Analytical and Programmable Drug Delivery Systems

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CRS 2022 Annual Meeting & Expo
July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada
Advanced Delivery Science

Advanced Functional Drug Delivery Systems

The research objective of our group is to develop advanced **functions** of delivery systems

1. Programmable controlled release
   - For personalized medicine

2. Derivative controller
   - Rapid, pre-emptive action
   - Stimuli-responsive

To mimic the controls of chemical plants using materials

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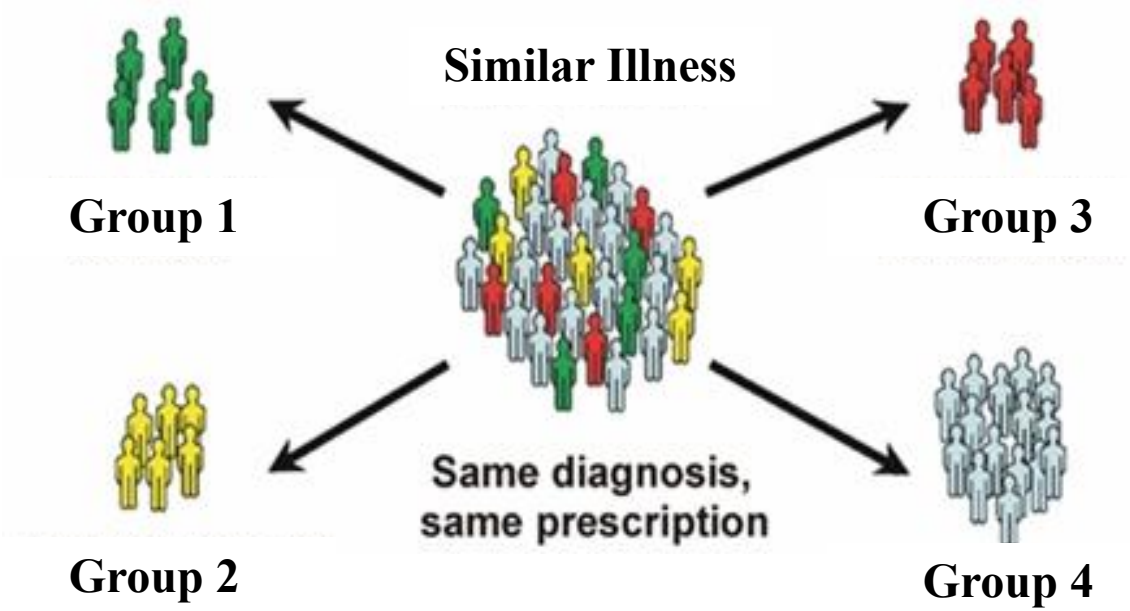
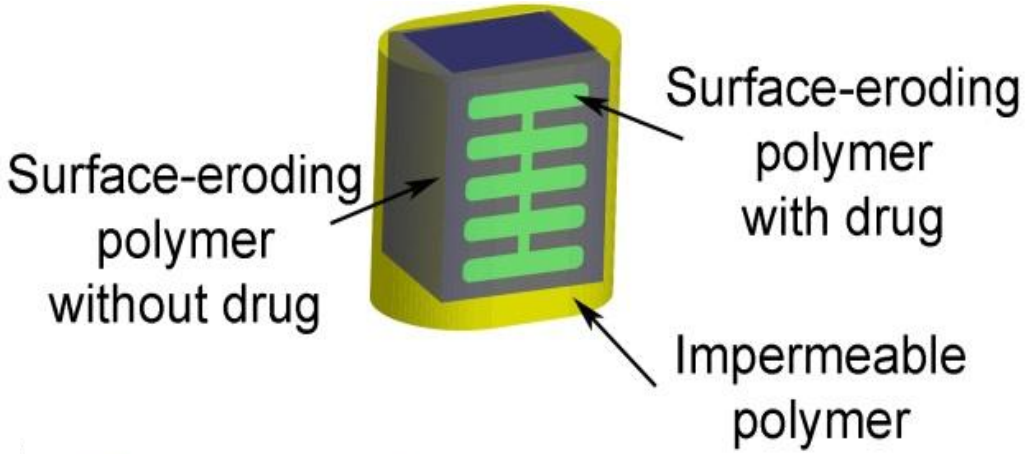
Programmable Drug Delivery for Personalized Medicine

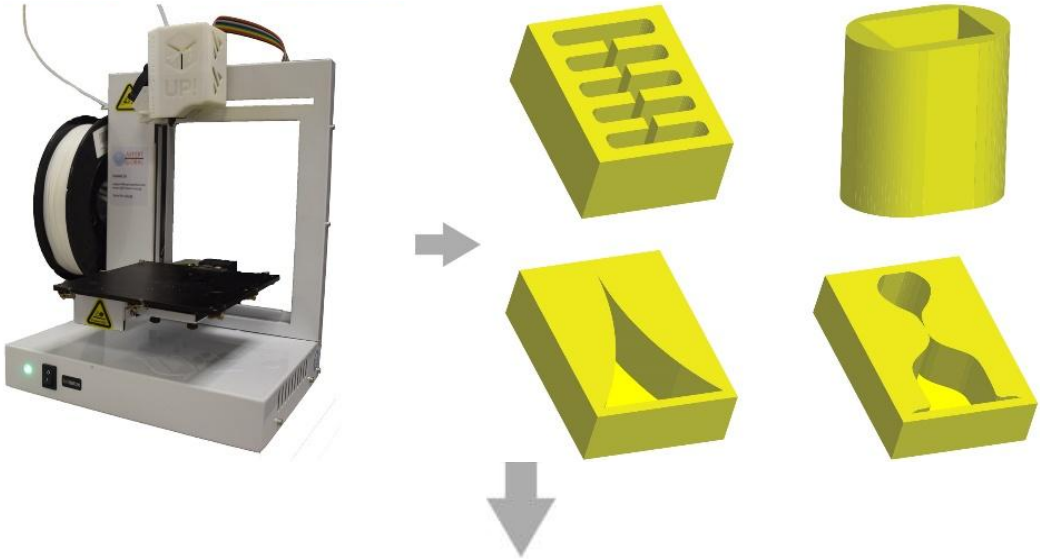


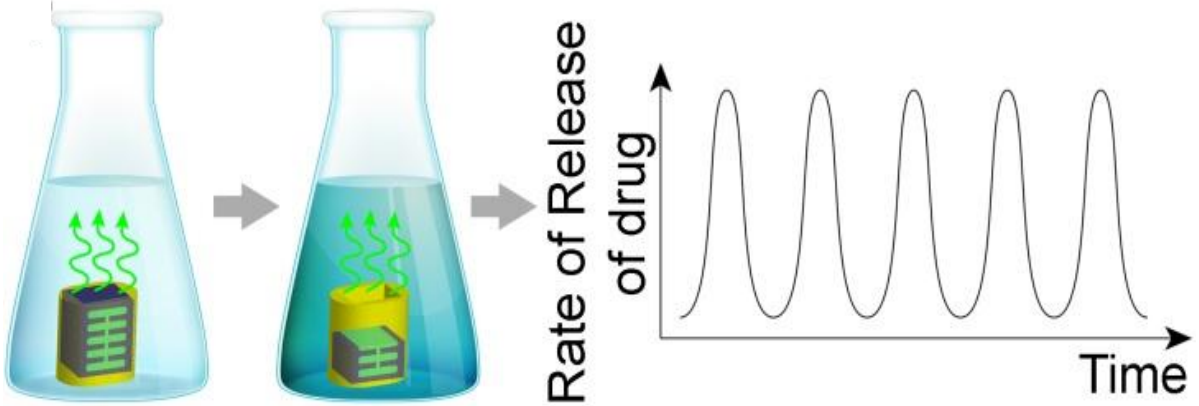
- Biological differences (e.g., genetics)
- Physical differences (e.g., age, sex, body mass, etc)
- Different types of illness
- Different living/ working conditions
- Different types of consumption (e.g., drinks, food, herbs, etc)

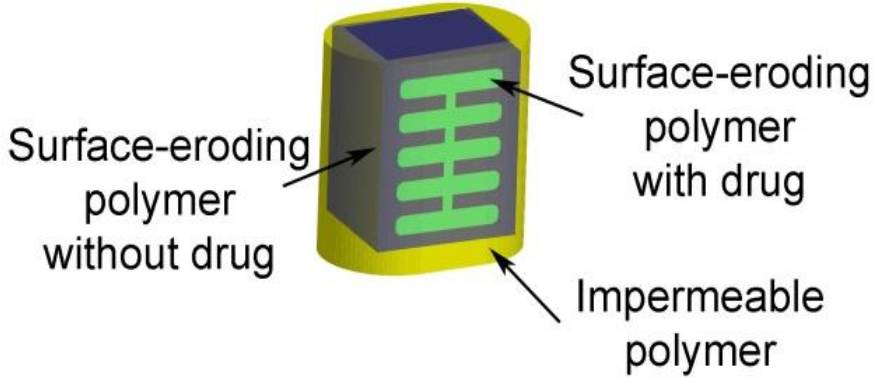
All individuals are different !

