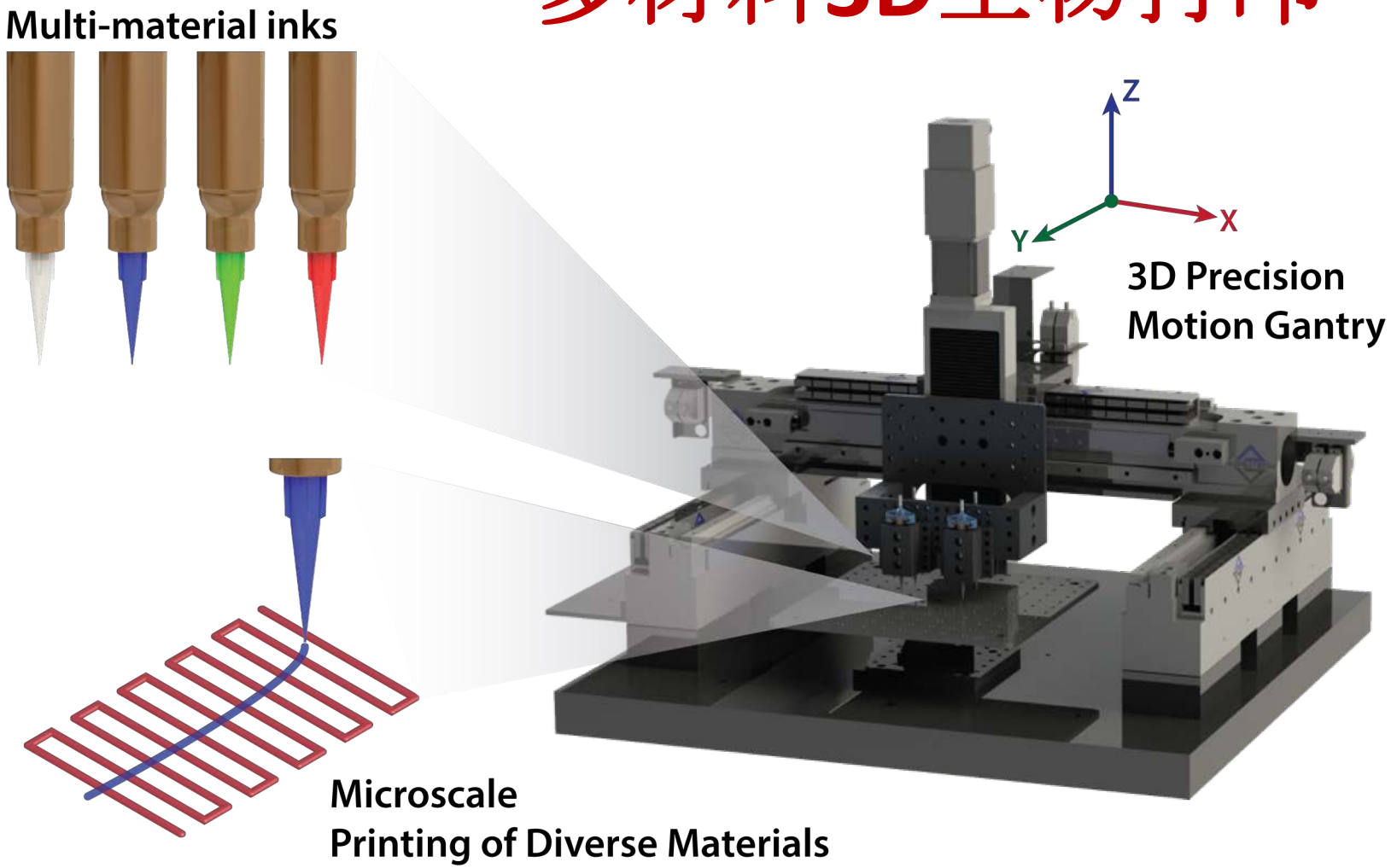


Hydrogel bandage水凝胶创可贴

Soft Living Machines
柔软活性机器

- **Personalized manufacture (3D/4D Printing)**
  个性化制造

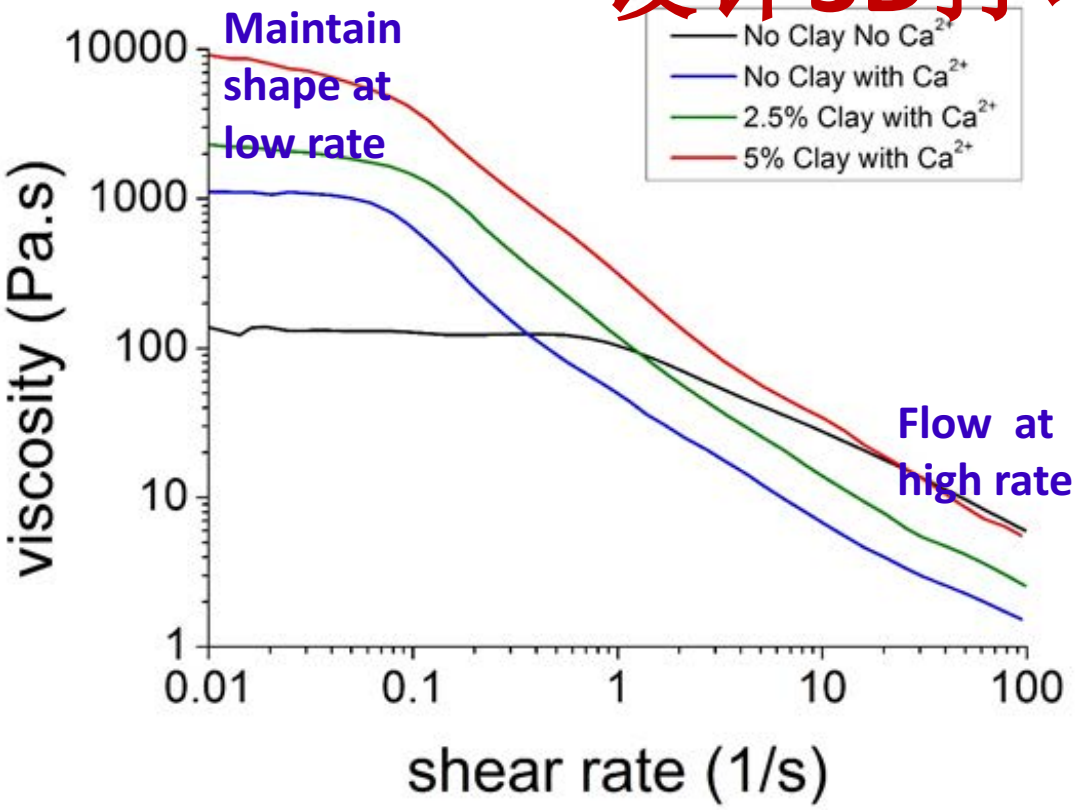
Multi-material 3D Bio-printer
多材料3D生物打印



- Micro-extrusion based
- Resolution up to **5um**.
- Printing **multiple** materials in one structure
- Particularly suitable for **soft materials with cells**.

Patent at MIT 在MIT专利

Design of Inks for 3D Printing
设计3D打印墨水



Ink: Shear-thinned polymer solution
剪切稀化墨水

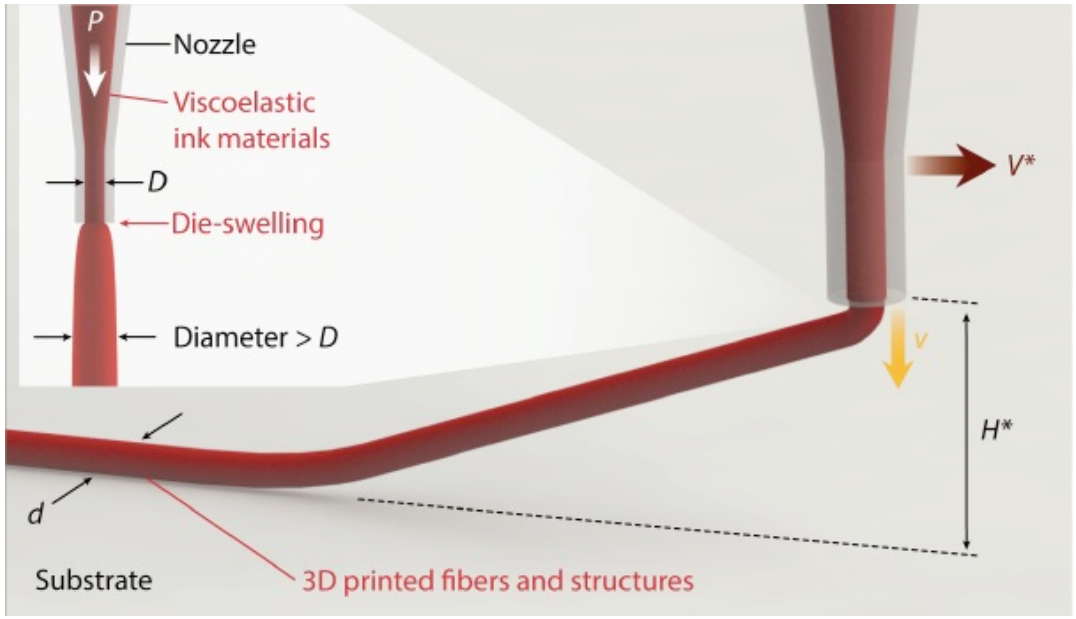
Hong et al Advance Materials, 27, 4035 (2015)

