Een computer gemaakt van een netwerk van moleculen

Albert Wong
Universiteit Twente



Fuligo Septica

Woudschoten Chemie Conferentie | 6-11-2026

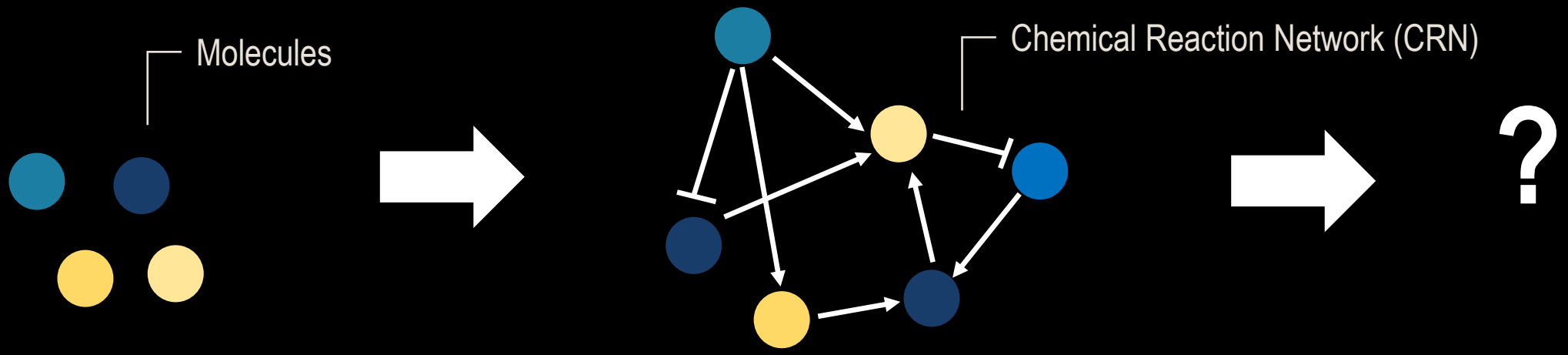
Een computer gemaakt van een netwerk van moleculen

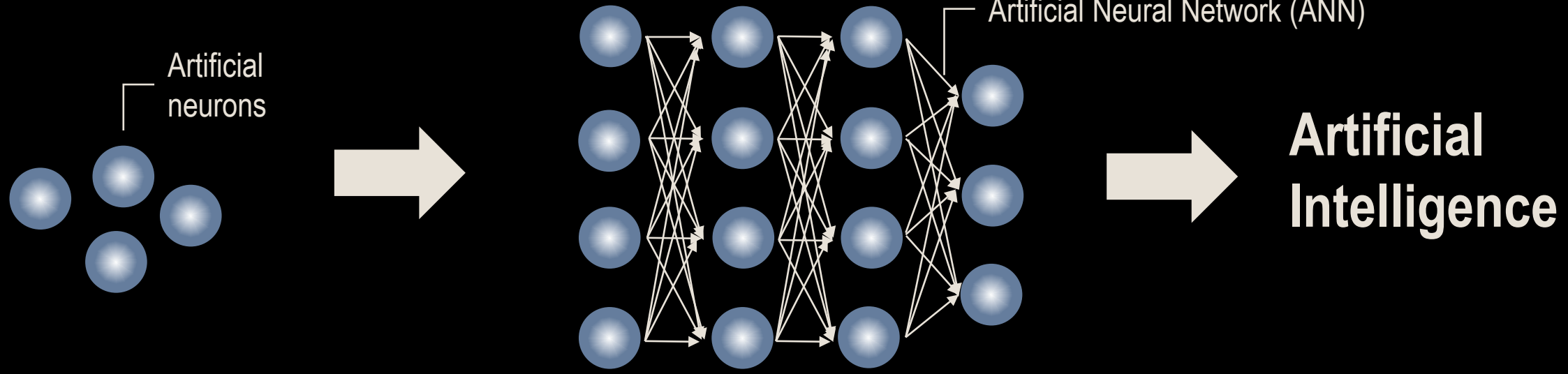
YouTube: Solving shortest path problem with *Physarum plasmodium*





Can a molecule be **intelligent**?





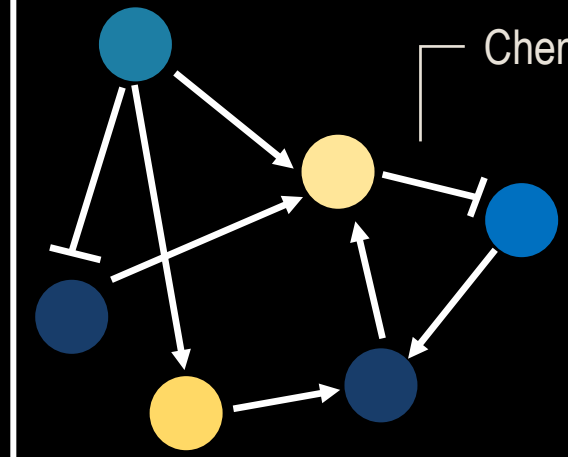
Single units

Collective

Can a molecule be **intelligent**?

Molecules

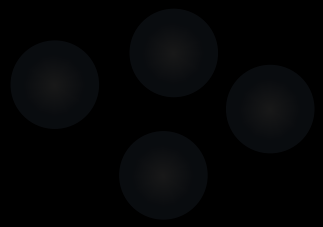




?

How can a CRN become intelligent?

Artificial neurons



Single units

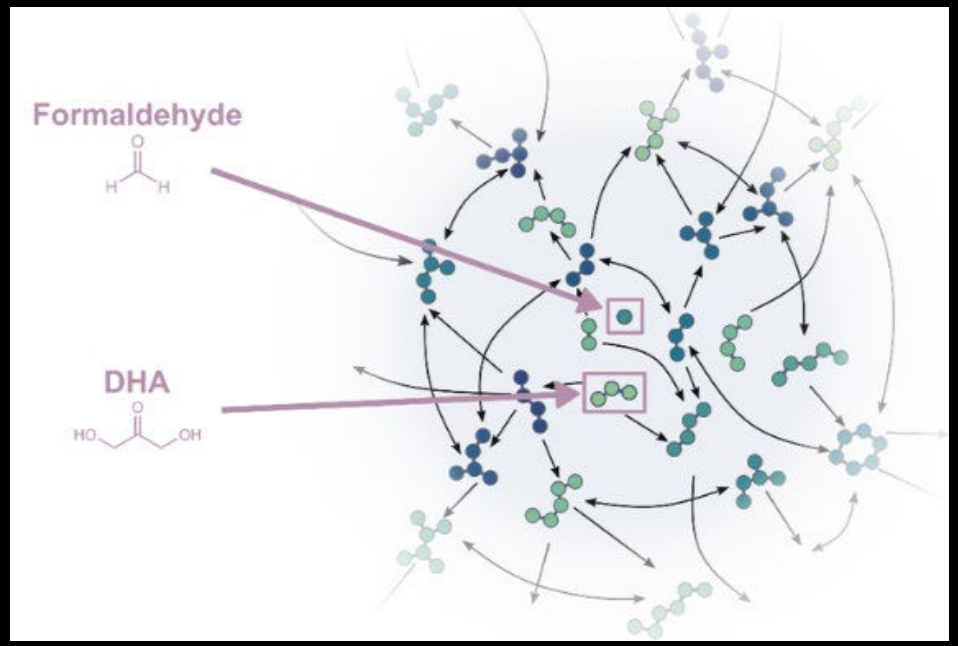


Collective

Artificial Intelligence

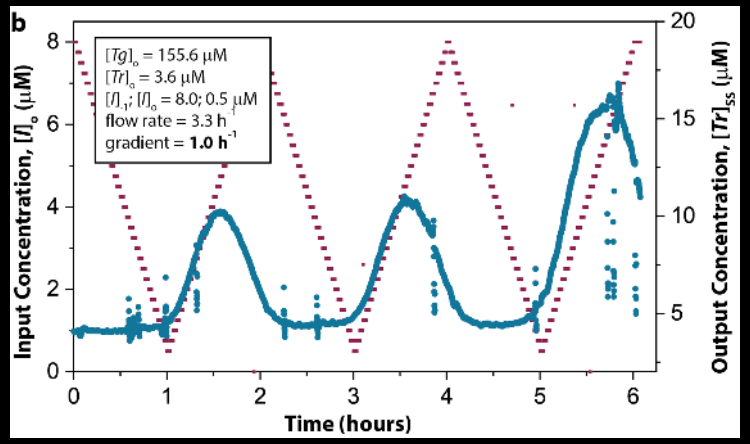
State of the art: CRNs that compute, through…