Programming Fully Customizable Tablet for Personalized Medicine









Components of the Fully Customizable Tablet

Drugs tested:

- Paracetamol (high-dosage drug)
- Phenylephrine hydrochloride (low-dosage drug)
- Diphenhydramine hydrochloride (low-dosage drug)

High-dosage drug excipient:

- Hydroxyethyl cellulose (HEC)

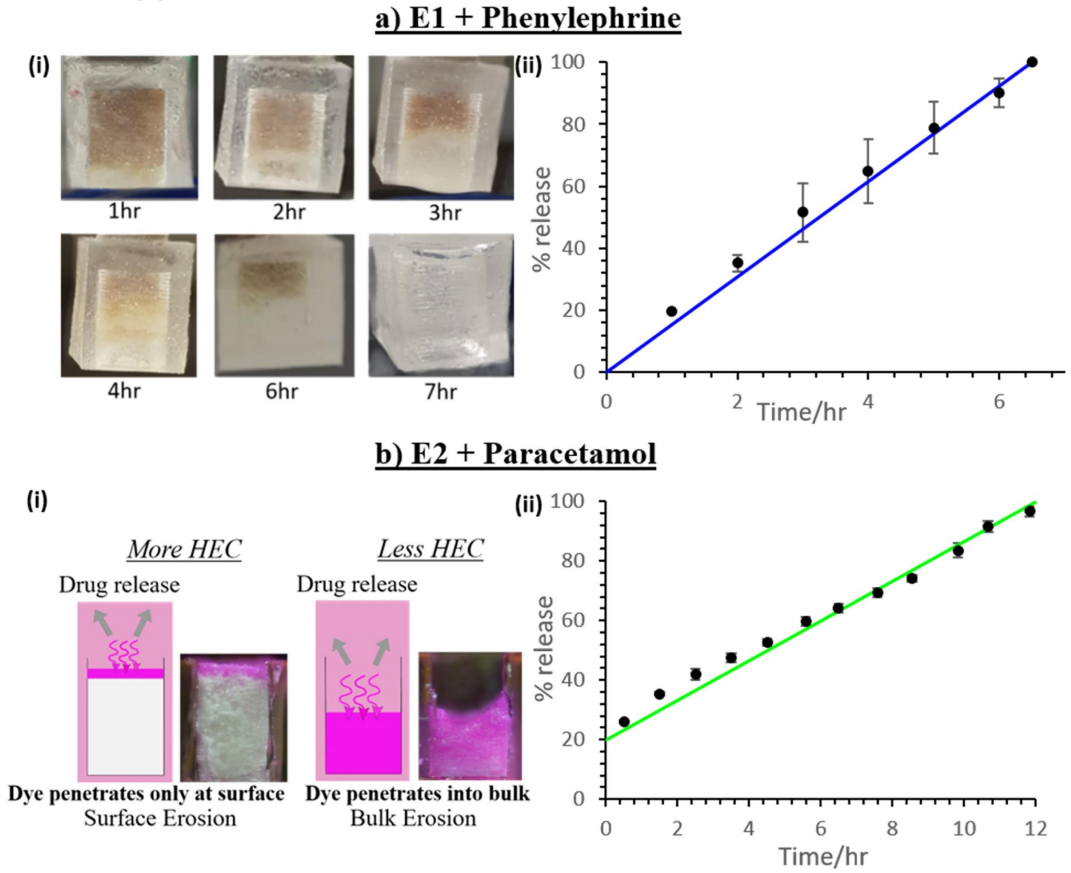
Low-dosage drug excipient:

- Carnauba wax
- Sodium alginate
- Croscarmellose sodium (CNa)

Coating:

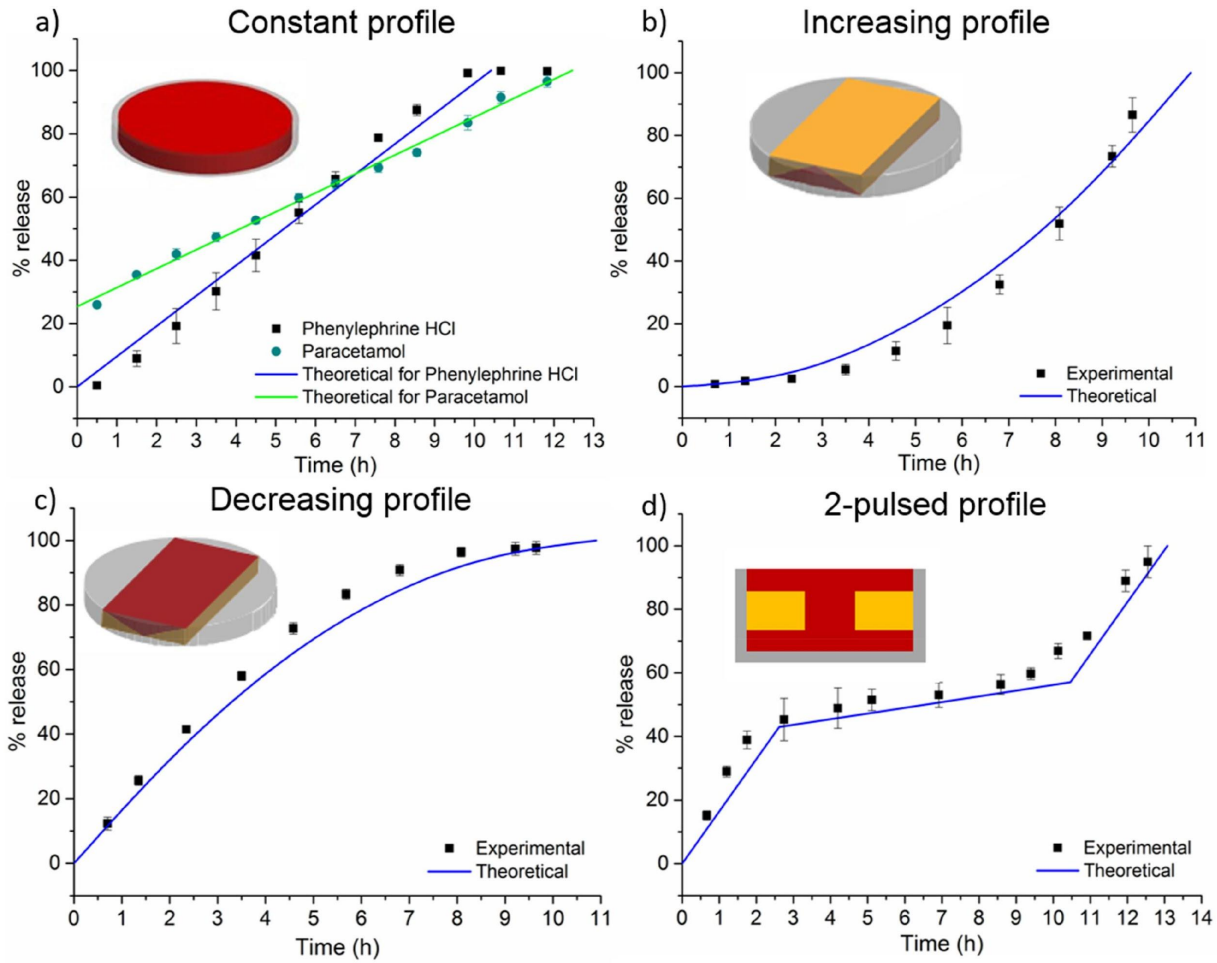
- White wax

Surface-eroding excipient

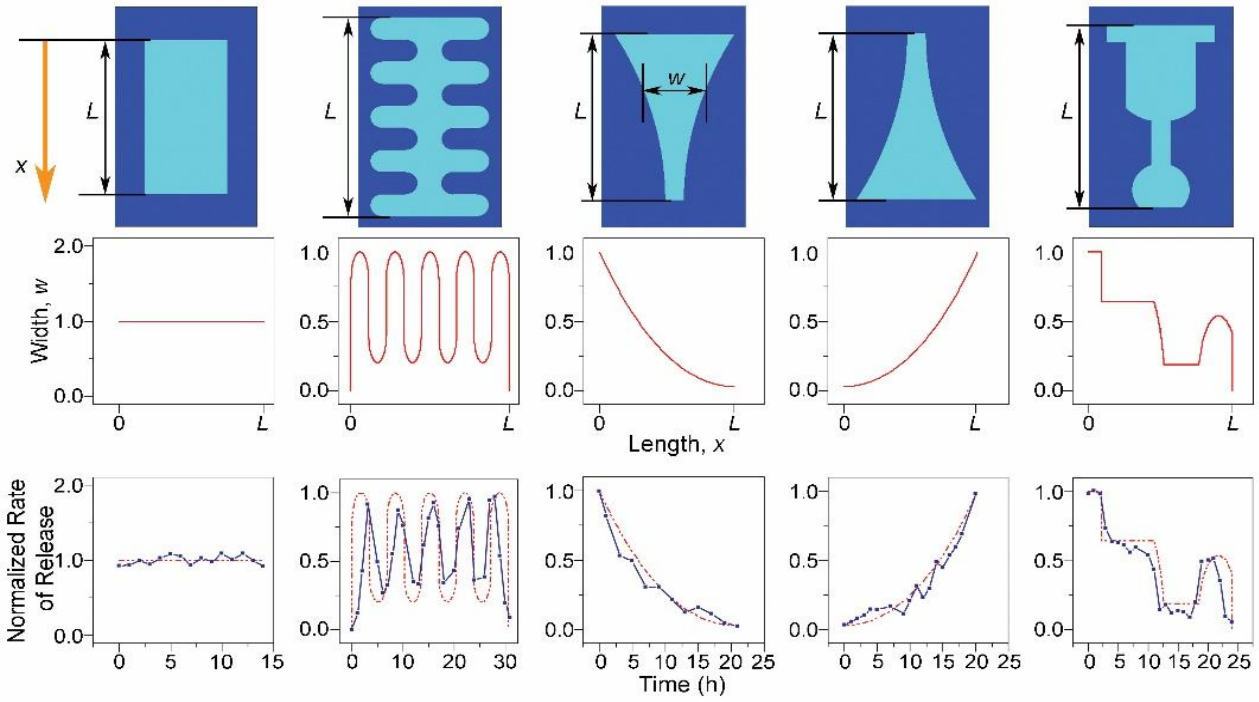


Fully Customizable Release Profile

Phenylephrine hydrochloride or Paracetamol

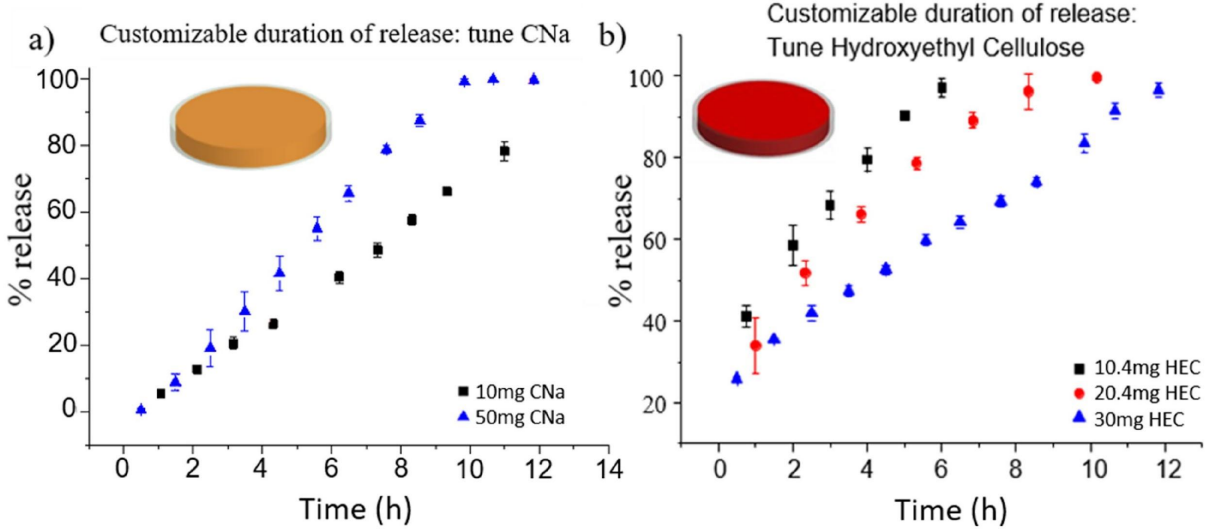


Any arbitrary profiles



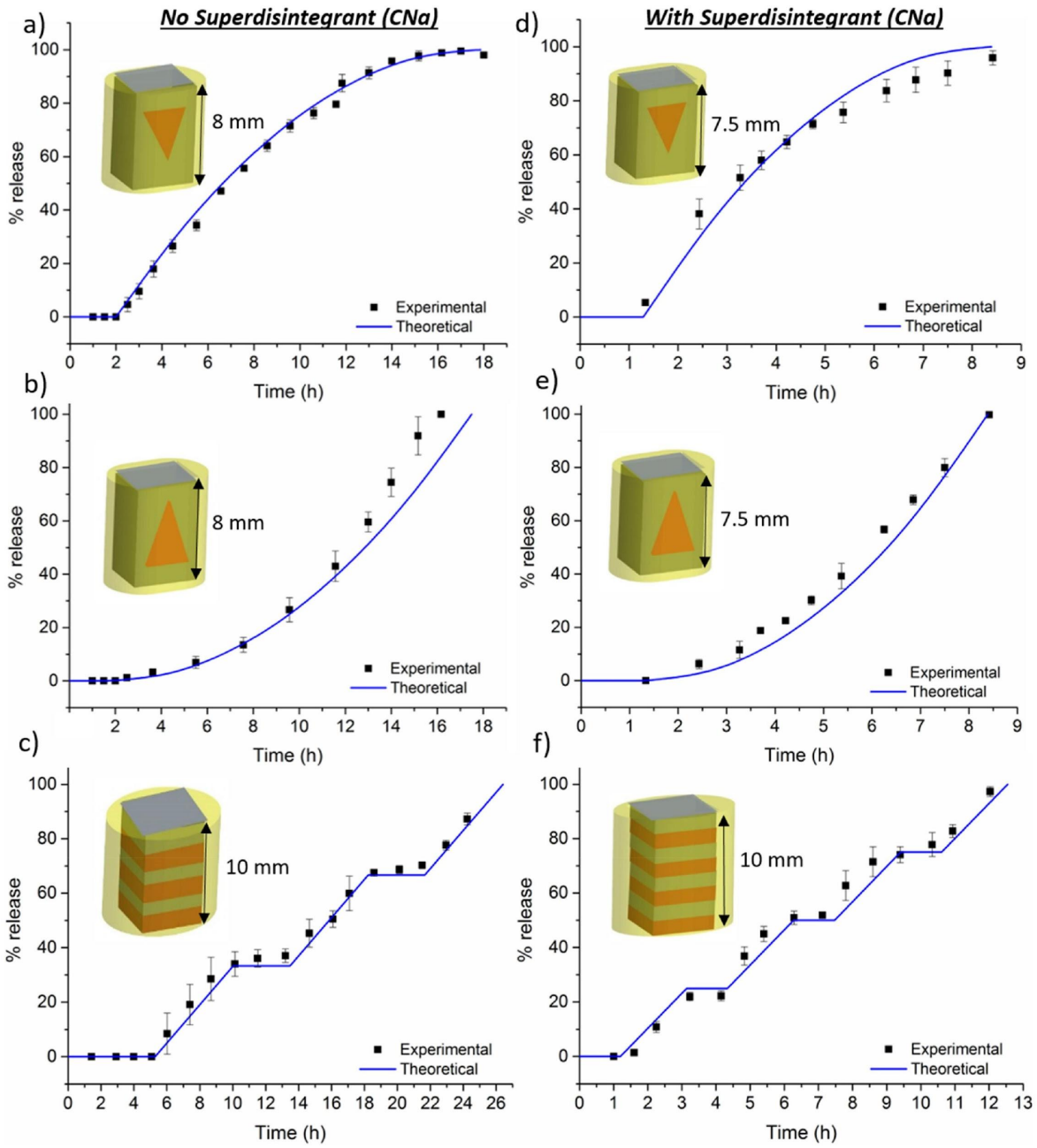
Fully Customizable Duration of Release

Pills

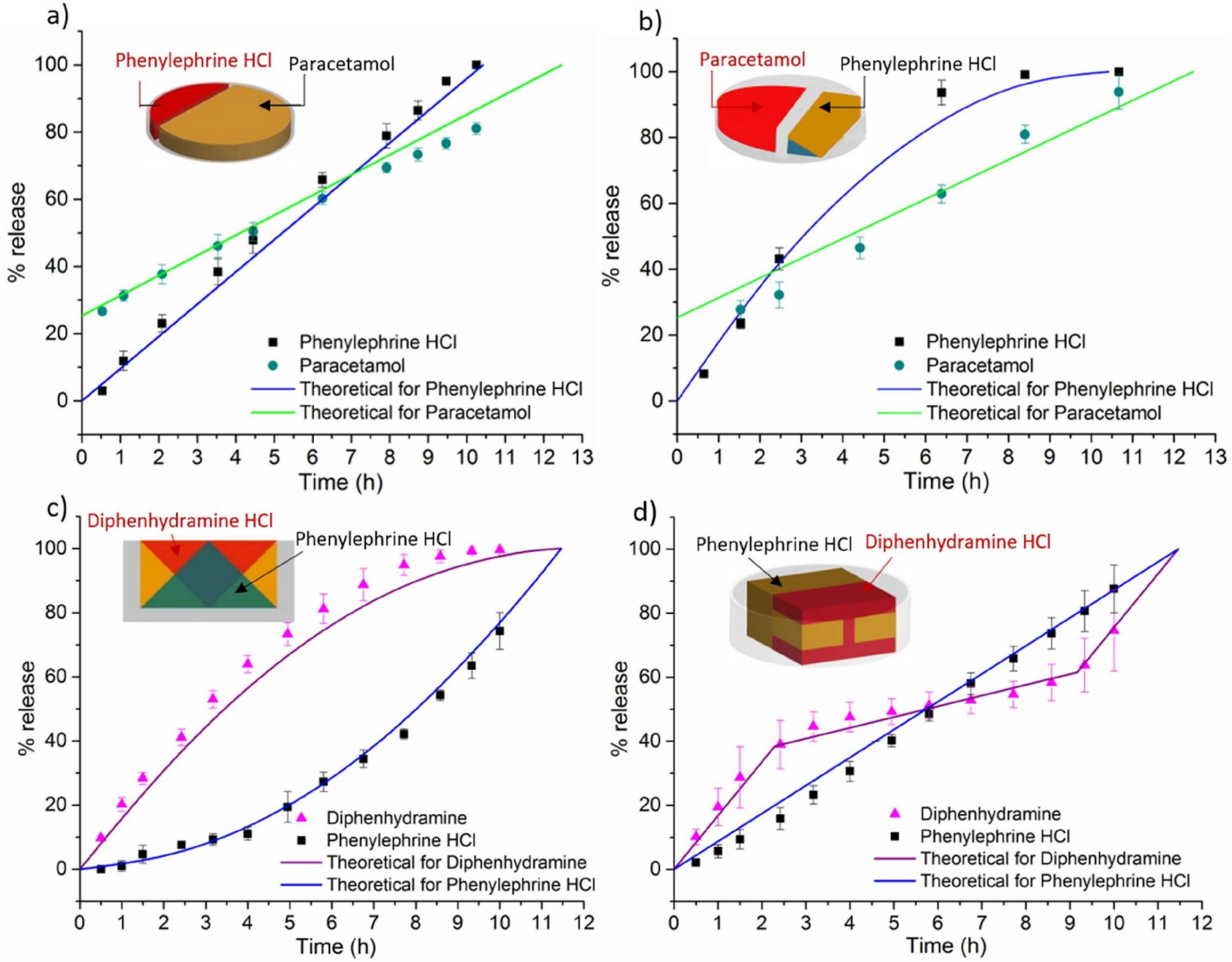


1. Changing the geometry of tablet
2. adding superdisintegrant,
3. tuning the composition of the excipient, or

Long Capsule



Fully Customizable Multi-Drug Tablet



Programmable Fully Customizable Tablet for Personalized Medicine