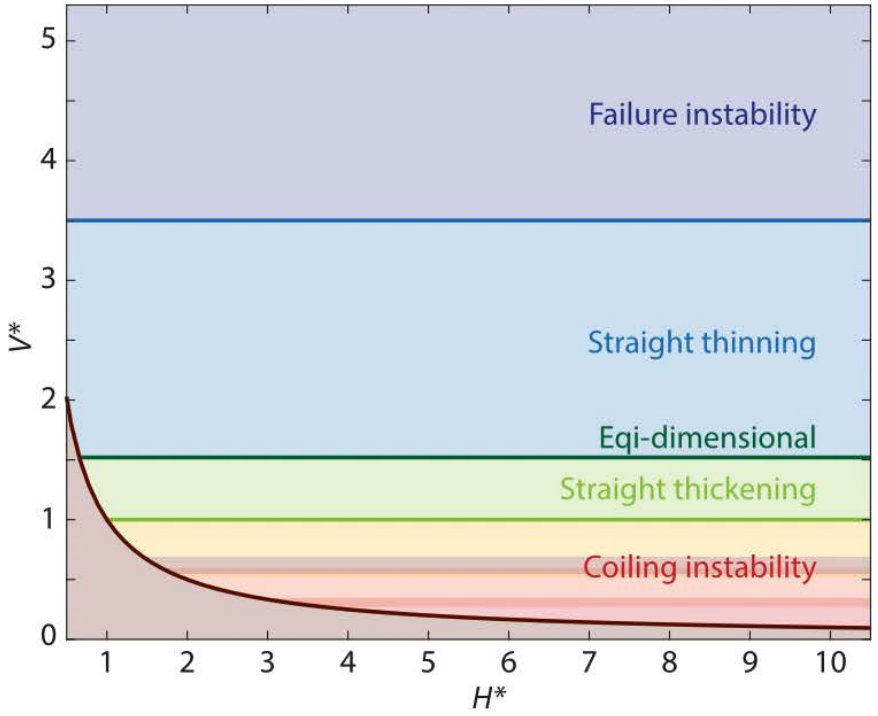
Patent at MIT

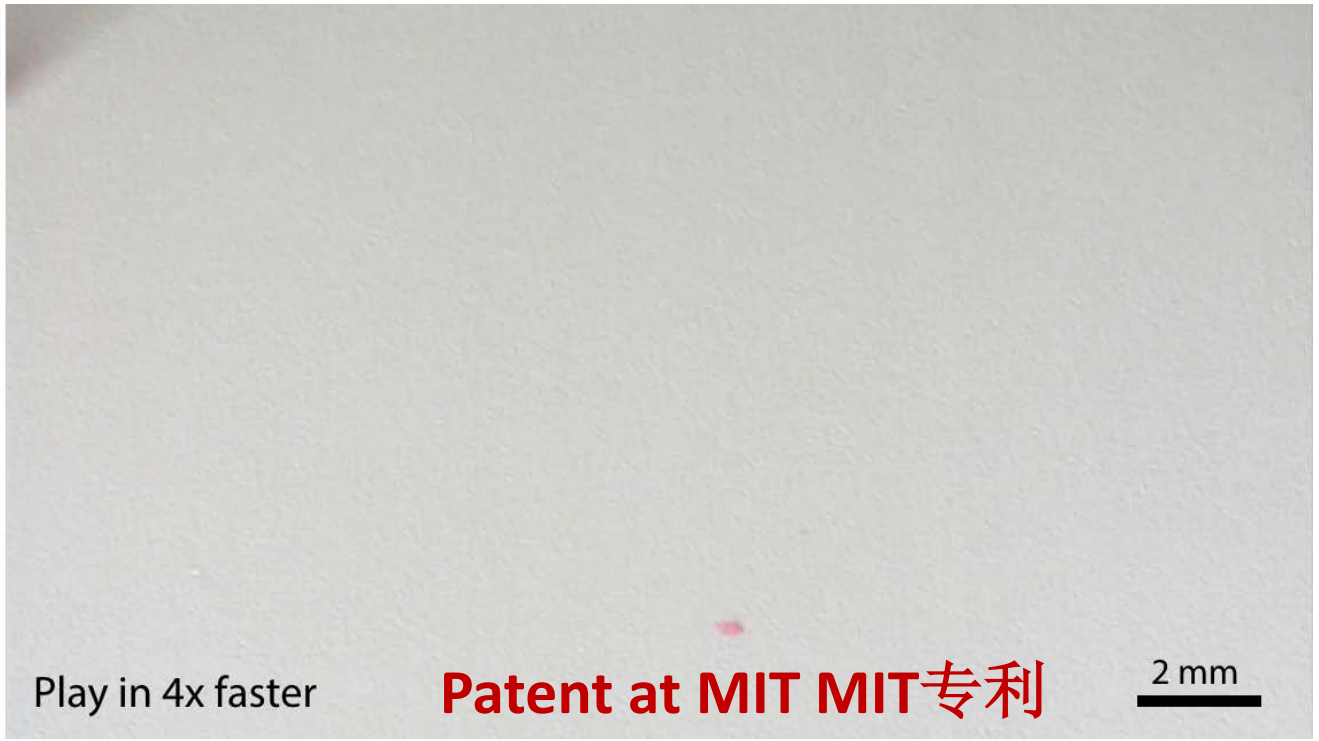
Design of Printing Process and Pattern
设计3D打印过程和模式

$$P=P(V^*, H^*)$$

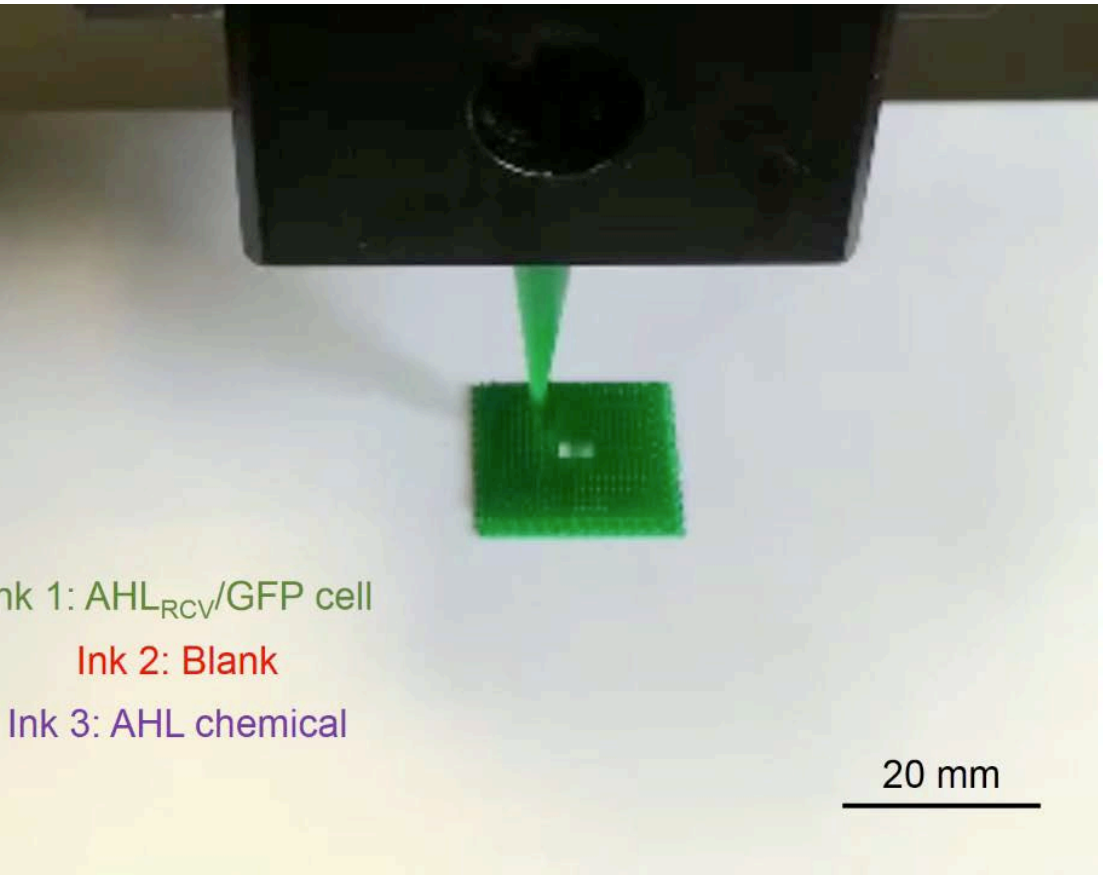
Yuk et al, Advanced Materials, In Press

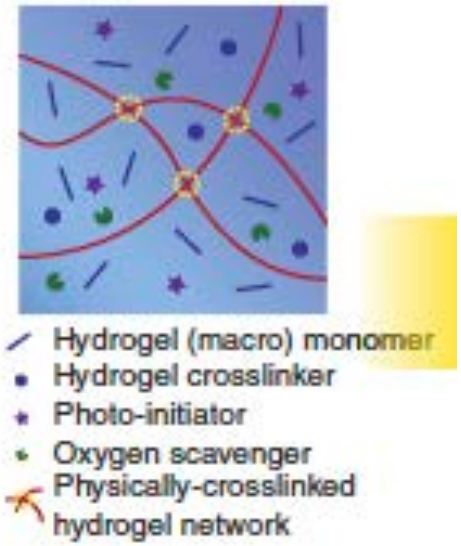




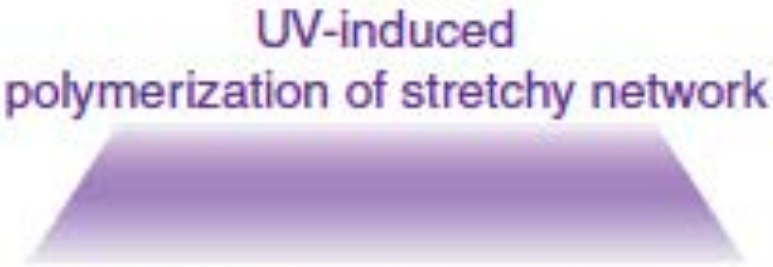


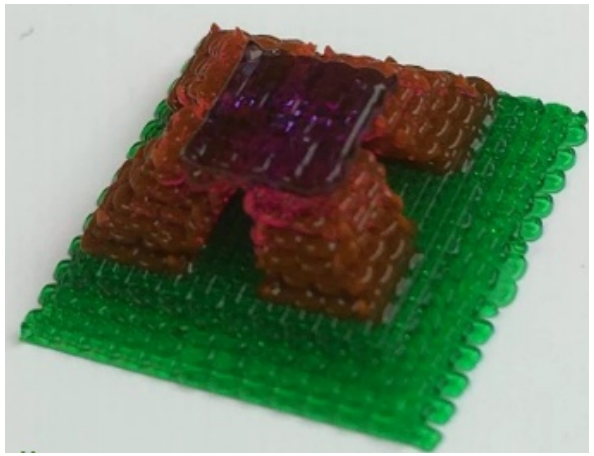
Step 1: Shape
3D Printing
Reversible Networks





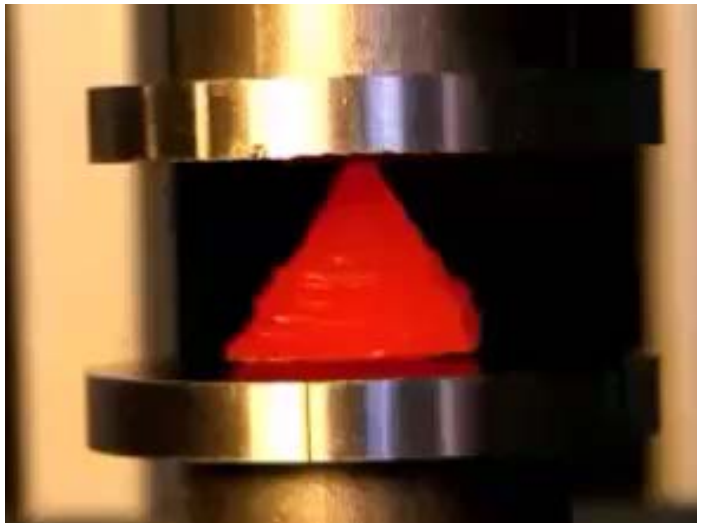
Step 2: Robustness
UV Crosslinking
Covalent Network