… emergent behaviors



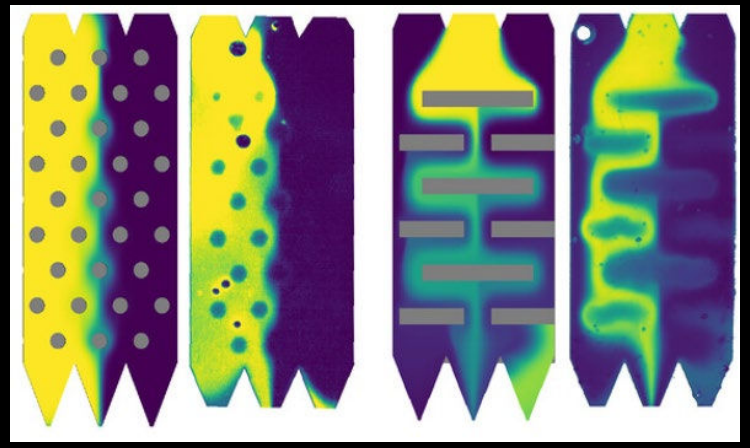
Huck-lab: *Nature* **2024**; *Nat. Chem.* **2025**
Cronin-lab: *Nat. Commun.* **2024**

… history-dependency



Wong-lab: *Nat. Commun* **2024**;
Prins-lab: *JACS* **2024**

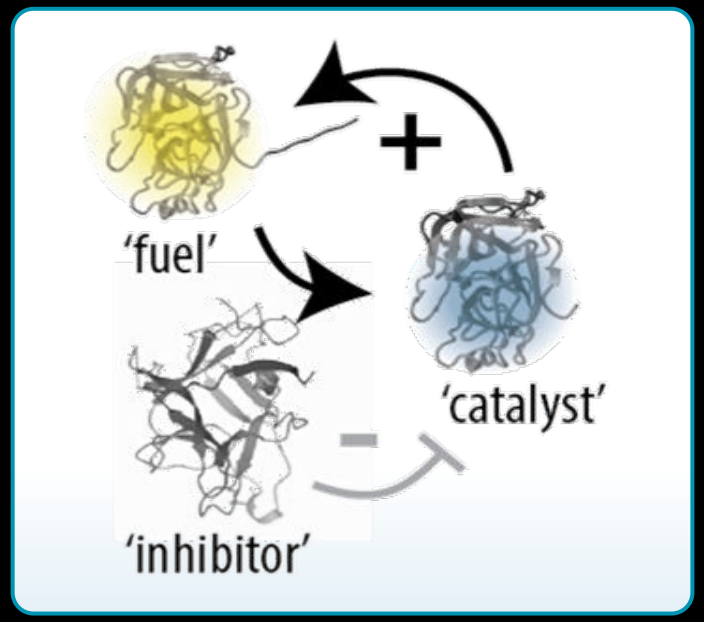
… spatially-organized feedback



Walther-lab: *Adv. Mater* **2026**

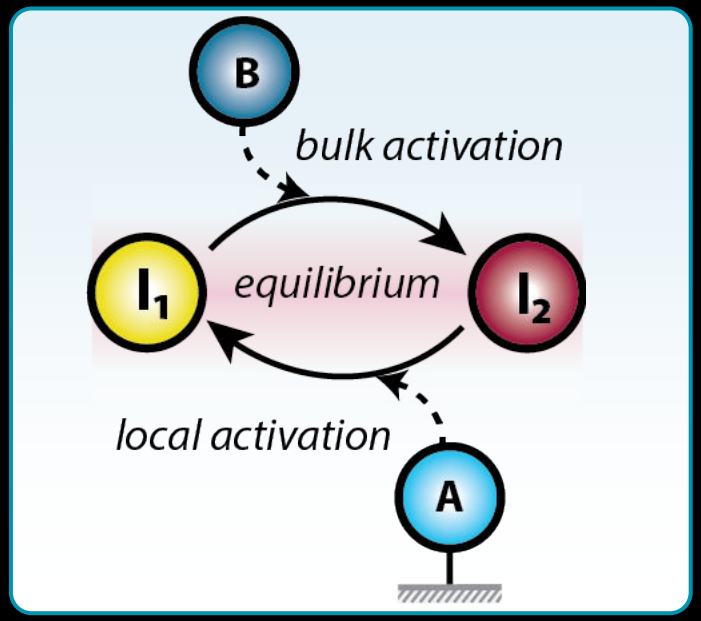
Our approach: Investigate how CRNs can …

… be programmed



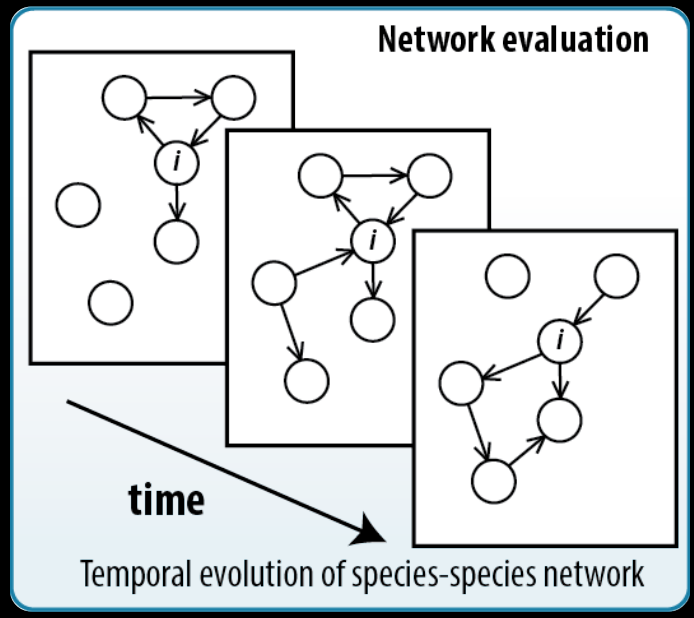
D. Kriukov *Small* **2022**;
D. Kriukov *Nat. Commun.* **2024**