Fully Customizable tablet

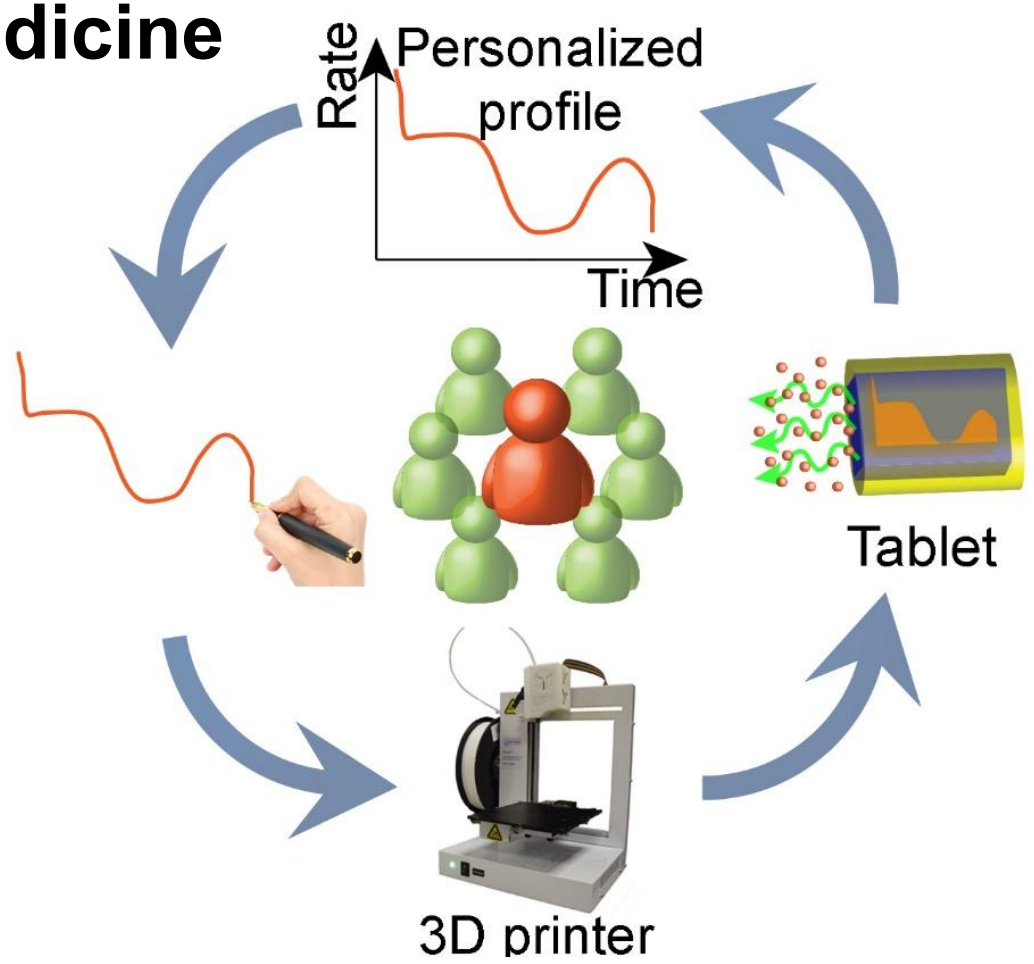
- Customizable dosage
- Customizable duration
- Customizable release profile
- Customizable multi-drug tablet

Advantages

- Low cost: commercially available 3D printers
- Easy to use: shape drawn corresponds directly to release profile

Customization on-the-spot

- Local neighborhood clinics, Hospitals, Drug stores, Automated dispenser



Advanced Materials 2015, *27*, 7847-7853.
Journal of Controlled Release 2020, *322*, 42-52.
International Journal of Pharmaceutics 2021, *598*, 120370. (Invited Article)