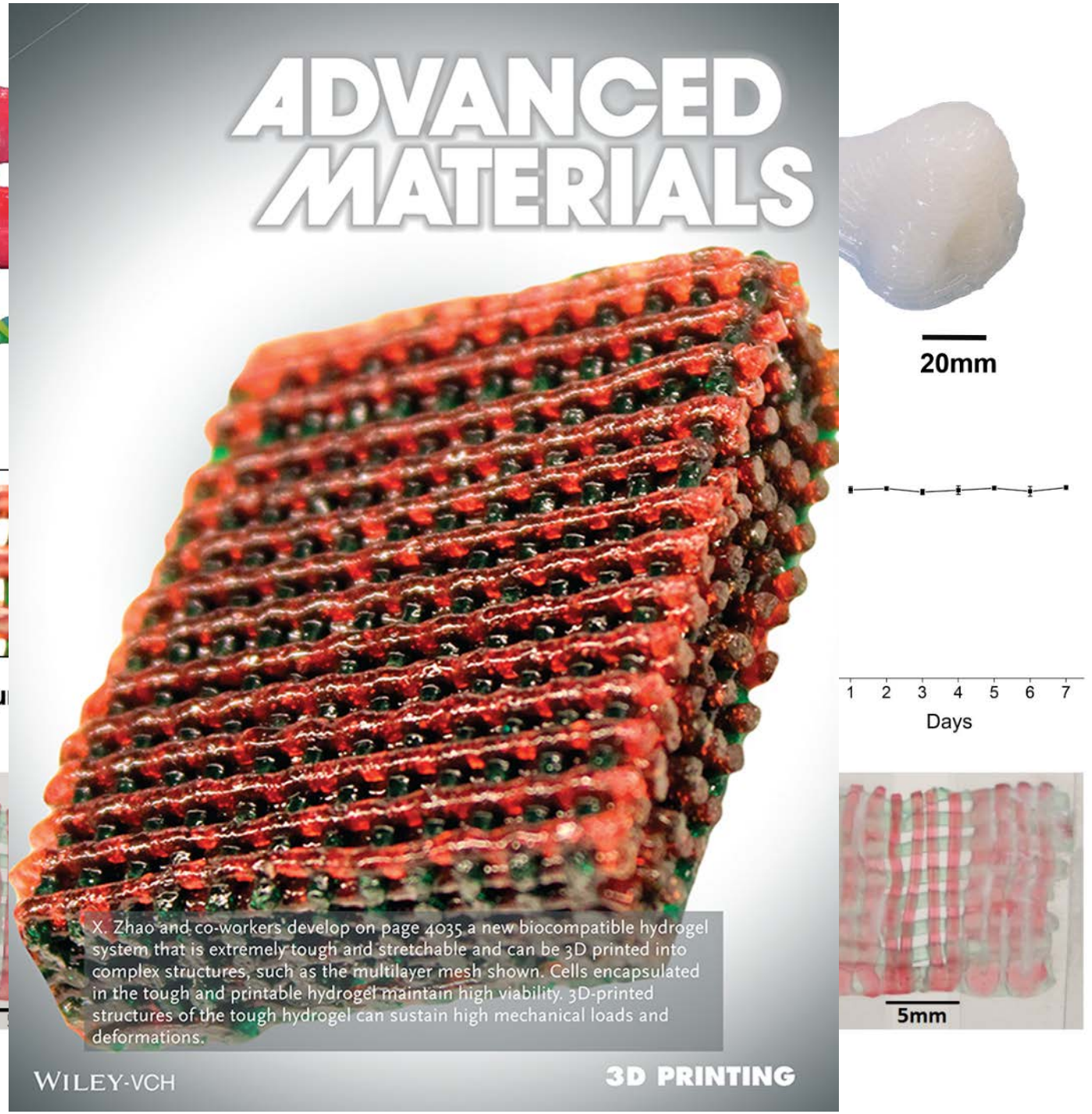


Hong et al Advance Materials, **27**, 4035 (2015)

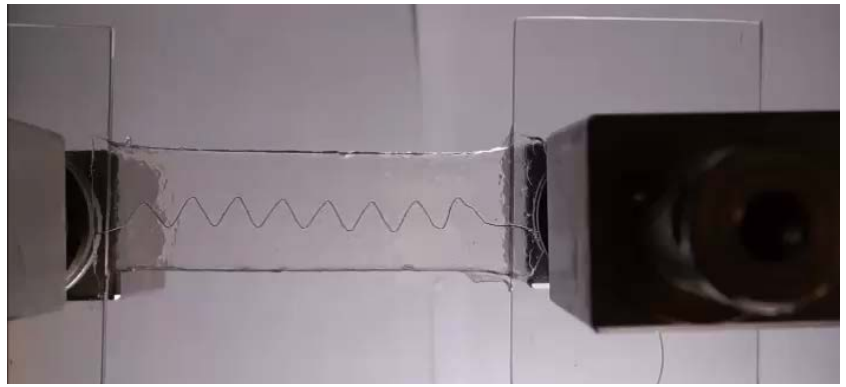
Robust Microstructures by 3D Printing



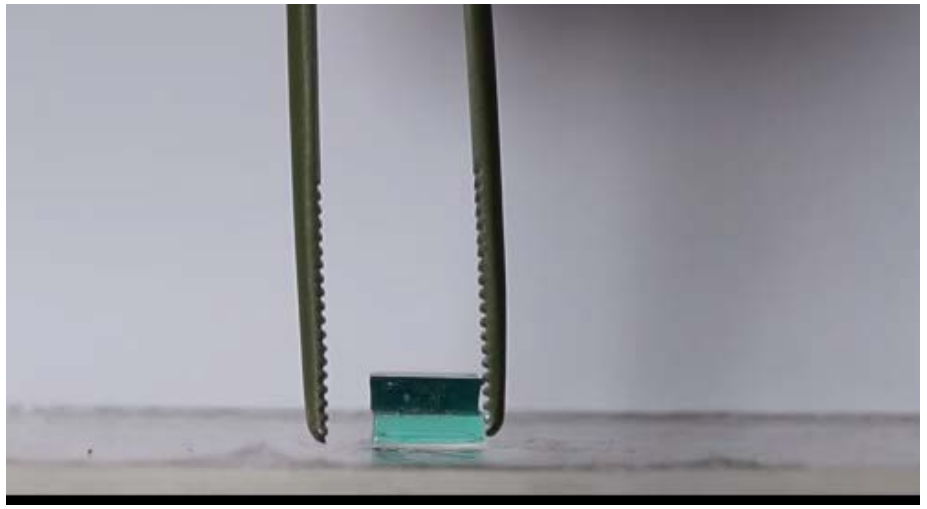
Hong et al Advance Materials, **27**, 4035 (2015)



Integrating Electronics with hydrogels (70~90% water)
在水凝胶中集成电子元件

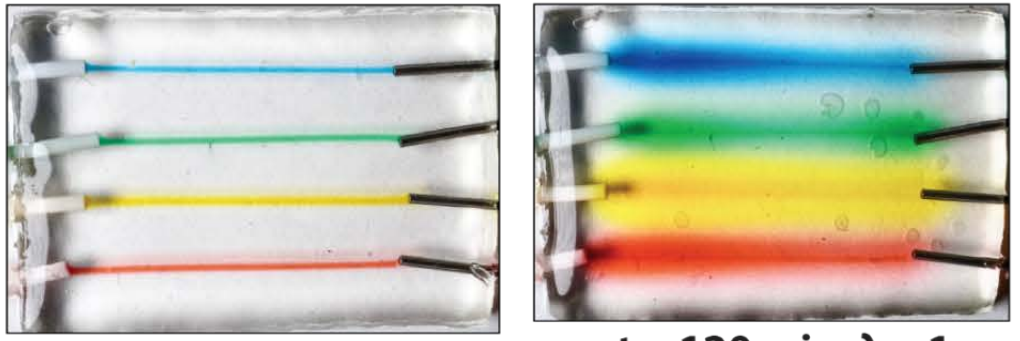


Conductive wires



Functional islands

LED arrays



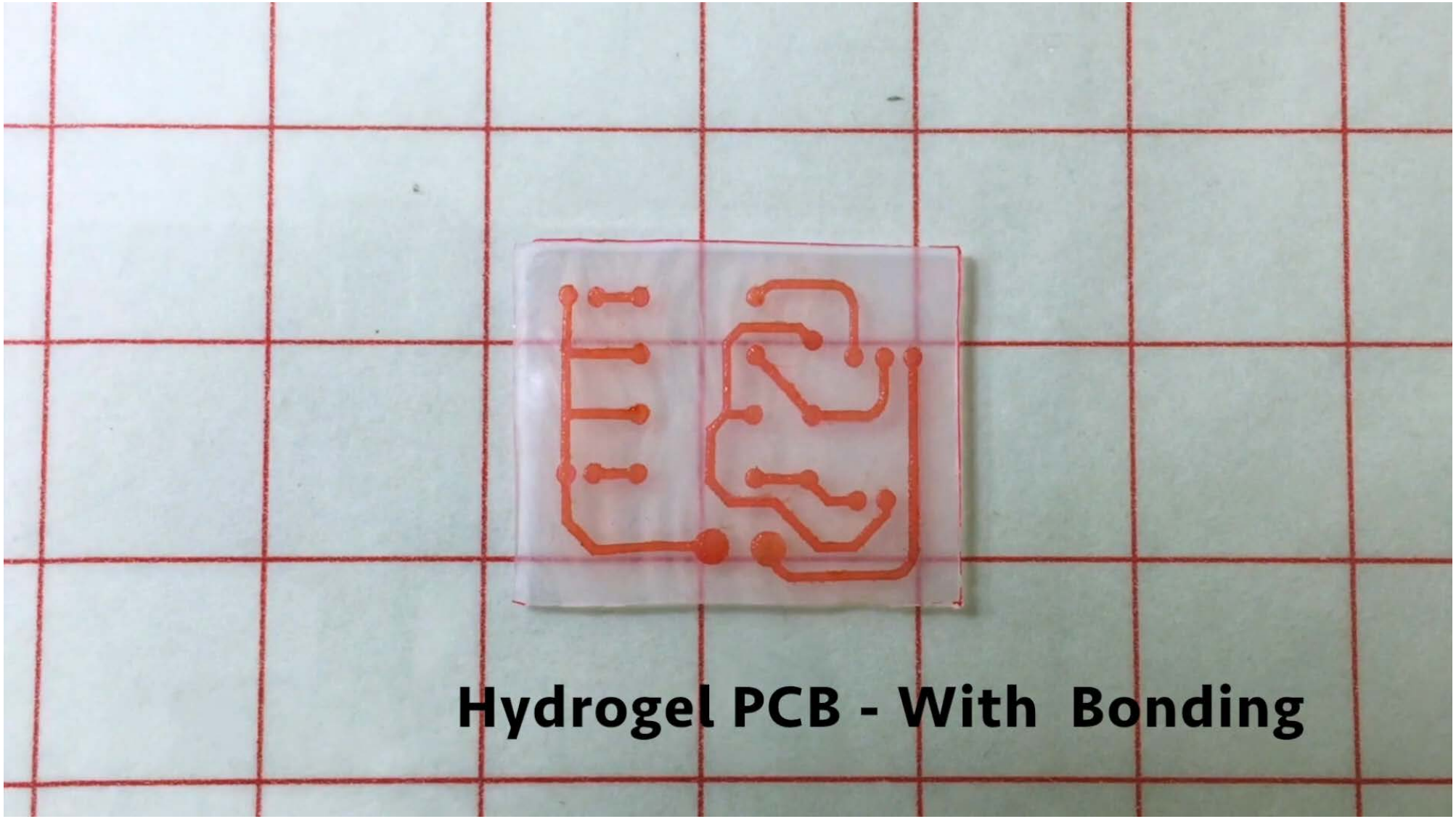
t = 0 min, λ = 1

t = 120 min, λ = 1

Drug delivery channels

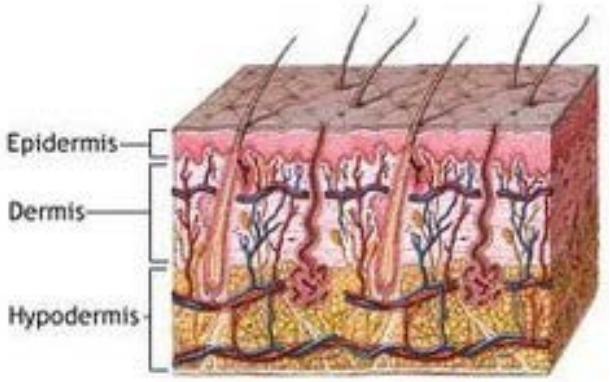
Lin, et al, Advanced Materials, 28, 4497–4505(2016)