… process information



H. Koyunçu *ChemSysChem* **2023**
Tyumina, A. & Vasylkiv, I. *JACS* **2026**

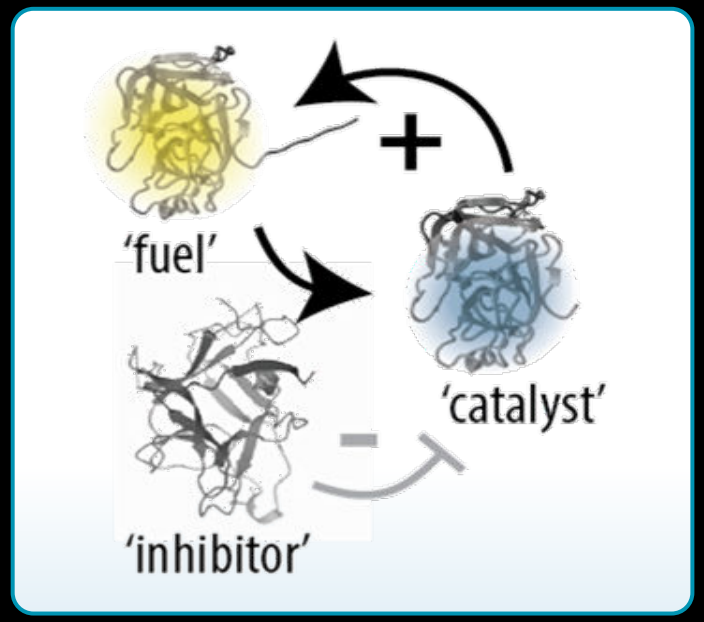
… create emergent functions



E. Da Cunha & Y. Kraakman *Chem. Sci.* **2025**

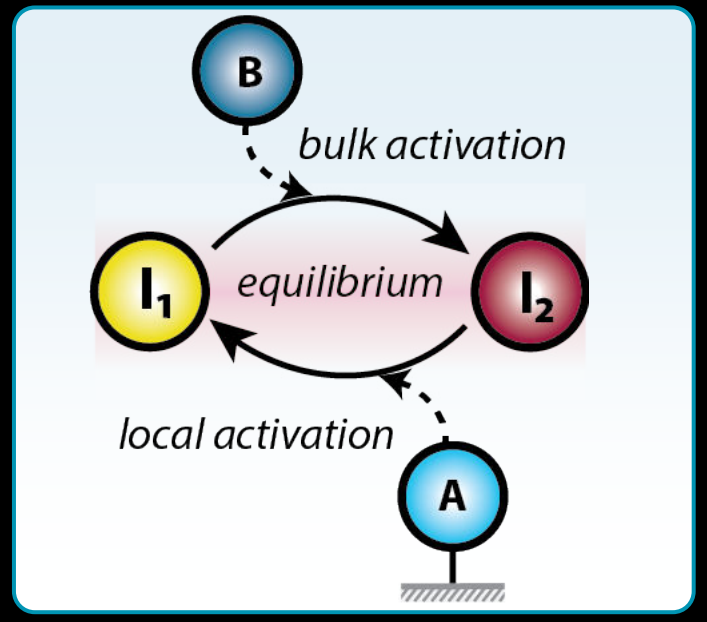
Our approach: Investigate how CRNs can …

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D. Kriukov *Small* **2022**;
D. Kriukov *Nat. Commun.* **2024**

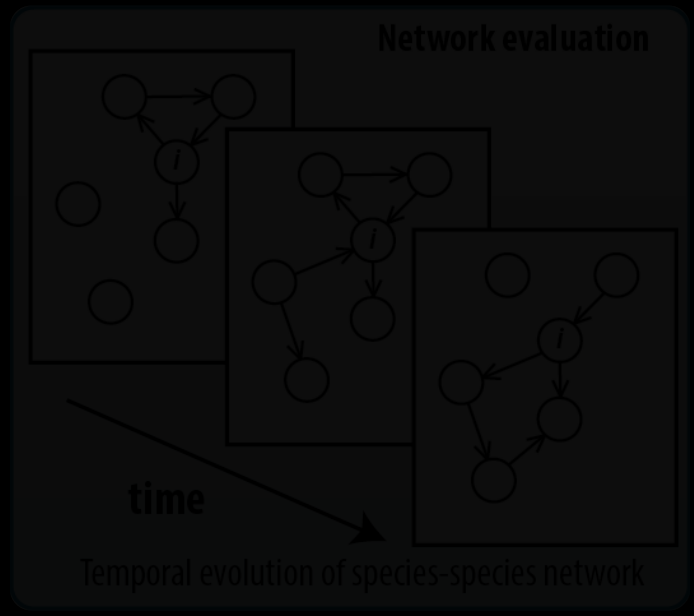
… process information



H. Koyunçu *ChemSysChem* **2023**
Tyumina, A. & Vasylkiv, I. *JACS* **2026**

Today's topic

… create emergent functions



E. Da Cunha & Y. Kraakman *Chem. Sci.* **2025**

How can you contribute!?

Dus, waar gaan we het vandaag allemaal over hebben?

Dus, waar gaan we het vandaag allemaal over hebben?

Inleiding

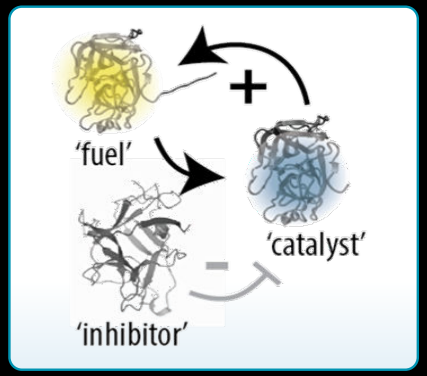


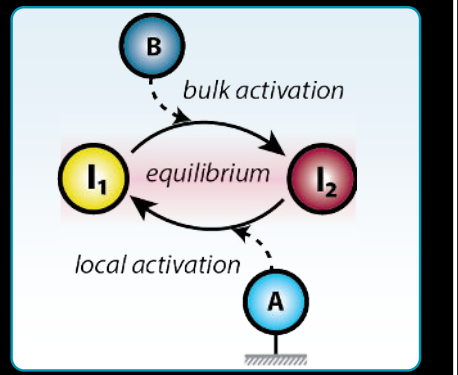
?

Focus:

Rekenen zonder brein

Kern





?

Focus:

Rekenen met chemische netwerken

Dus, waar gaan we het vandaag allemaal over hebben?

Inleiding

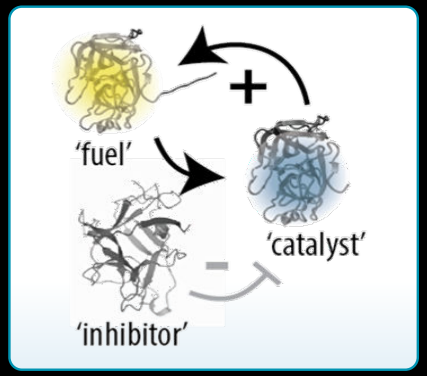


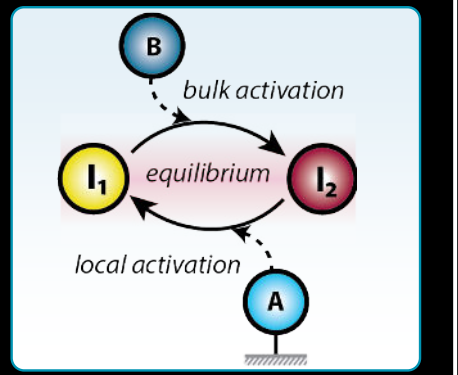
?

Focus:

Rekenen zonder brein

Kern





?