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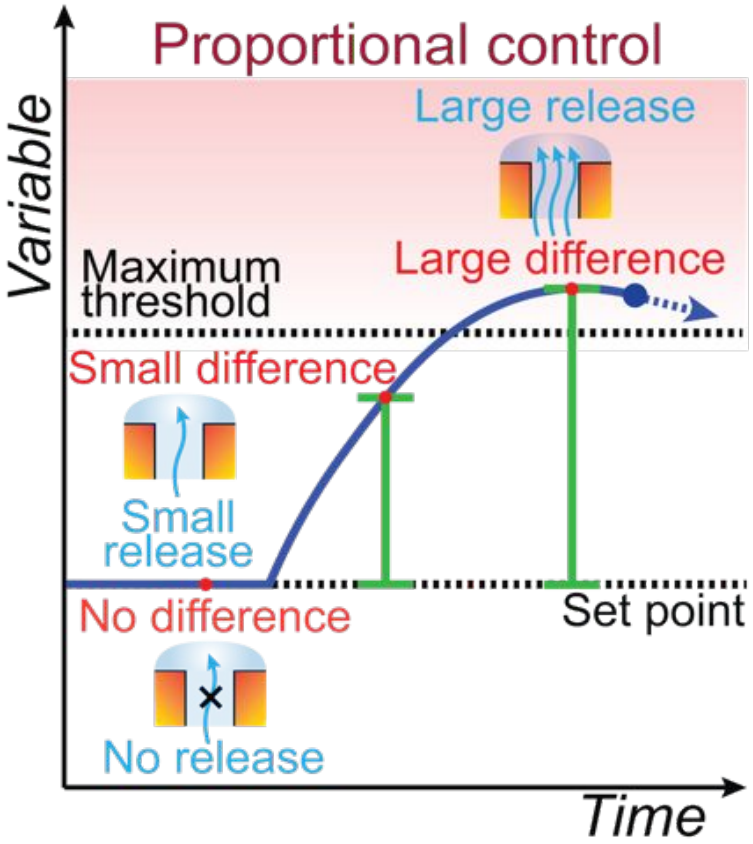
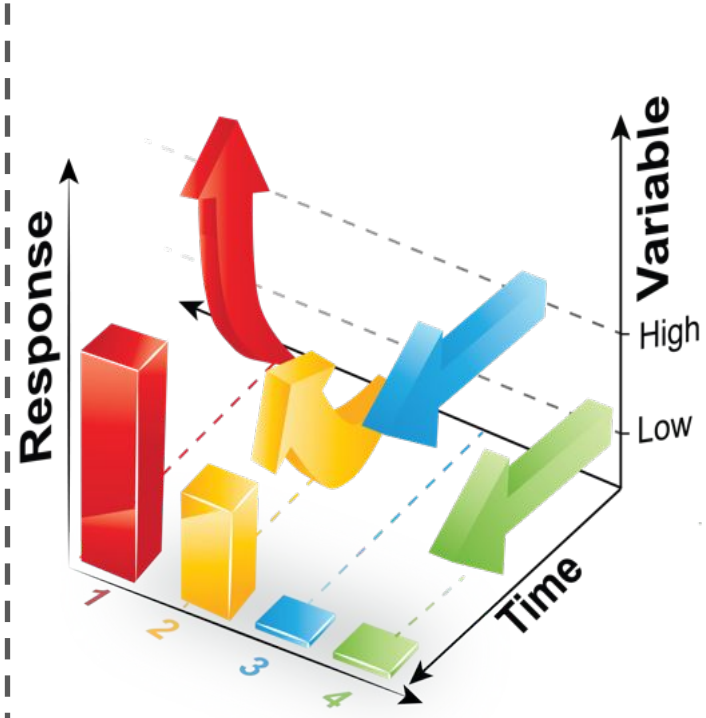
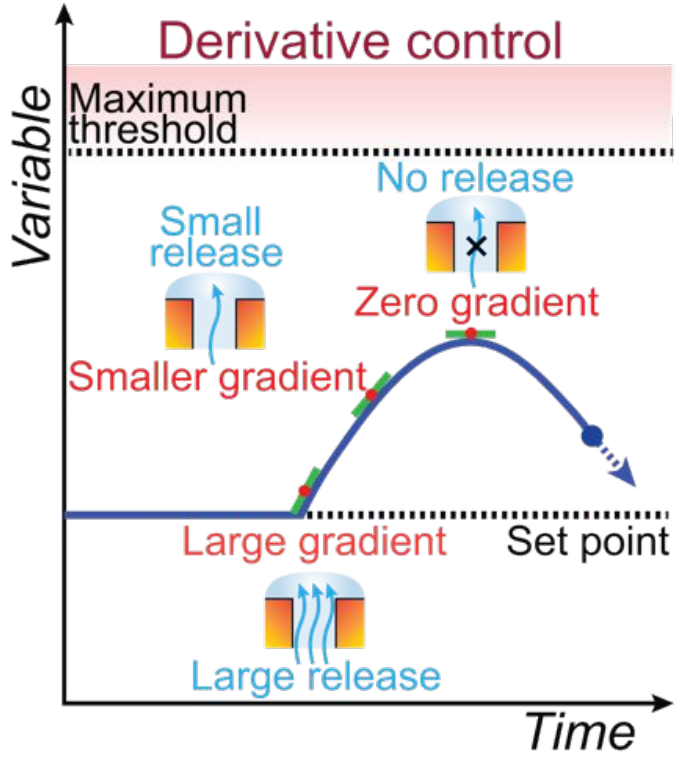
Performing Calculus by Stimuli-Responsive Derivative Controller



Large response only with large difference

Derivative Control





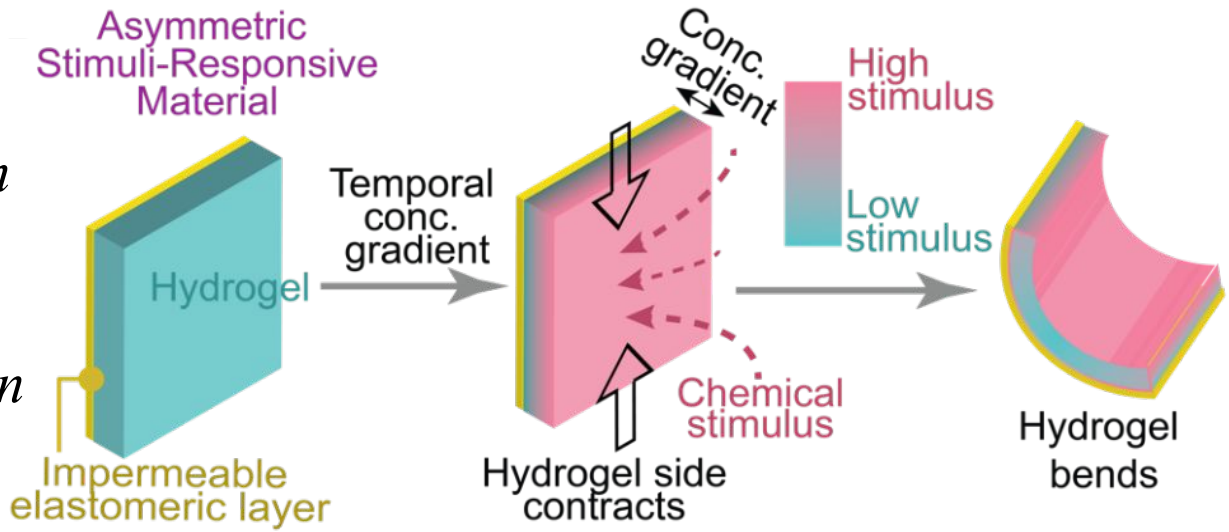
Large response even with small difference

- Derivative has always been performed by computers ...
  - *How do we perform Derivative by simple materials?*