Printed Hydrogel Circuit Boards 打印水凝胶电路



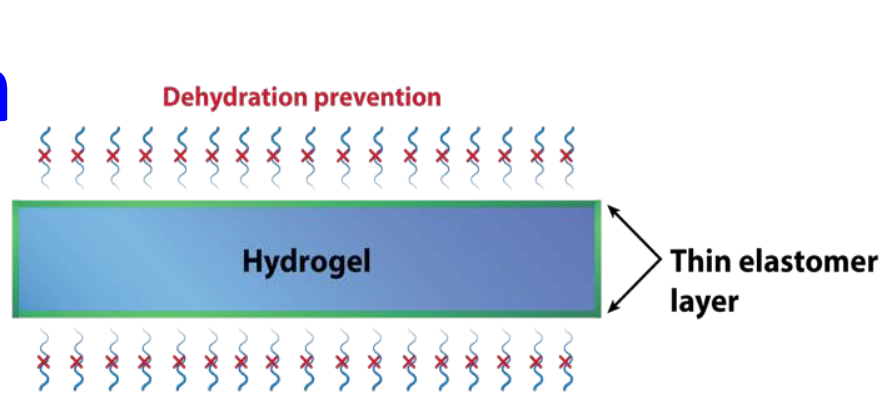
Yuk et al, Nature Communications, 7, 12028 (2016)

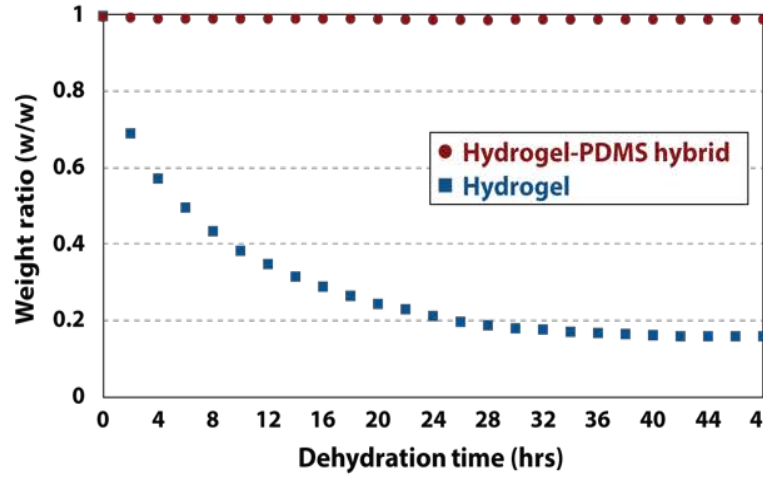
Anti-dehydration Hydrogel
抗干燥水凝胶

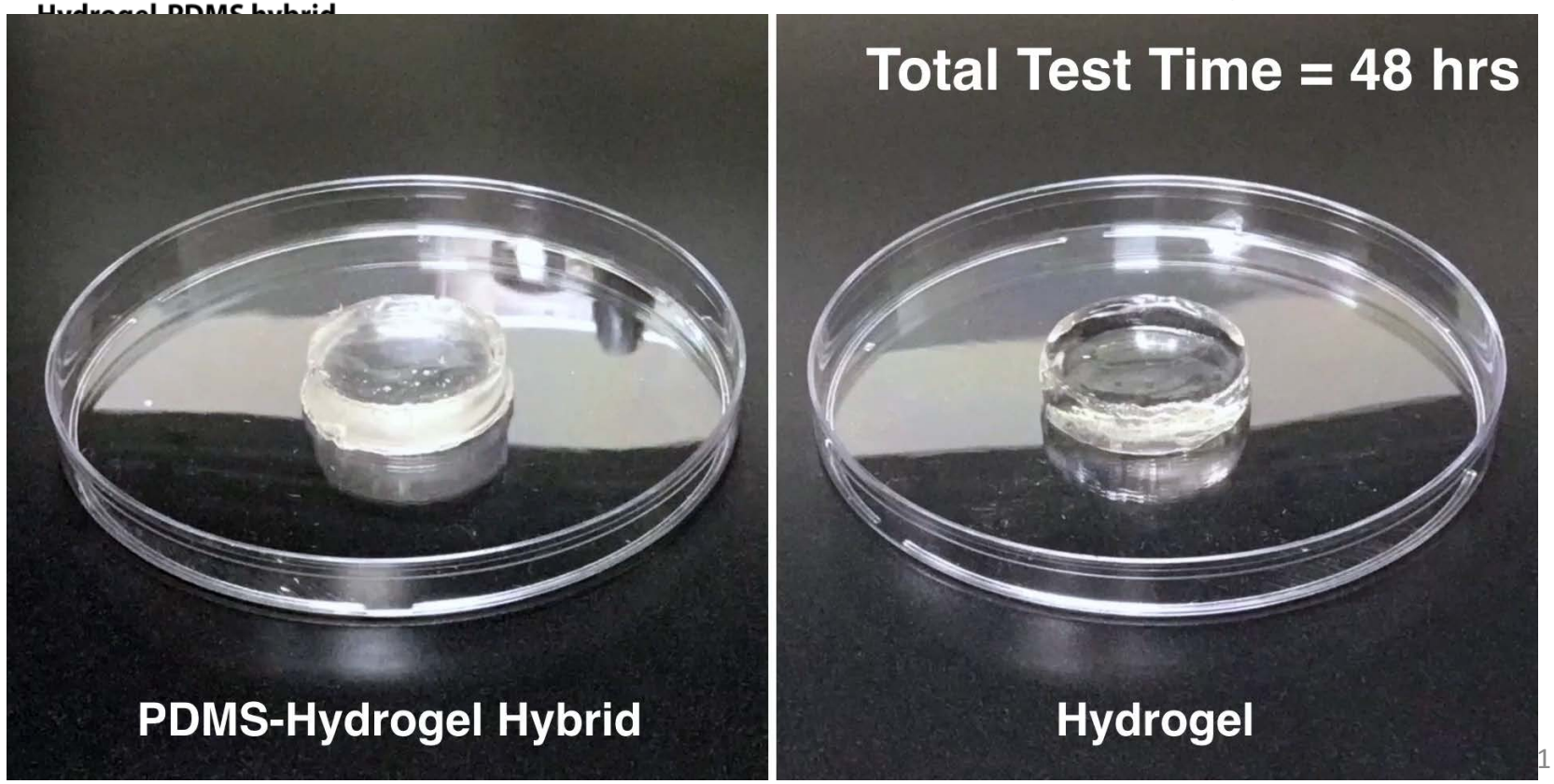


Yuk et al, Nature Communications, 7, 12028 (2016)

Patent at MIT, Liscenced by cirsinc.com



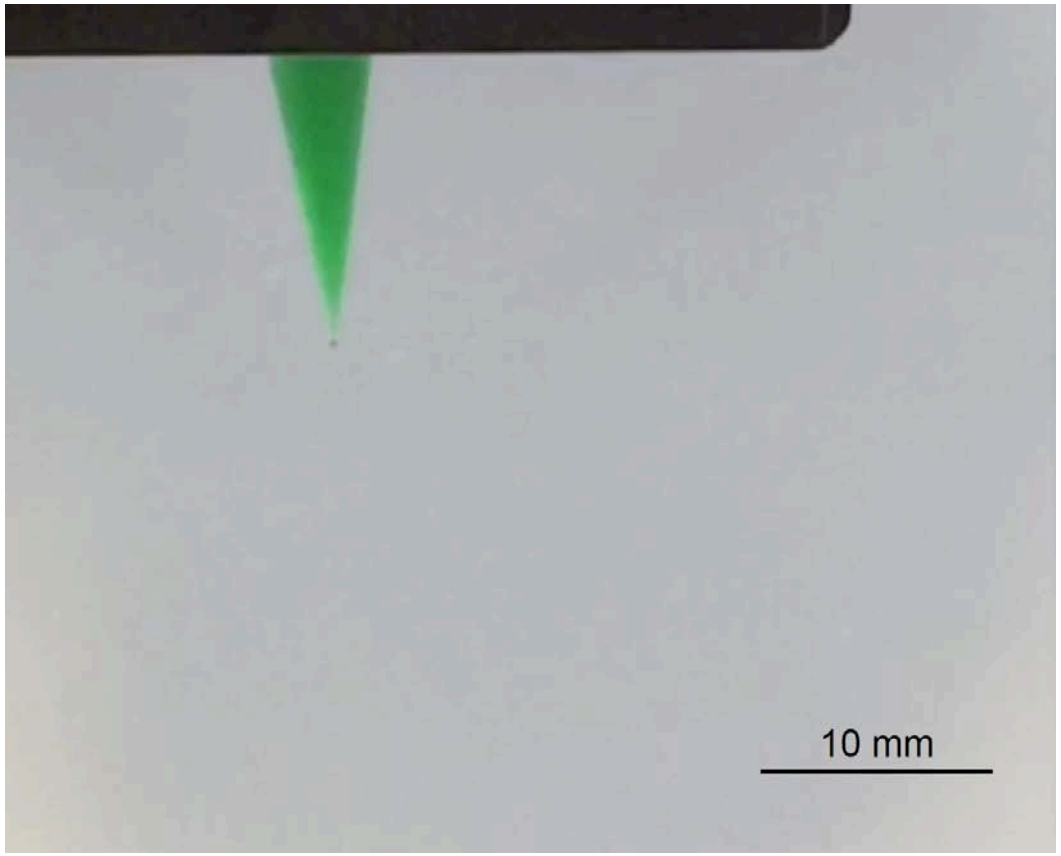




Merging Human Body and Machines: Examples

- Merging Skin and Machines 皮肤
- Merging Body Cavities and Machines 身体空道
- Merging Brain and Machines 大脑
- Merging Stomach and Machines 胃