Focus:

Rekenen met chemische netwerken

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NWO

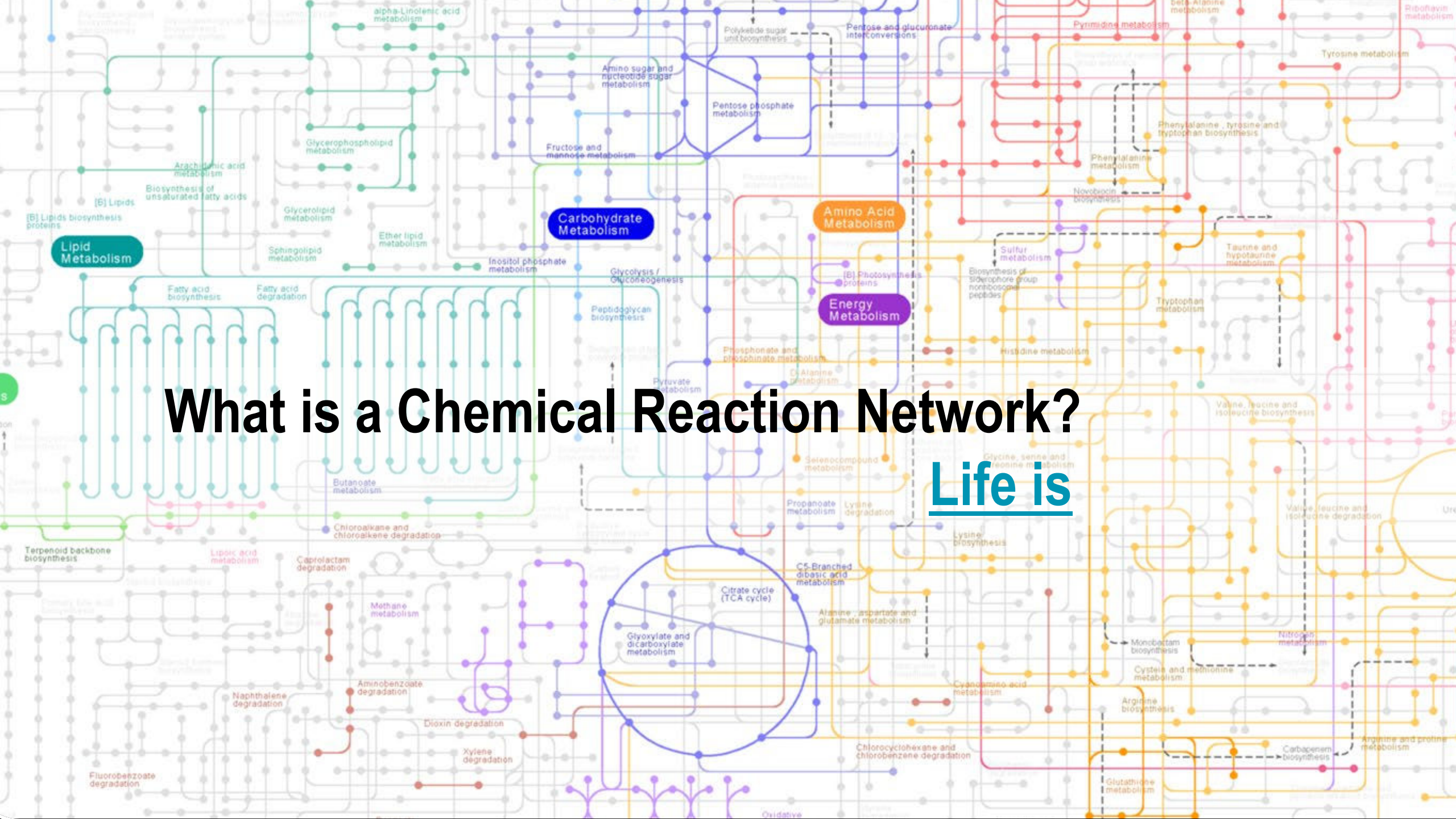
wetsus

ChemistryNL



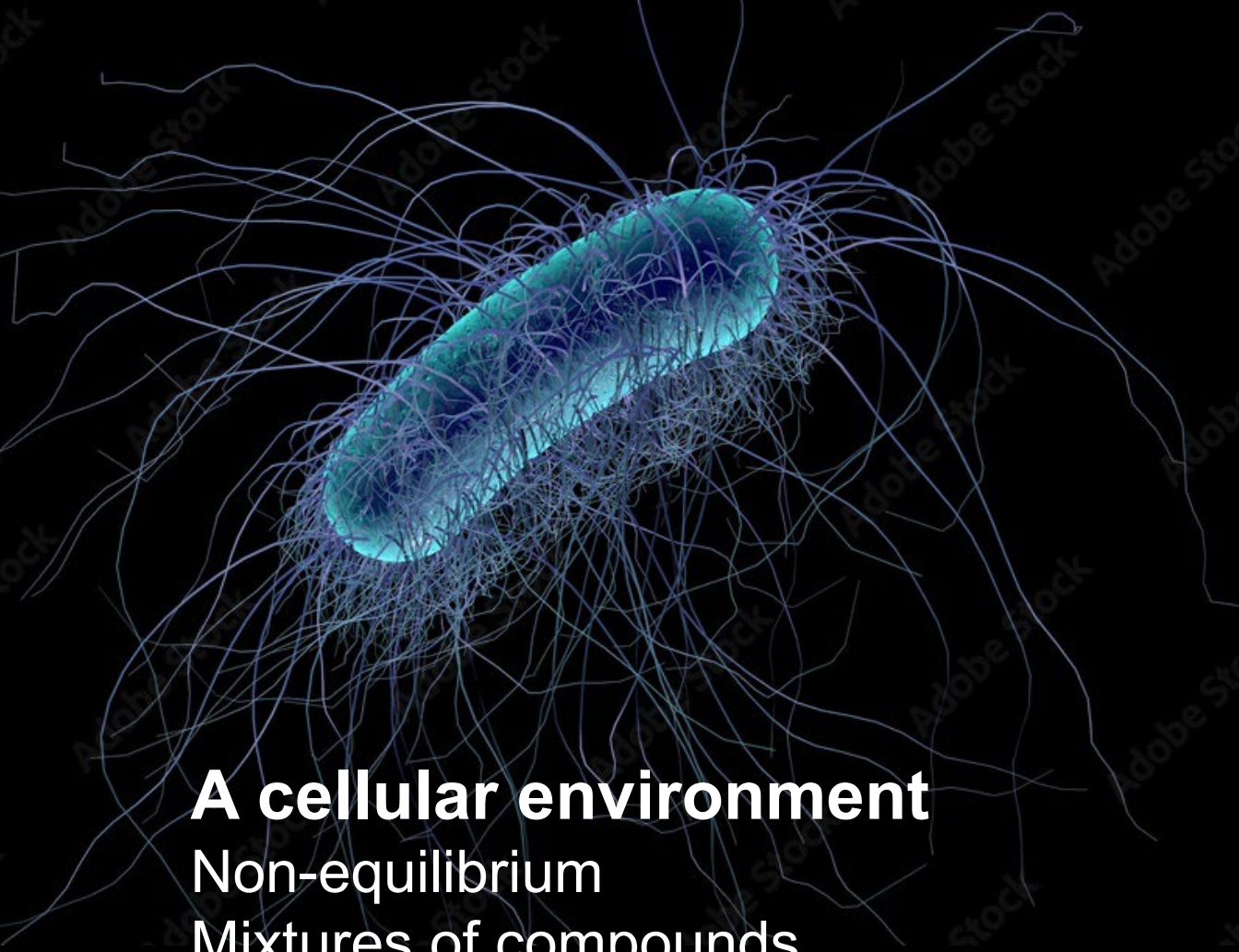
NRO NATIONAAL REGIEORGAAN ONDERWIJSONDERZOEK

What is a Chemical Reaction Network?



What is a Chemical Reaction Network?