Performing Calculus by Stimuli-Responsive Derivative Controller

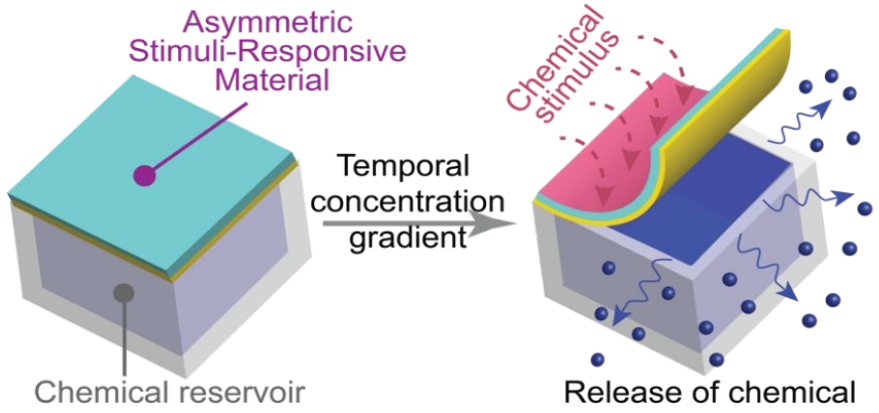
Asymmetric Stimuli-Responsive Polymer

Reaction-diffusion process with one impermeable boundary condition



Rate of bending depends on the derivative of concentration

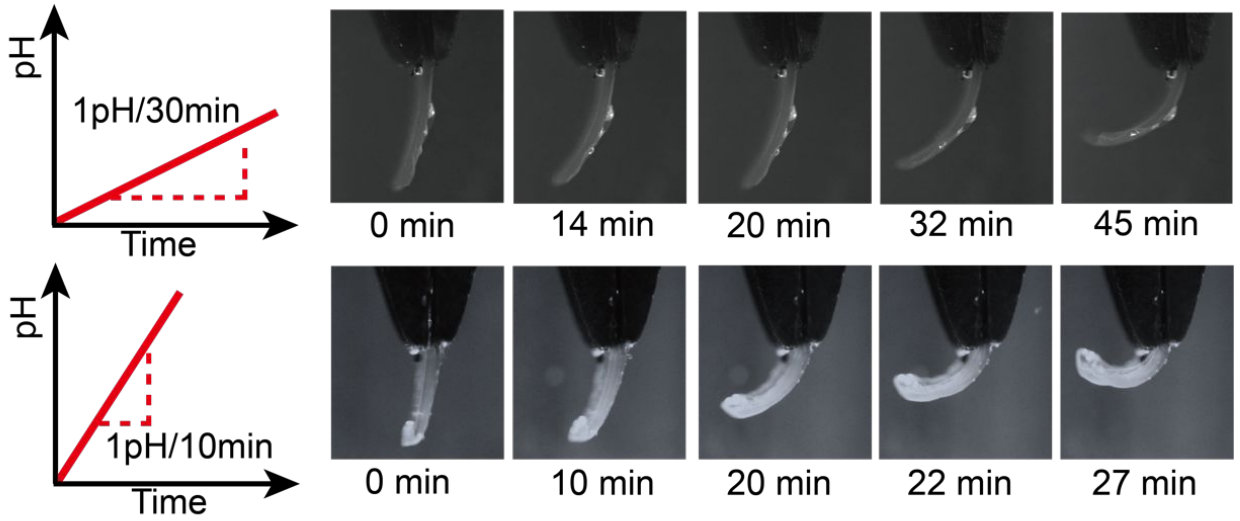
Controller and Self-Regulation based on temporal Derivative



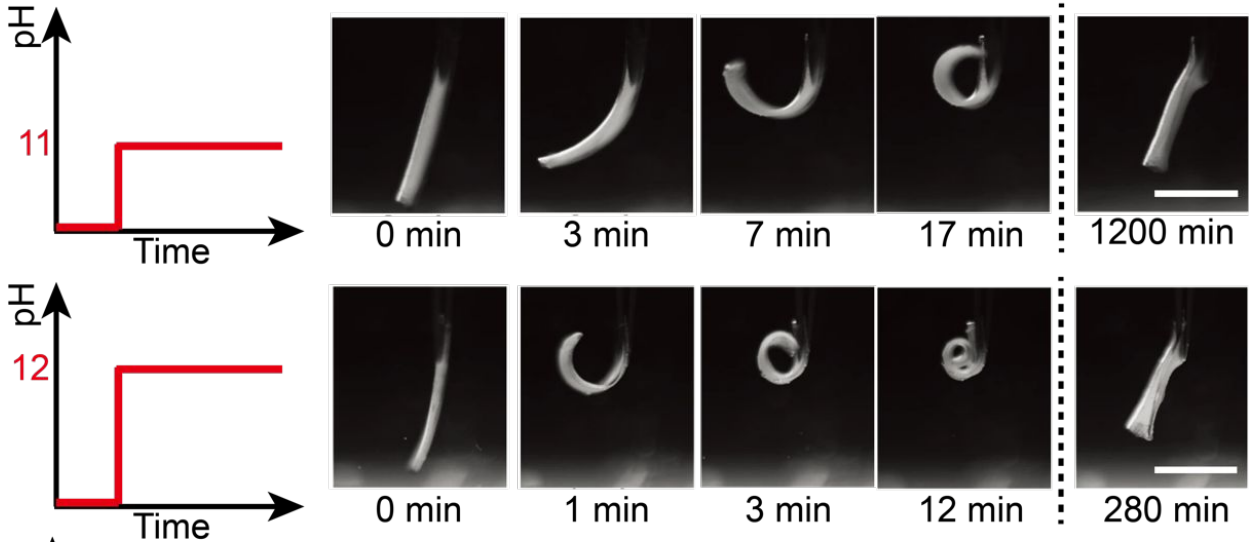
Performing Calculus: Asymmetric Adaptive Stimuli-Responsive Material for Derivative Control.
Science Advances 2021, *7*, eabe5698.