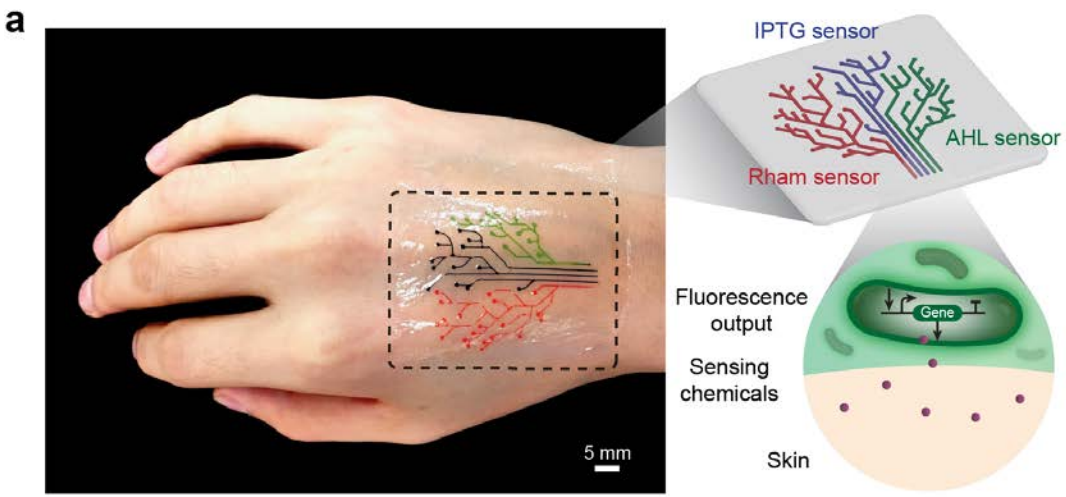
Merge With Skin: Living Tattoo

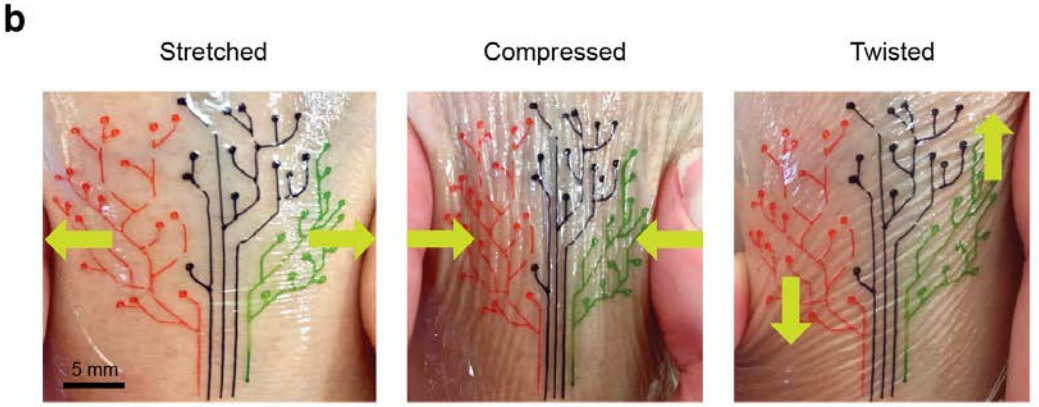


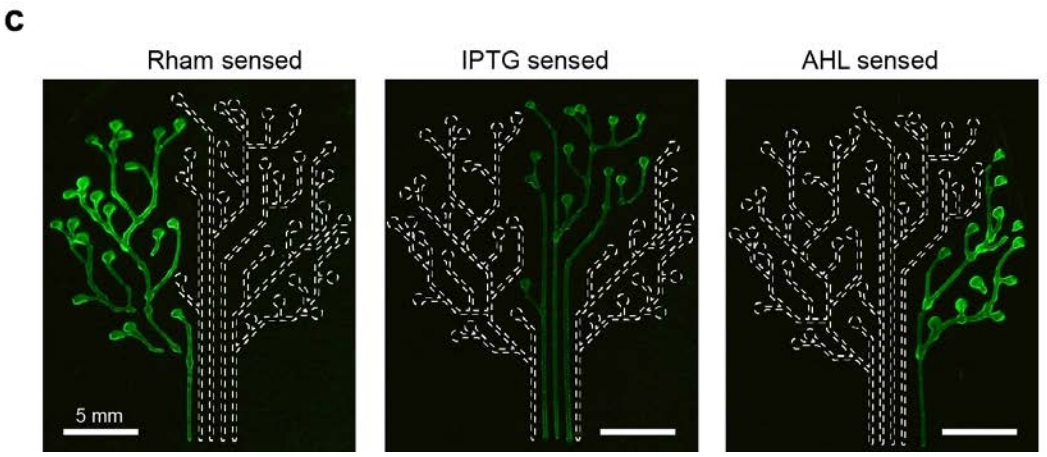
Liu et al, Advanced Materials, In Press

In collaboration with Tim Lu

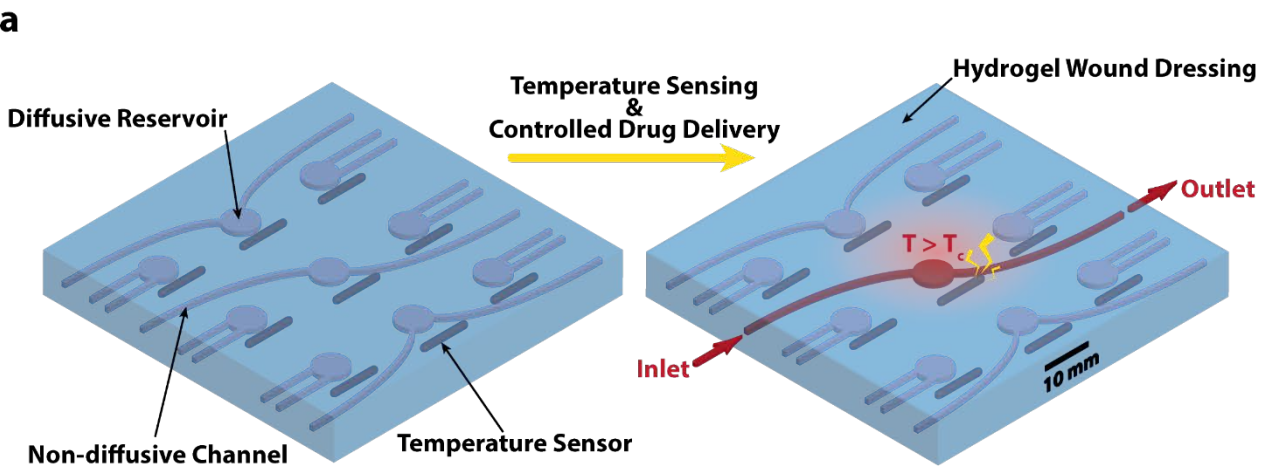
Patent at MIT

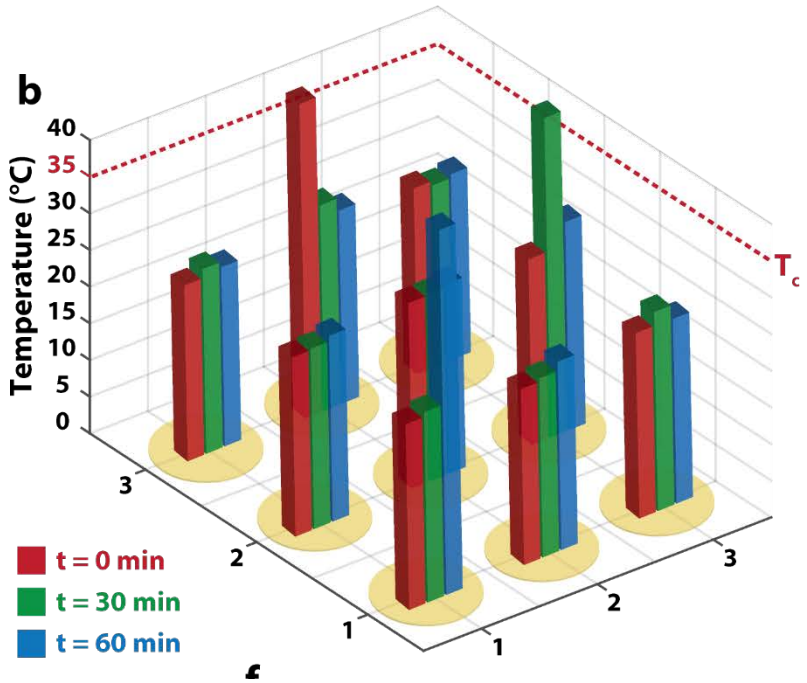


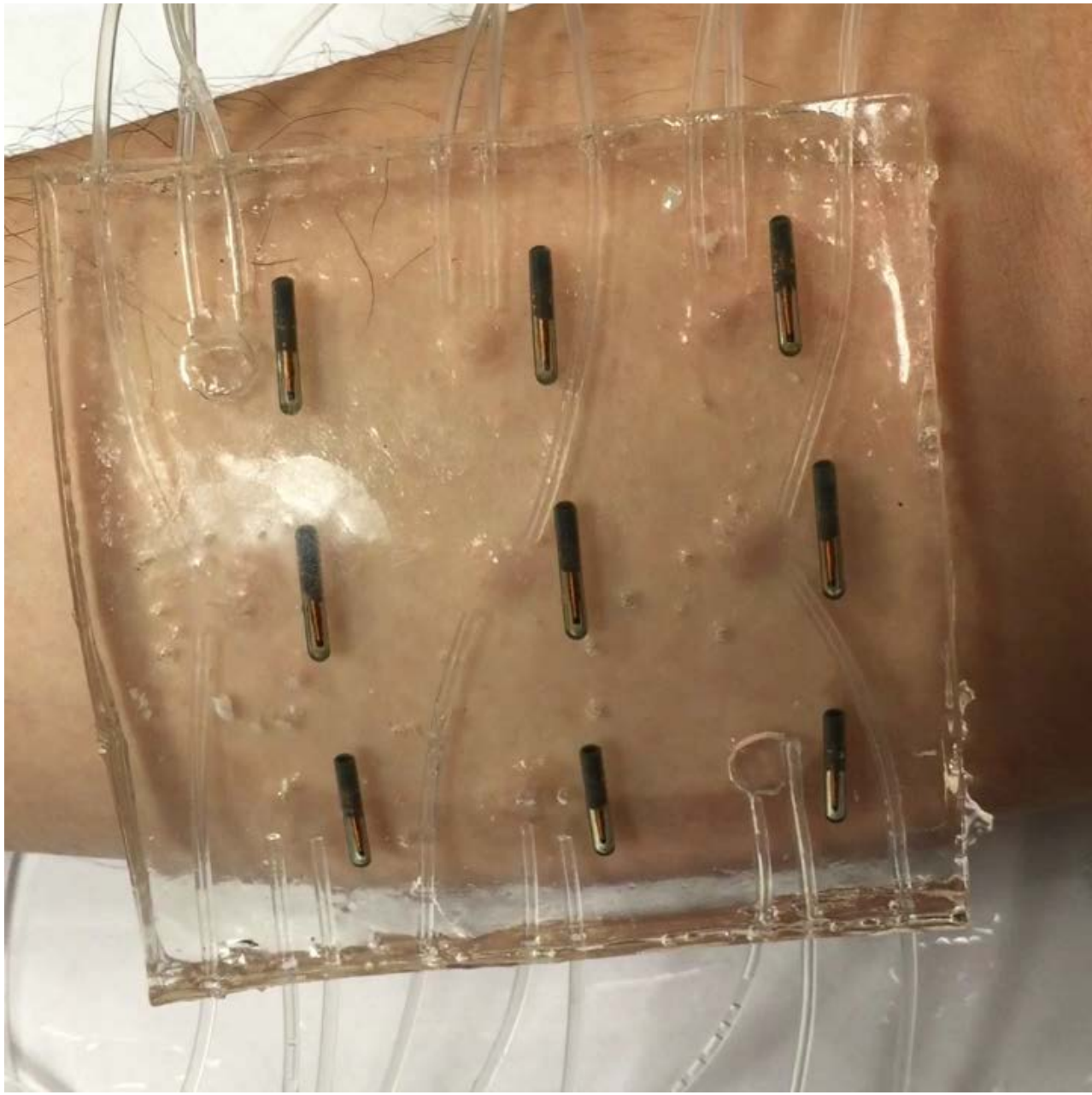




MIT Smart Hydrogel Band-Aid



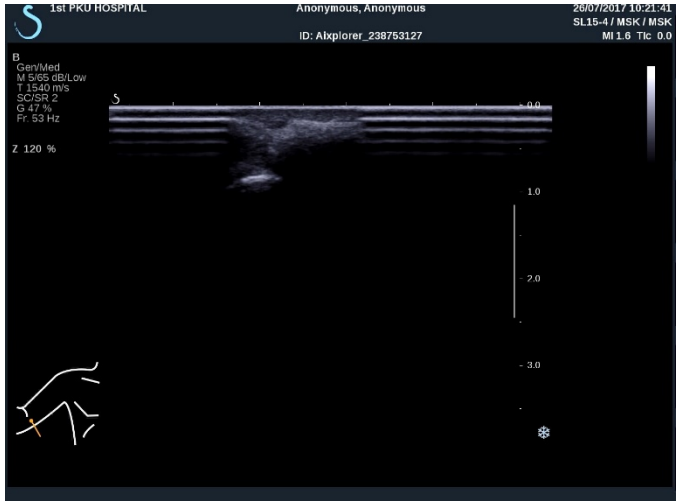




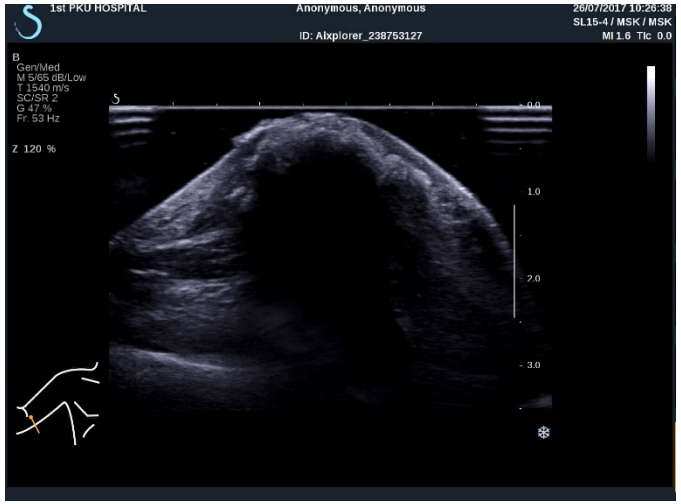
Lin, et al, Advanced Materials, **28**, 4497 (2016) **Patent at MIT**

Solid Ultrasound Gel 固态B超水凝胶介质

Liquid Gel



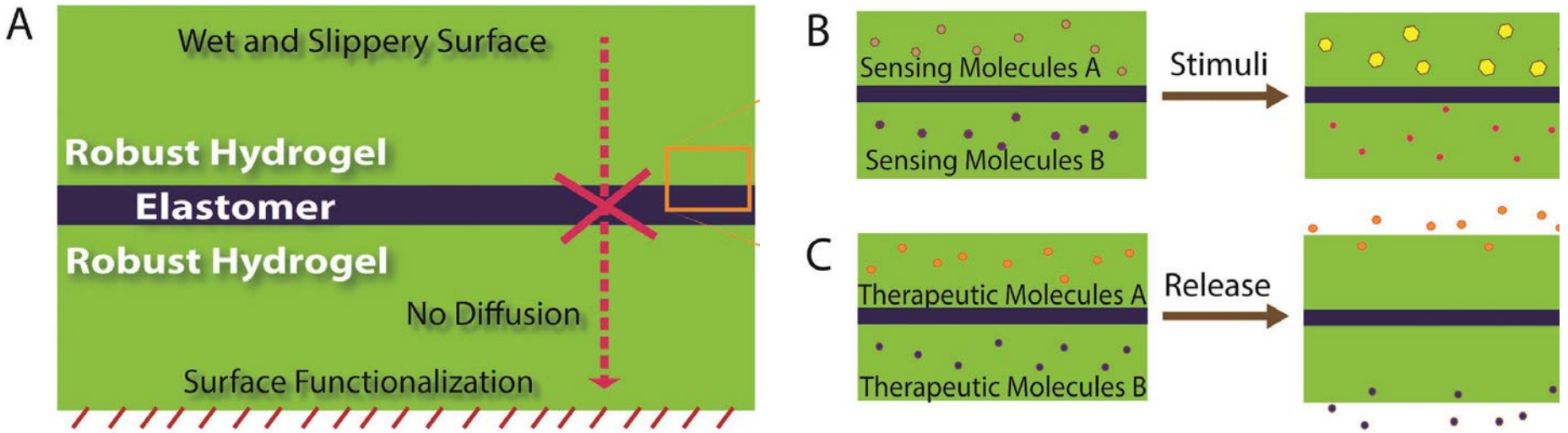
Solid Gel



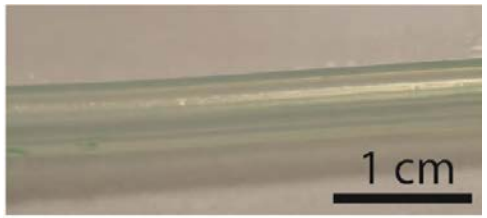
In collaboration with Dr. LZ. Chen from PKU