Life is



A cellular environment

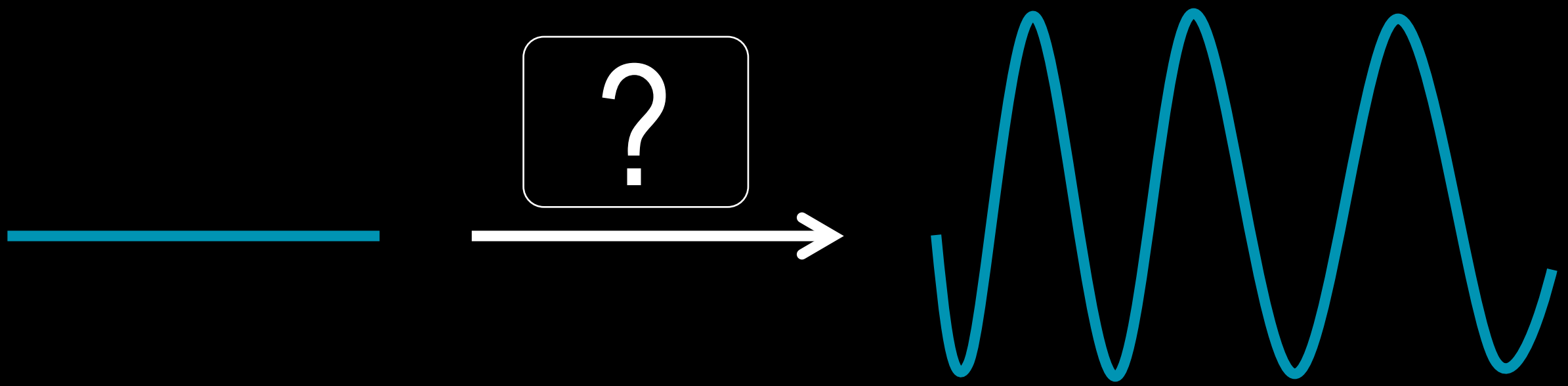
Non-equilibrium
Mixtures of compounds
Networks of reactions
Heterogeneous (but with spatio-temporal precision)
…