Performing Calculus by Stimuli-Responsive Derivative Sensor

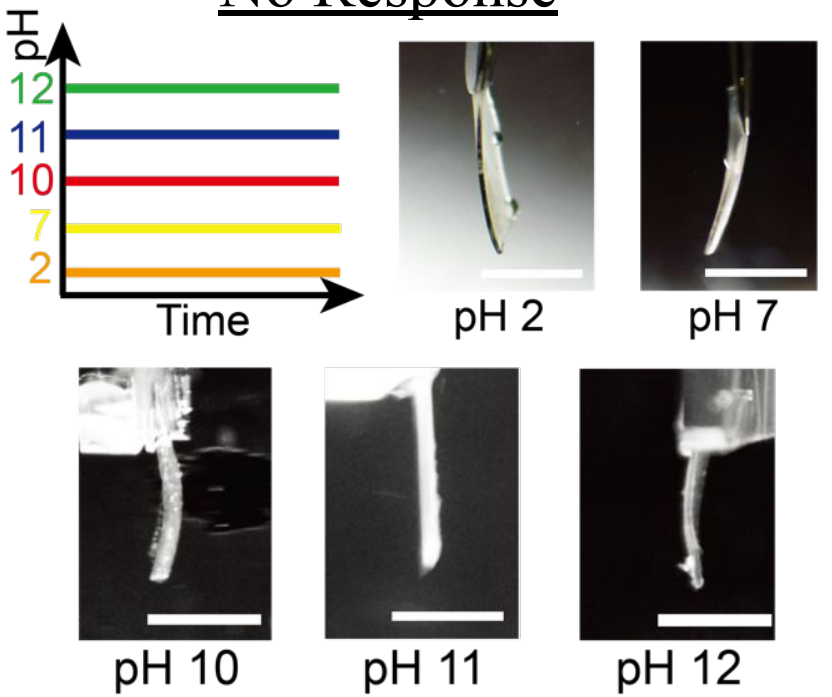
Gradient Response



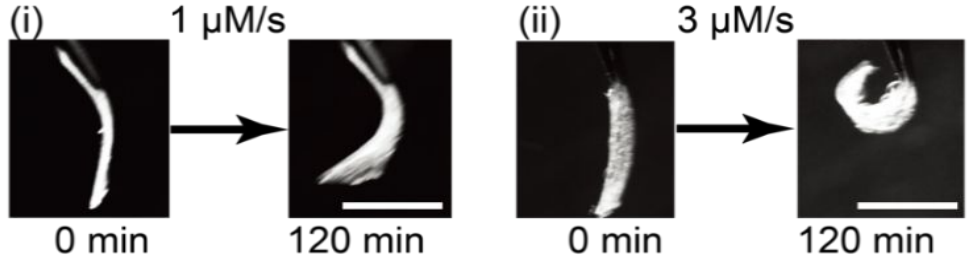
Step Response



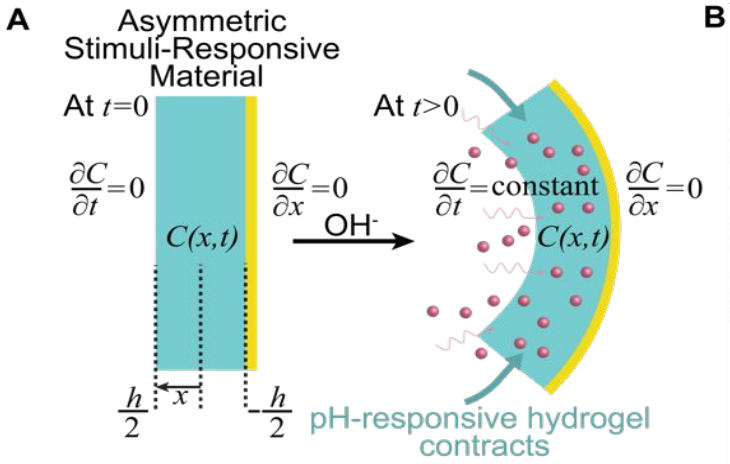
No Response

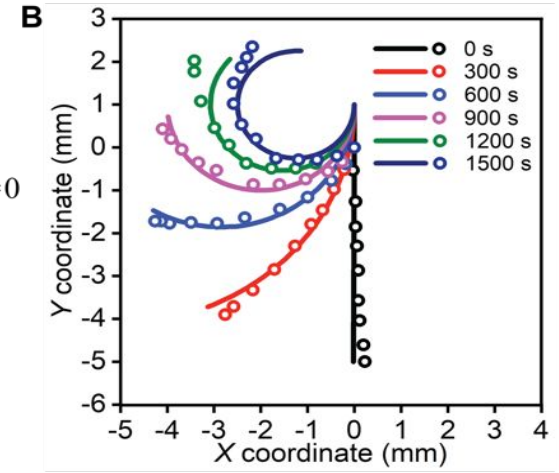


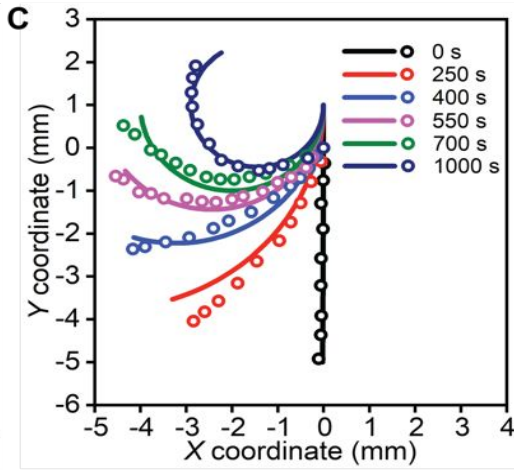
Glucose-responsive polymer

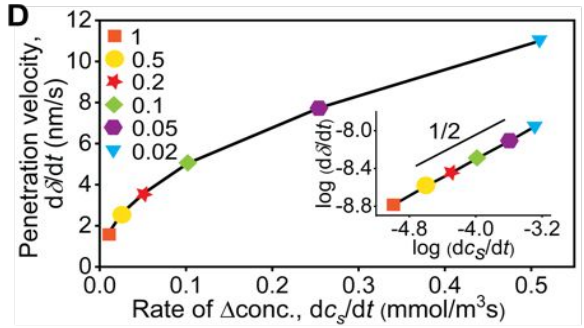


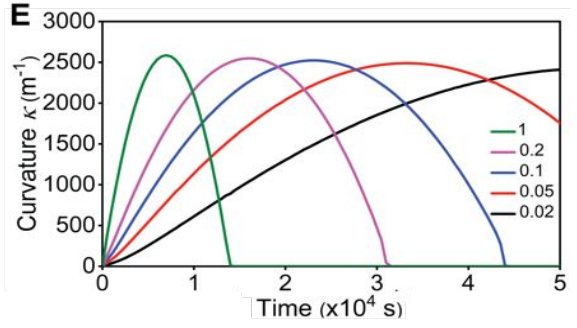
Mathematical Relationship between Rate of Bending and Derivative

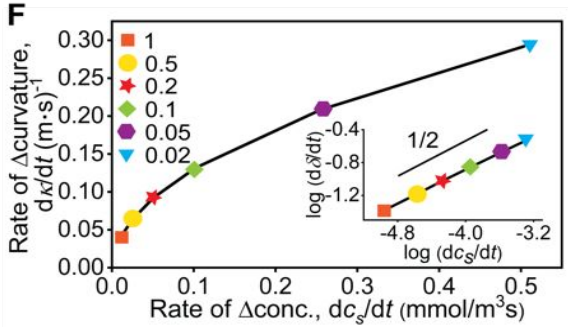












Reaction-Diffusion

$$\frac{\partial c(x,t)}{\partial t} = D\frac{\partial^2 c(x,t)}{\partial x^2} + k_-(s_0 - s(x,t)) - k_+ s(x,t)c(x,t)$$

$$\frac{\partial s(x,t)}{\partial t} = k_-(s_0 - s(x,t)) - k_+ s(x,t)c(x,t)$$

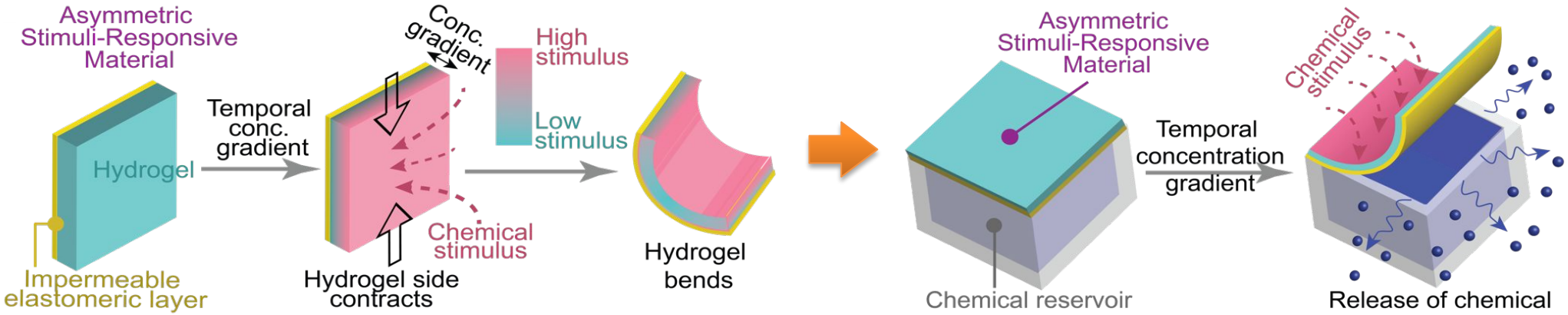
Curvature due to Contractile Strain

$$\kappa(t) = \frac{12\varepsilon_{\max}}{h^3}\int_{-h/2}^{h/2}\left(\frac{x}{1+K/c}\right)dx$$

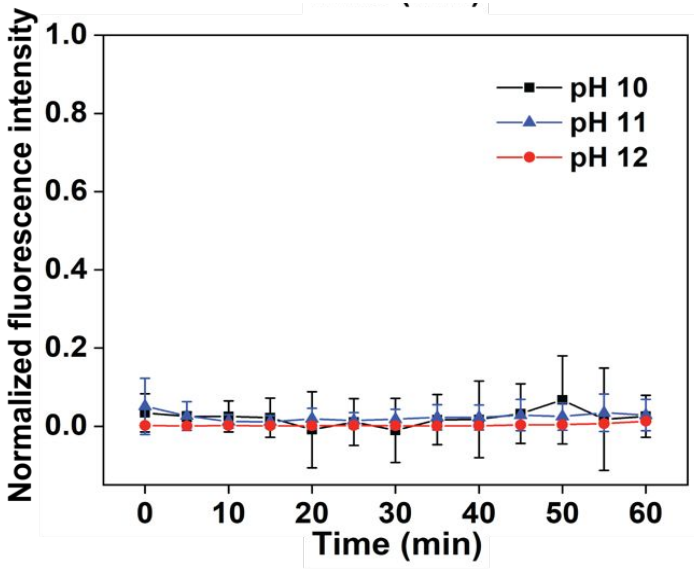
Rate of bending scales with temporal derivative mathematically:

$$d\kappa / dt \sim \sqrt{dc_s / dt}$$

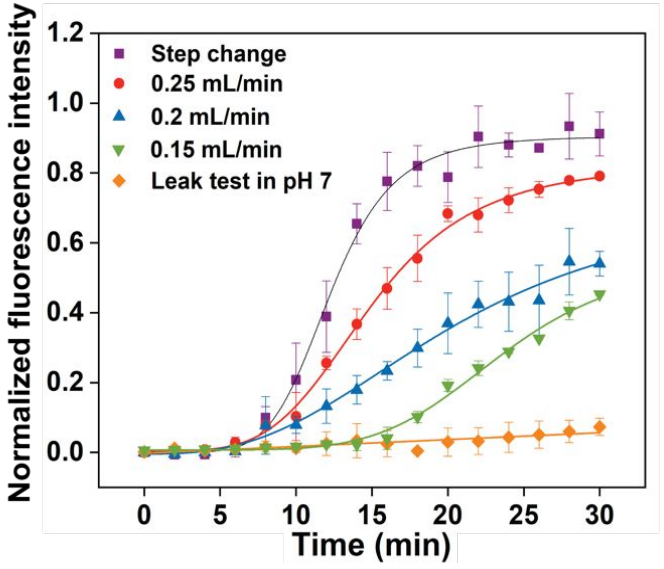
Controlled Release based on Derivative



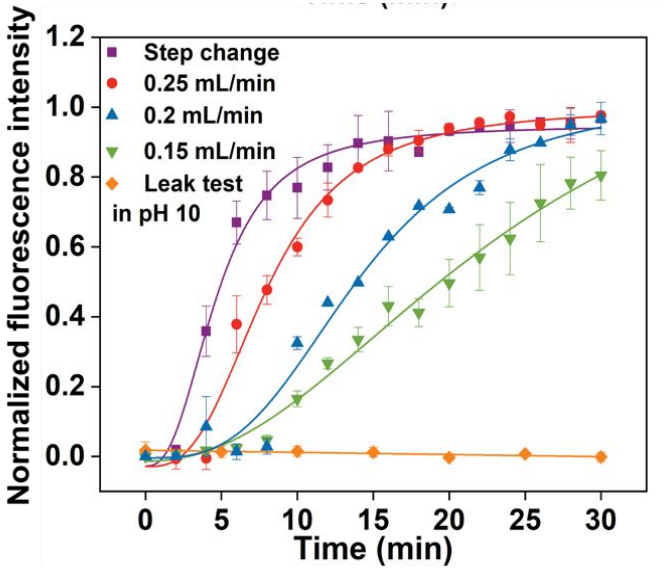
Constant pH



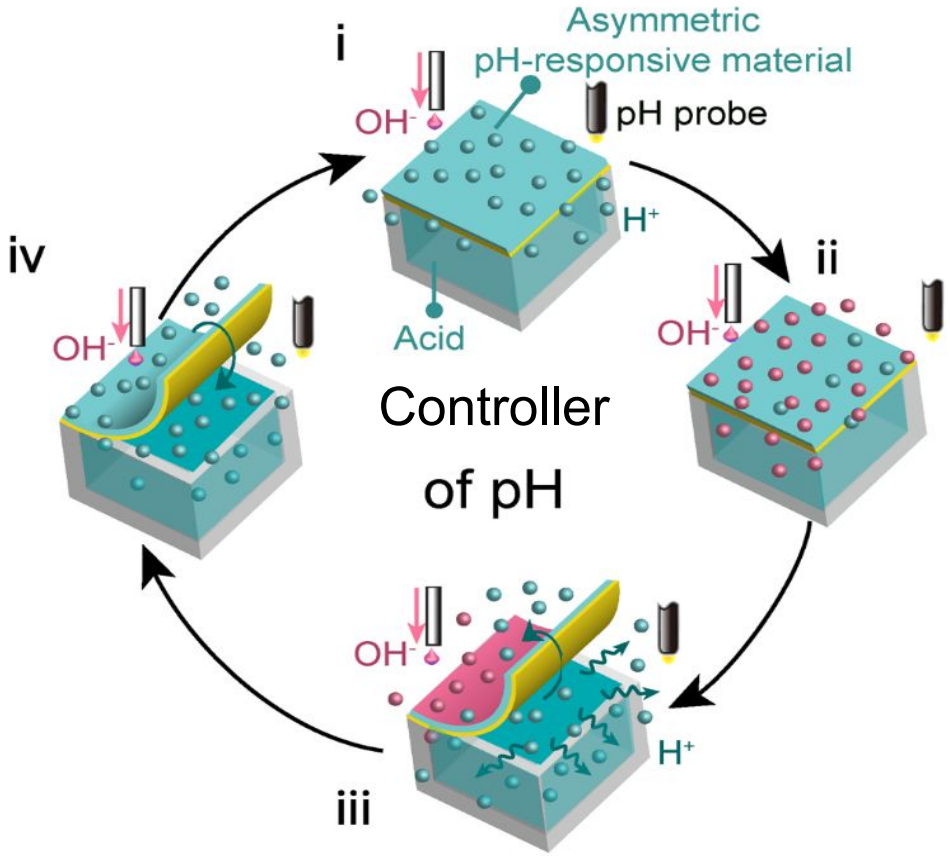
pH 7 to pH 11

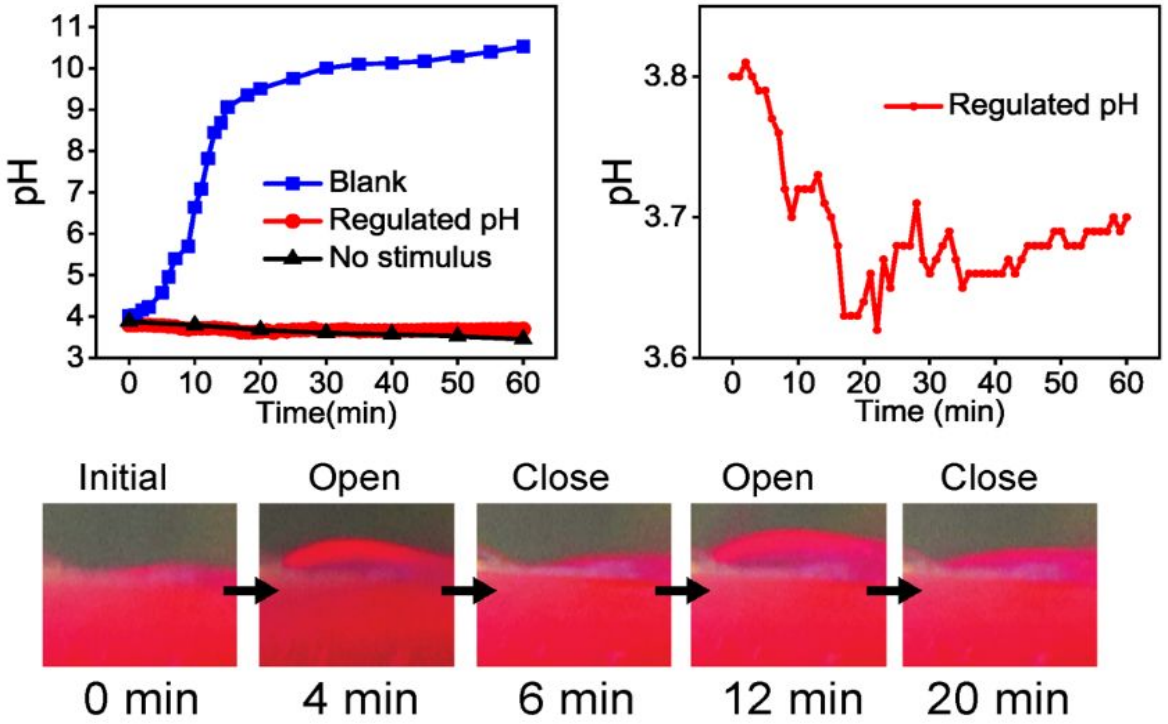


pH 10 to pH 11.48



Full Derivative Controller





- Full controller in a particle:
  - Sensing element
  - Computational ability
  - Actuation
  - Release

- First demonstration that calculus (derivative) can be performed without using a computer.

Science dvances 2021, *7*, eabe5698.

Questions?