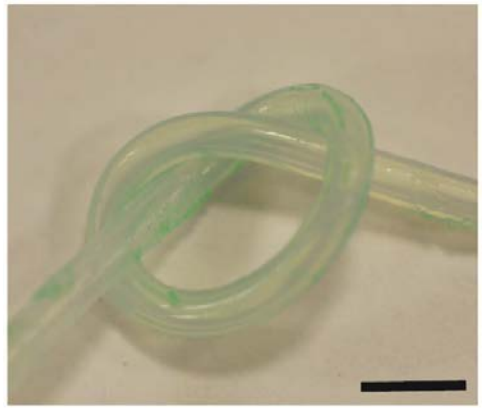
Patent from MIT 在通过CFDA审批

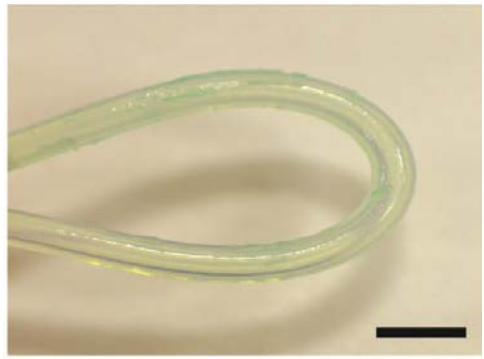
Merge with Body Cavity: Soft Slippery Antifouling Catheter



Surface Pair Condition	0.1 [s^{-1}]	0.5 [s^{-1}]
Steel on wet latex	0.269 ± 0.049	0.363 ± 0.144
Steel on hydrogel laminate	0.078 ± 0.008	0.096 ± 0.014
Steel on hydrogel	0.082 ± 0.018	0.106 ± 0.016
Latex on wet latex	0.216 ± 0.017	0.291 ± 0.081
Latex on hydrogel laminate	0.082 ± 0.016	0.114 ± 0.020
Hydrogel laminate on hydrogel laminate	0.022 ± 0.004	0.024 ± 0.001



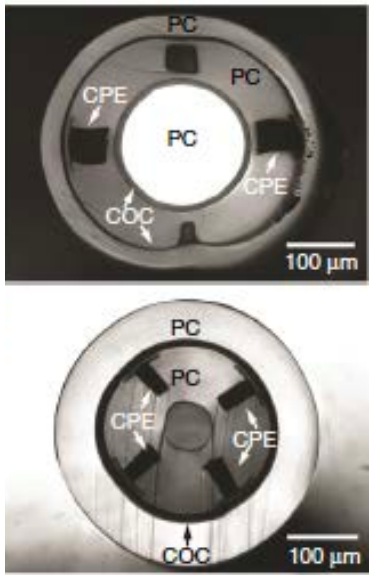




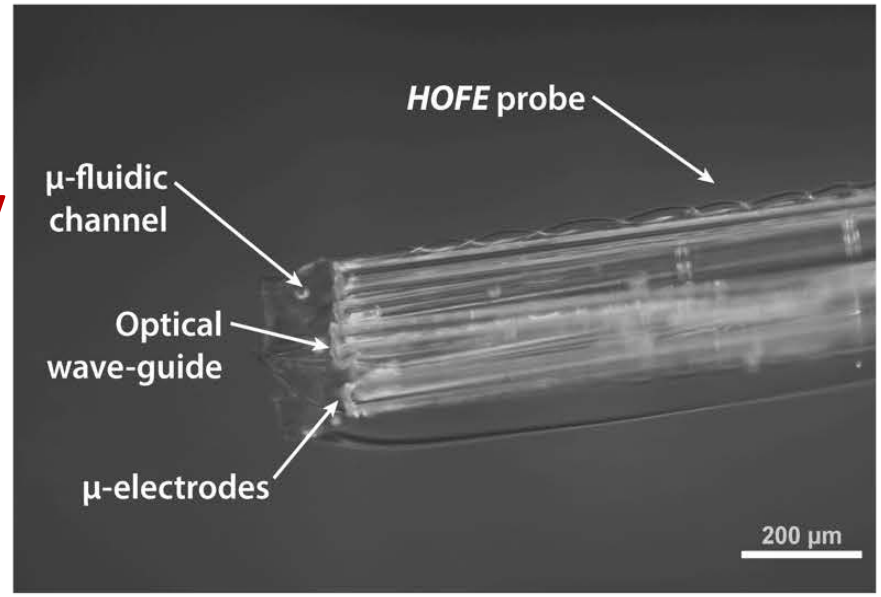
Parada et al, Advanced Healthcare Materials, **DOI:10.1002/adhm.201700520** (2017)