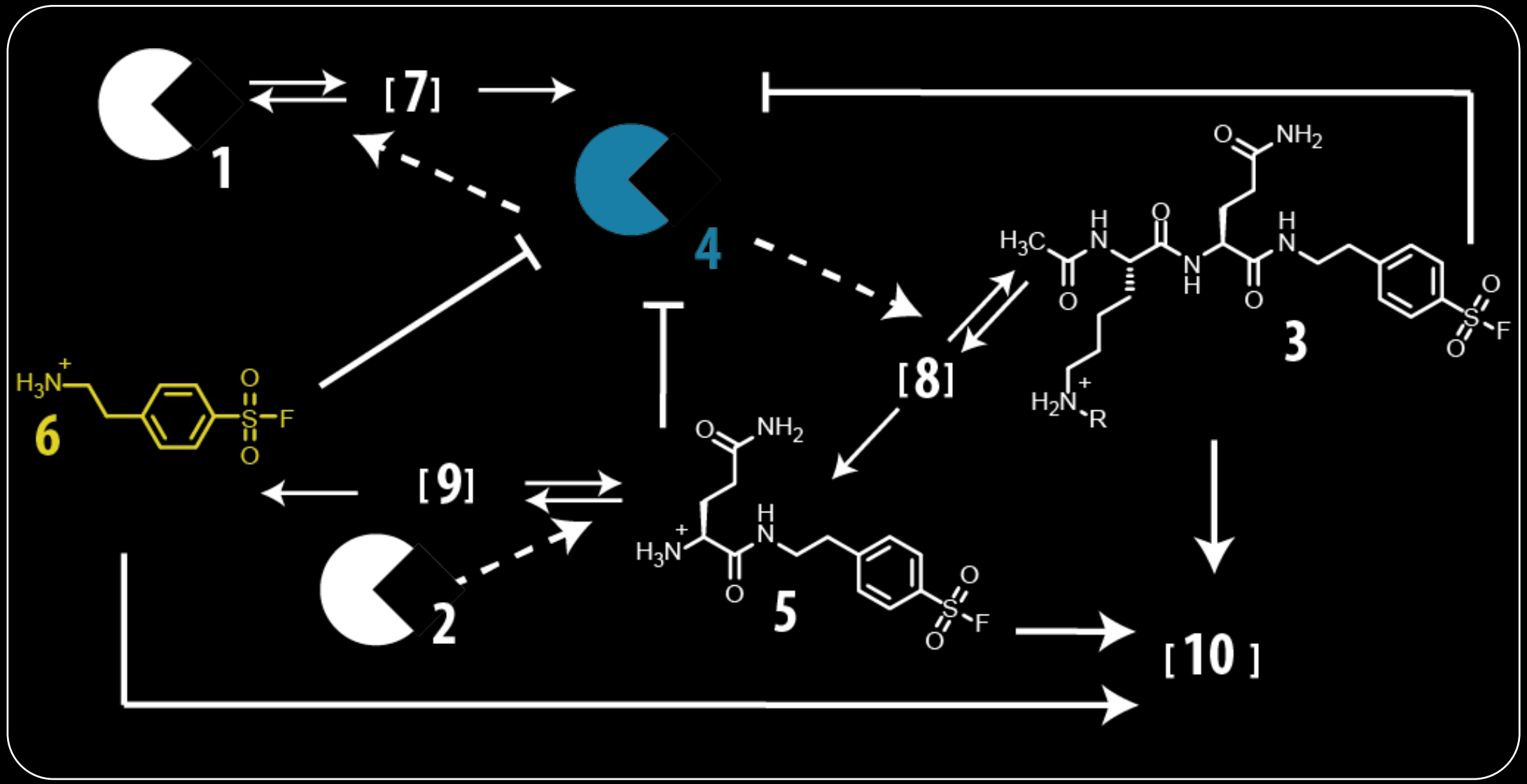
Laboratory conditions

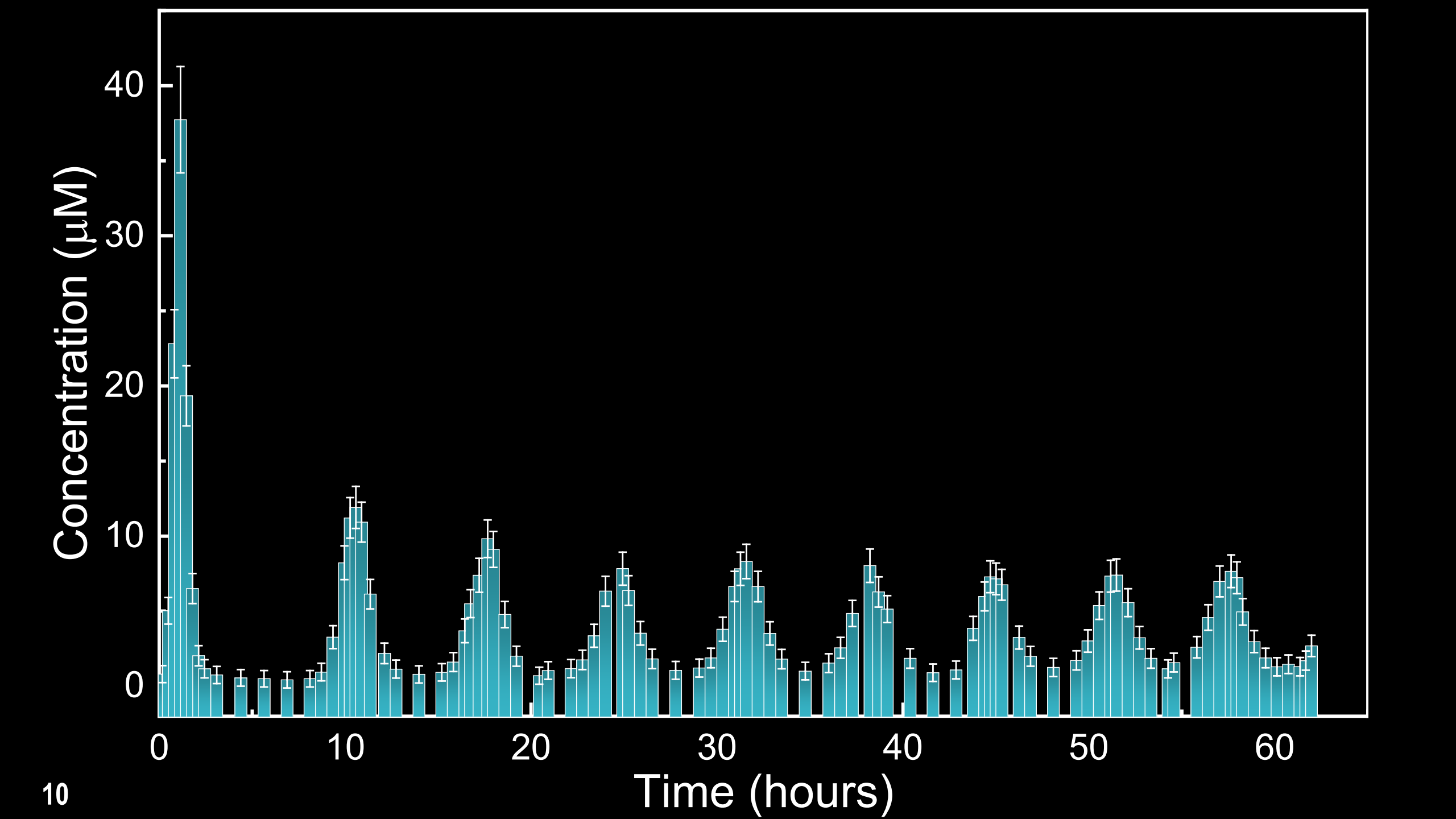
Equilibrium
Purified compounds
Reactions in isolation
Homogeneous (stirring)
…

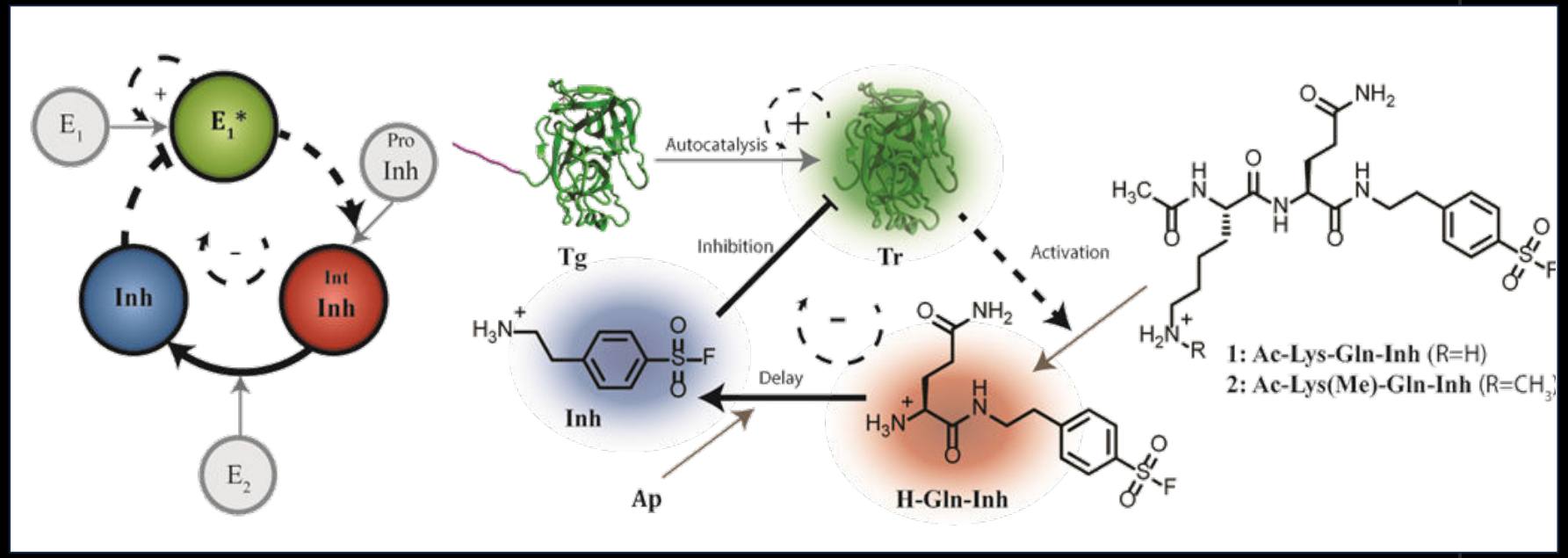







[7]
1
4
[8]
3
6
[9]
2
5
[10]

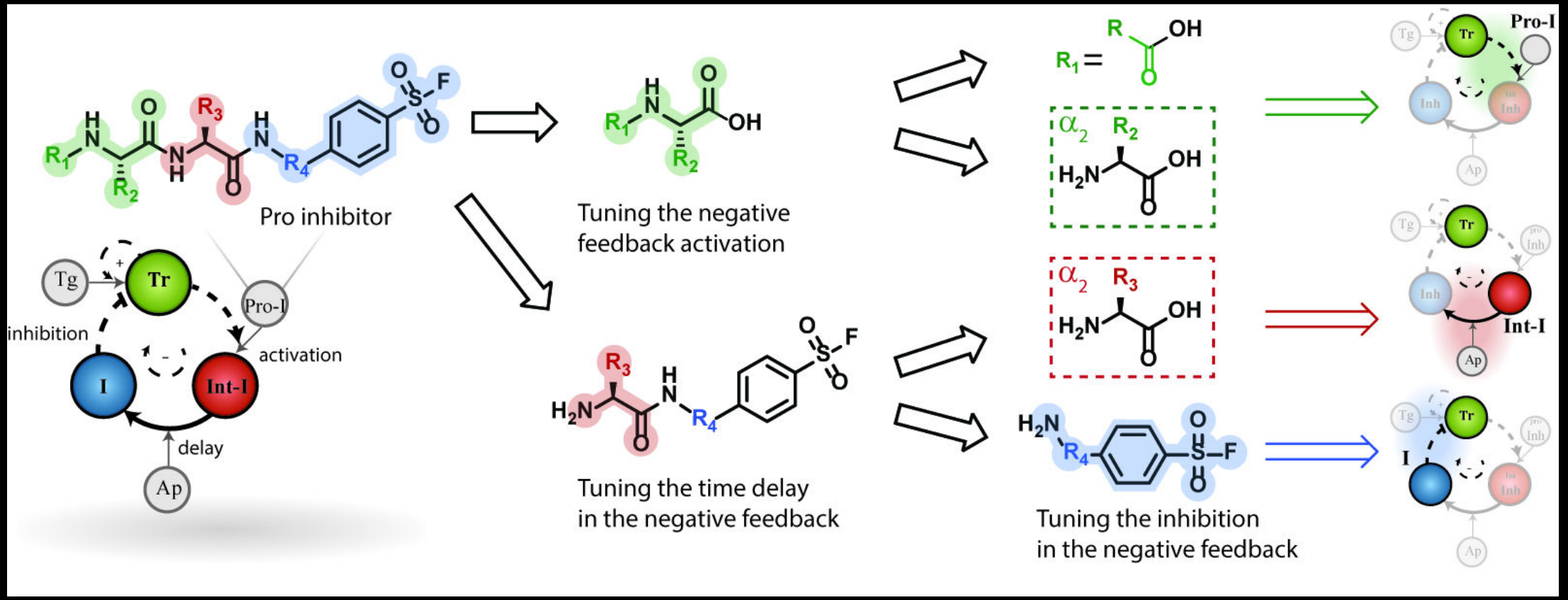

Concentration (µM)
0
10
20
30
40
0
10
20
30
40
50
60
Time (hours)



S. N. Semenov & **A. S. Y. Wong** *et al. Nat. Chem.* **2015**
A. S. Y. Wong *et al. J. Am. Chem. Soc.* **2015**
A. S. Y. Wong *et al. J. Am. Chem. Soc.* **2017**

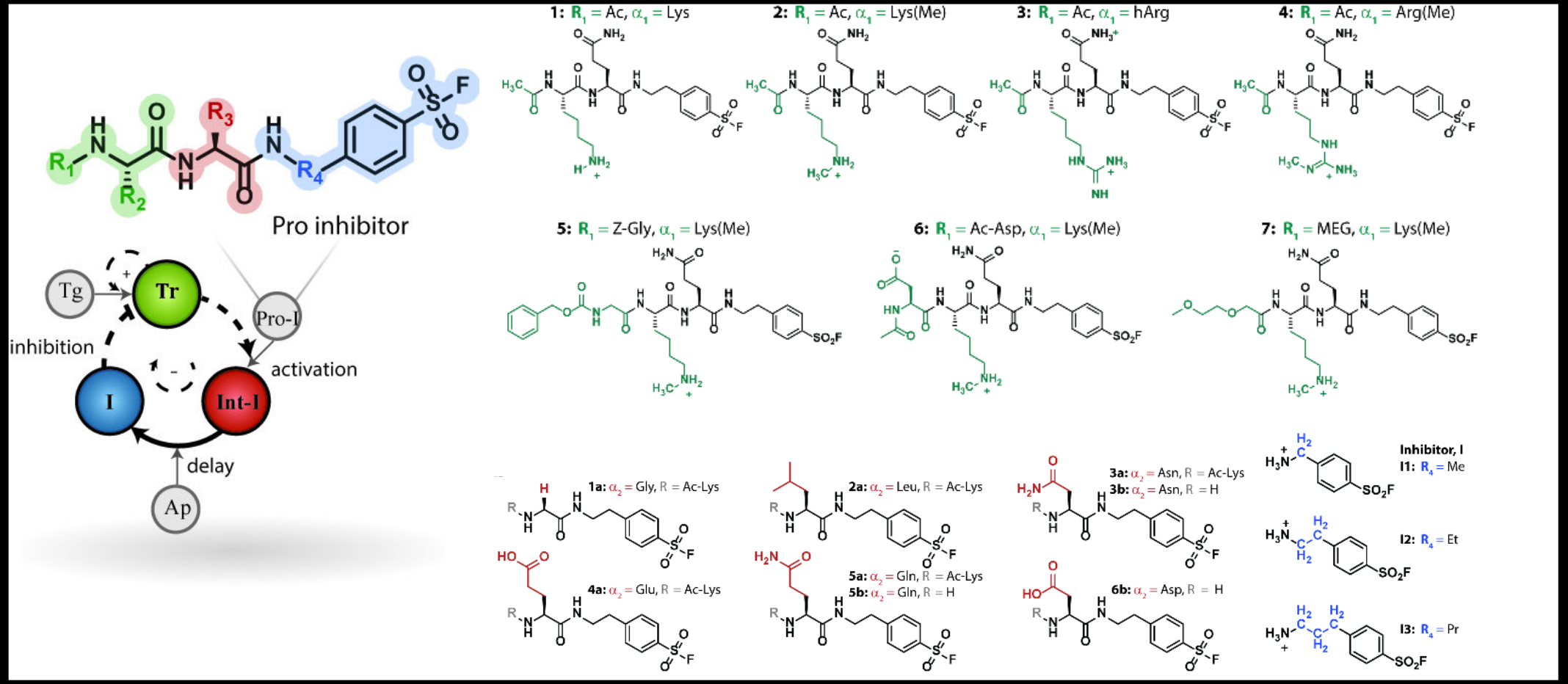
Exploit organic synthesis in designing feedback loops

Use retrosynthesis



Exploit organic synthesis in designing feedback loops

Use retrosynthesis



Oscillerend gedrag alleen mogelijk, indien

1. Er geen evenwicht optreedt
2. Netwerken gevormd

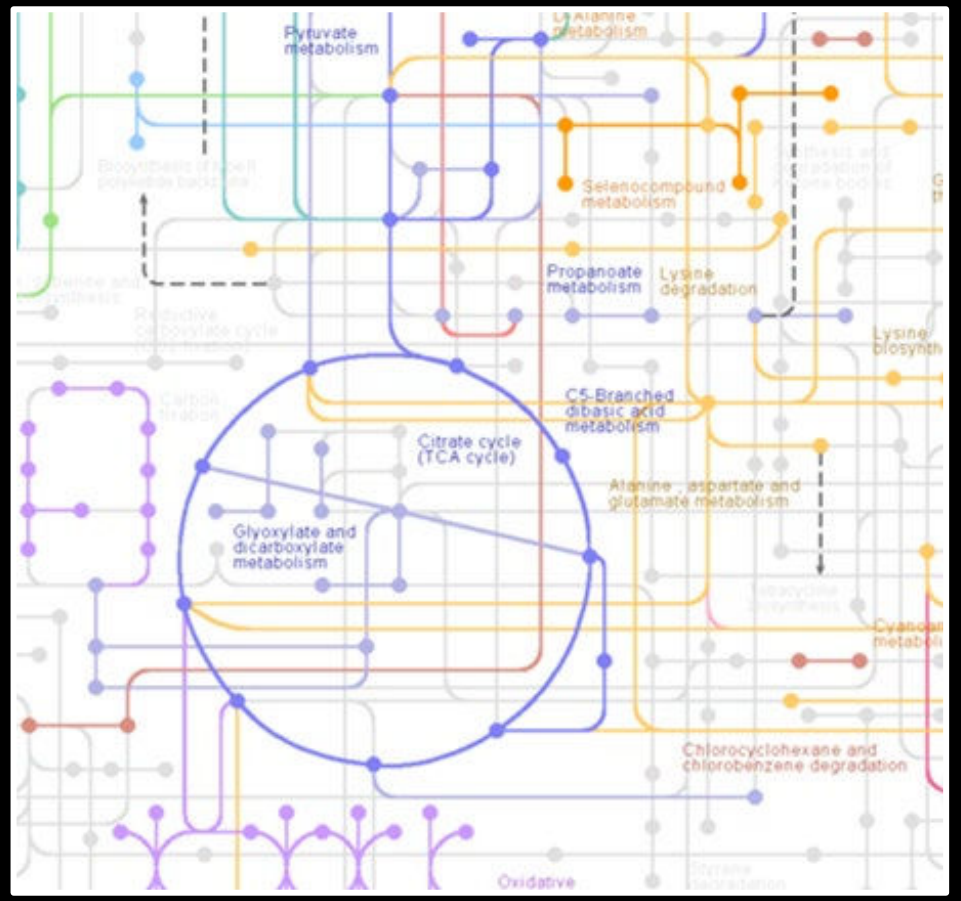
Continue vorming en afbraak is essentieel!



vimeo: Europe 24 (2014)

De nieuwe chemie heet “systeem chemie”