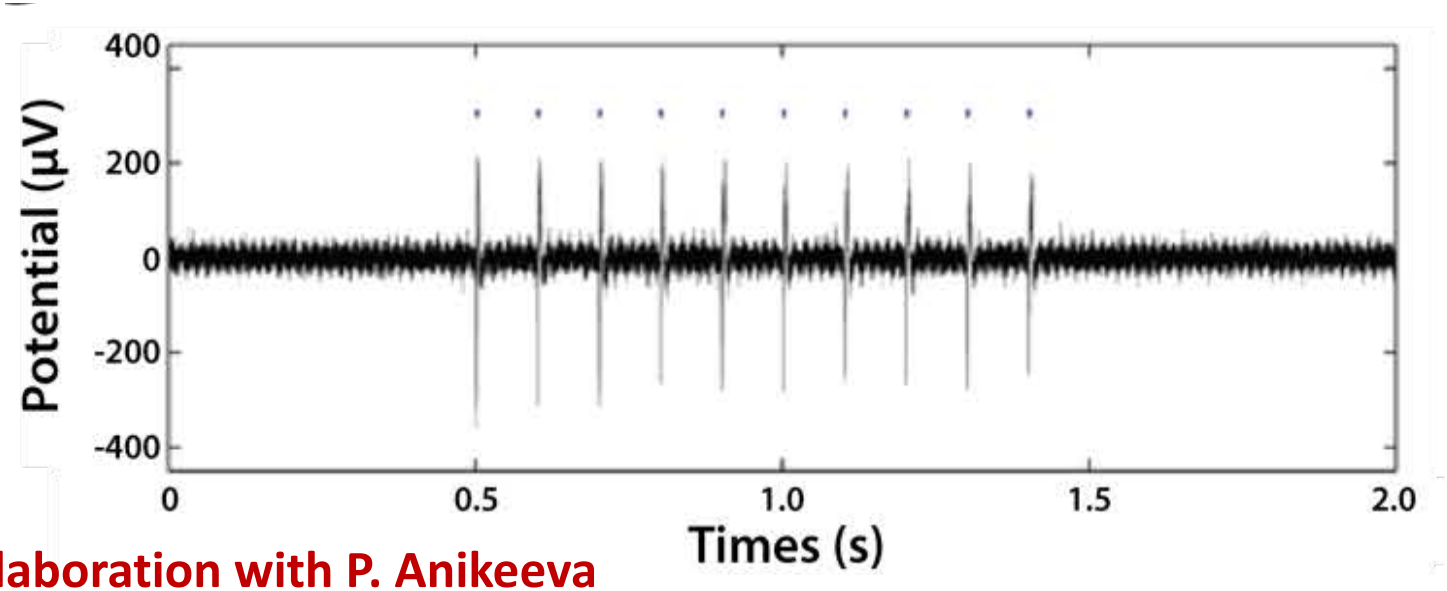
Patent at MIT

Merge With Brain: Hydrogel Neural Probe



Hydrogel Probe Body
Rigidity: 1~100kPa
Toughness: 1000Jm^{-2}



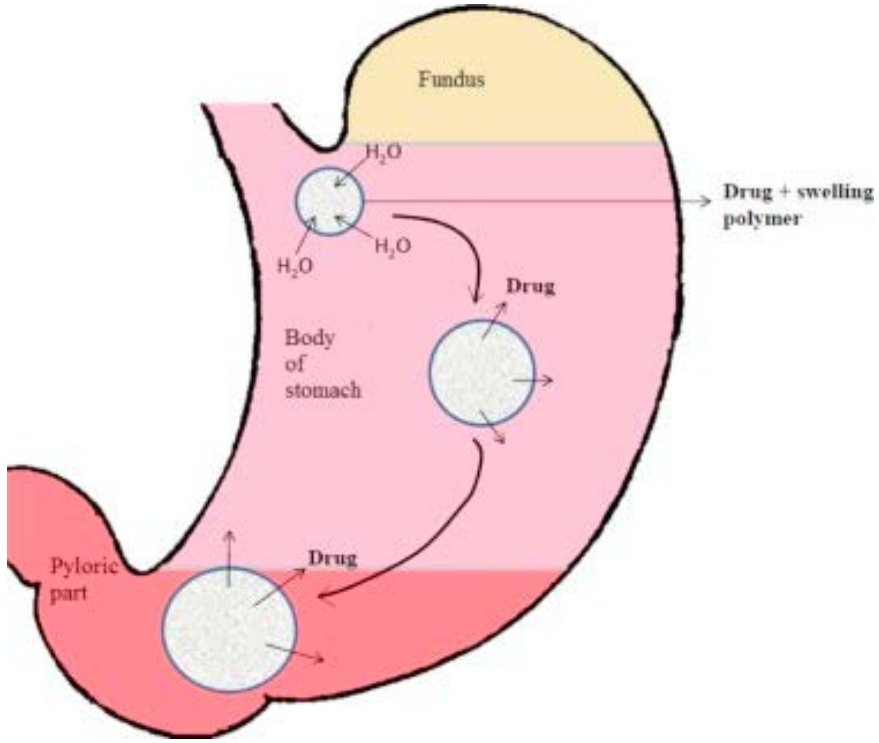


Yuk et al, Unpublished

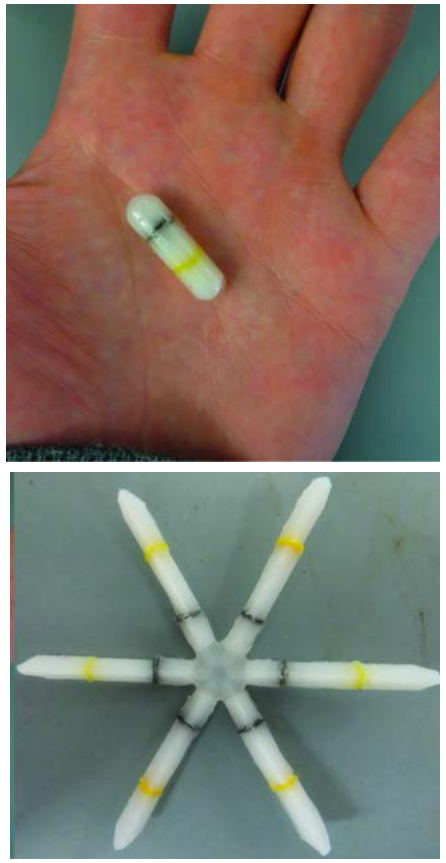
In collaboration with P. Anikeeva

Merge With Stomach: One Pill Per Week/Month

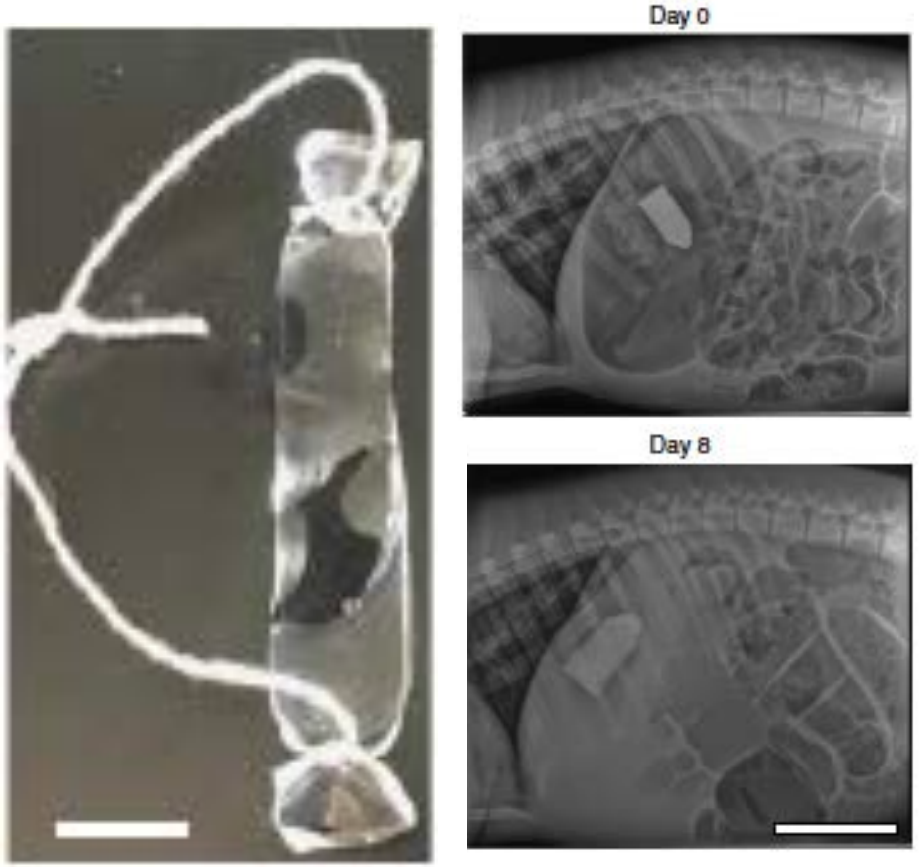
"One of the biggest issues in health care is noncompliance, people simply not taking their drugs", we need "to develop ultra-long-lasting capsules, which could be taken once a week or once a month." **Robert Langer MIT**



Gastric retentive system



Rigid-polymer based

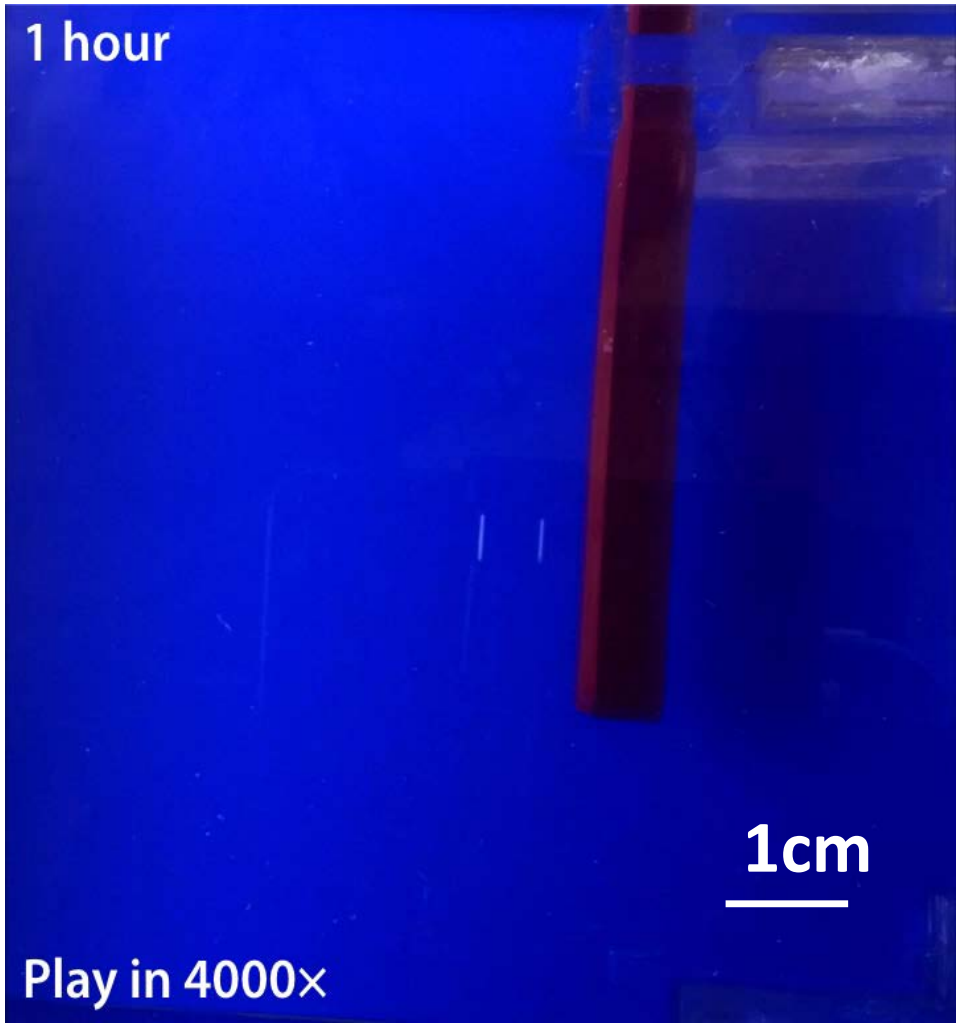


Robust-hydrogel based

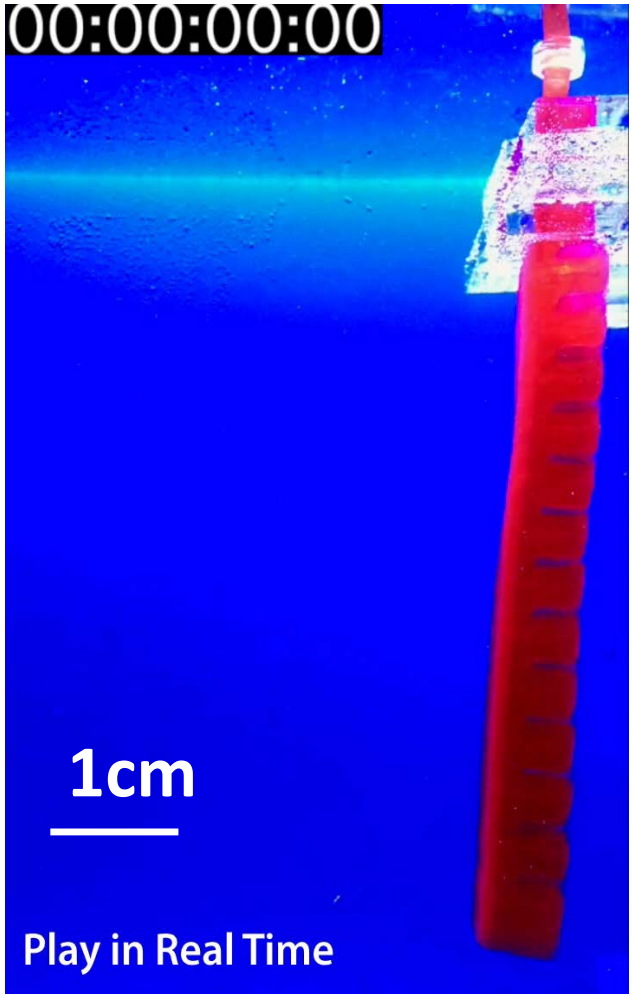
Langer, Nature Comm. DOI: 10.1038/s41467-017-00144-z

Muscle: Hydraulic Hydrogel Actuators and Robots

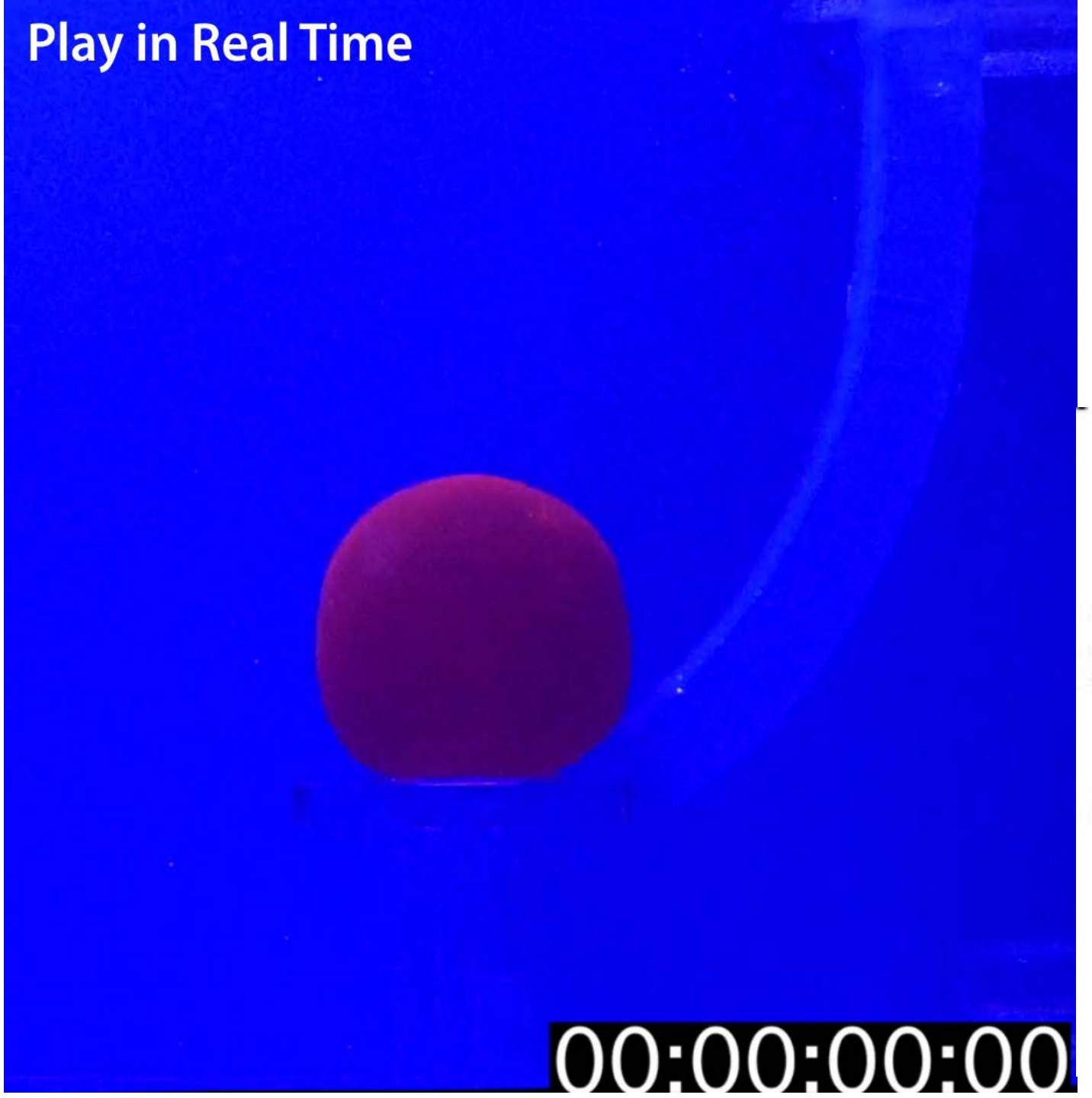
Osmotic Actuation



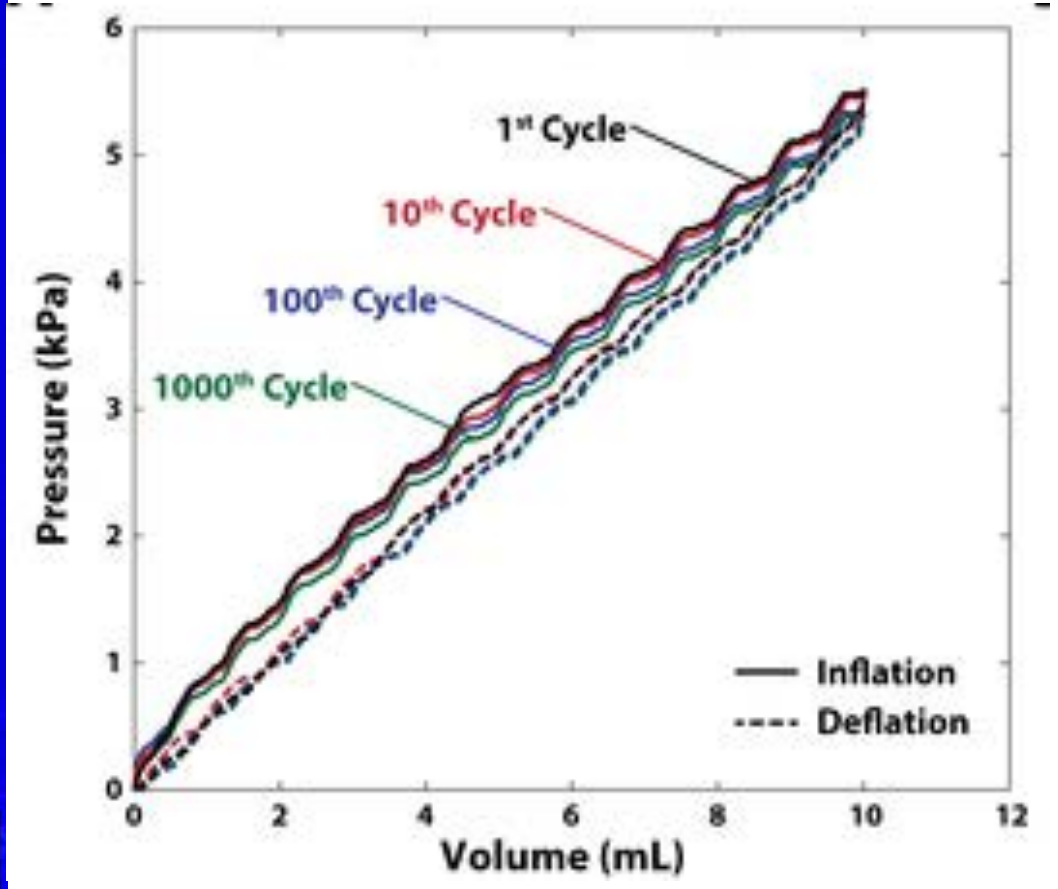
Hydraulic Actuation



Yuk et al, Nature Comm, **8**, 14230 (2017)



- Actuation force: >10N.
- Responsive time: <1s.
- Optically and sonically camouflaged in water




Play in Real Time
MIT CAC 1016-067-19
Yuk et al, Nature Communications,8, 14230
00:00:00:00

Acknowledgement

Group Members

- Hyunwoo Yuk
- Shaoting Li
- Xinyue Liu
- Teng Zhang
- German Alberto
- Yoonho Kim
- Ruike Zhao
- Vivas Chan
- Baoyang Lu
- Yan Yu
- Kai Zhang
- Grace Goon

Shaoting Li

Hyunwoo Yuk

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- Prof. Lallit Anand, MIT ME
- Prof. Nick Fang, MIT ME
- Prof. Zhigang Suo, Harvard
- Prof. David Mooney, Harvard
- Prof. Joost Vlassak, Harvard
- Prof. Kam Leong, Columbia
- Prof. Farshid Guilak, Duke

NSF CAREER Award

ONR YIP Award

Thank you! Questions?

Soft, Wet, Living
柔软,含水,生命

Soft living machines
活性软机器
zhaox.org

Hard, Dry, Non-living
坚硬,干燥,无生命