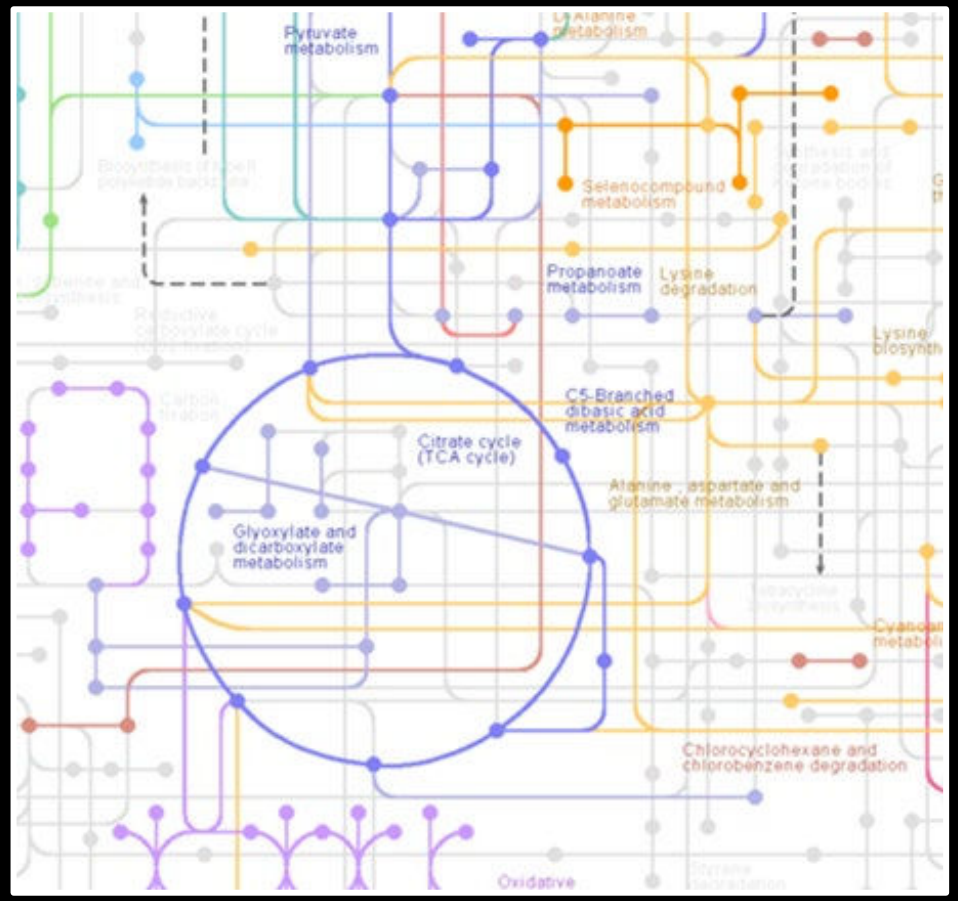




Geen evenwichten, netwerken, continue flow, heterogeen, …

De nieuwe chemie heet “systeem chemie”





De vraag is echter: welke regels gelden er dan?

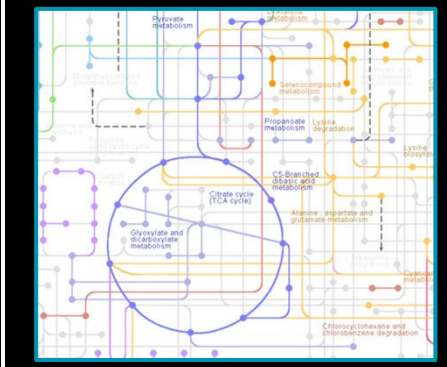
Inleiding



Focus:

Rekenen zonder brein

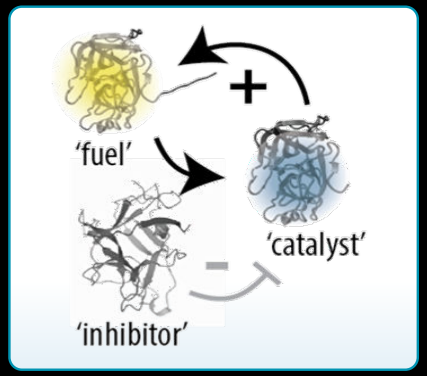
Kern 1

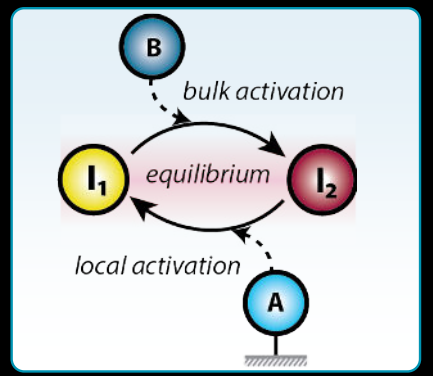


Focus:

Systeem chemie

Kern 2





Focus:

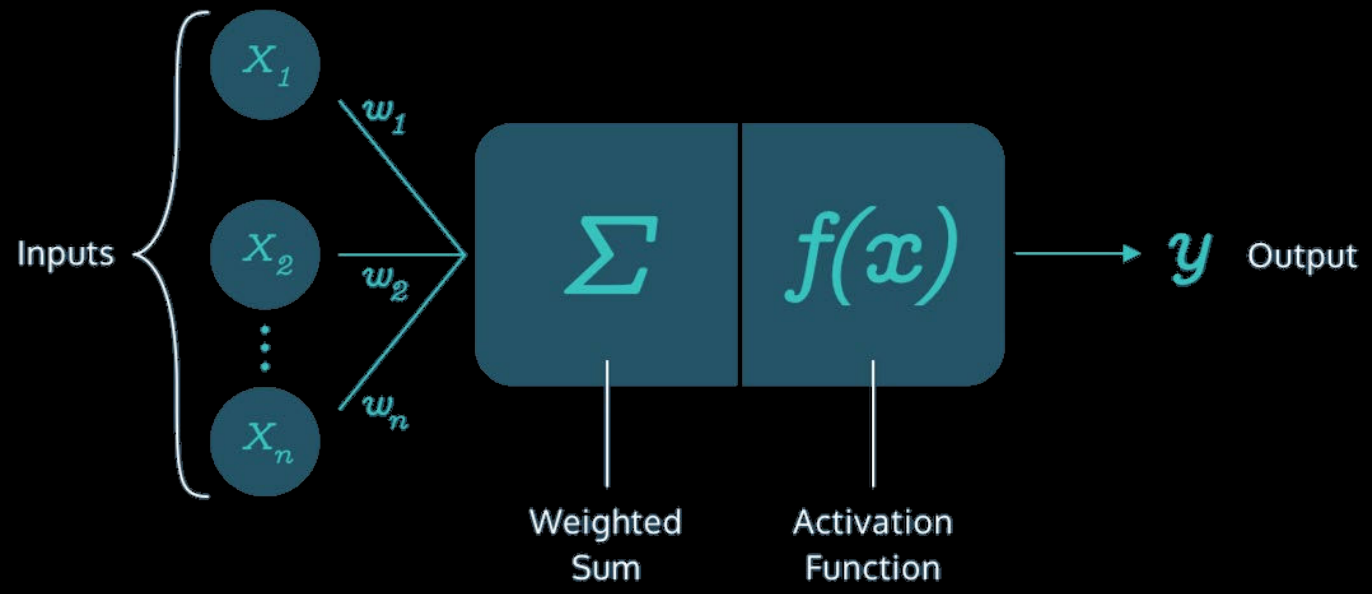
Rekenen met chemische netwerken

Kern 3

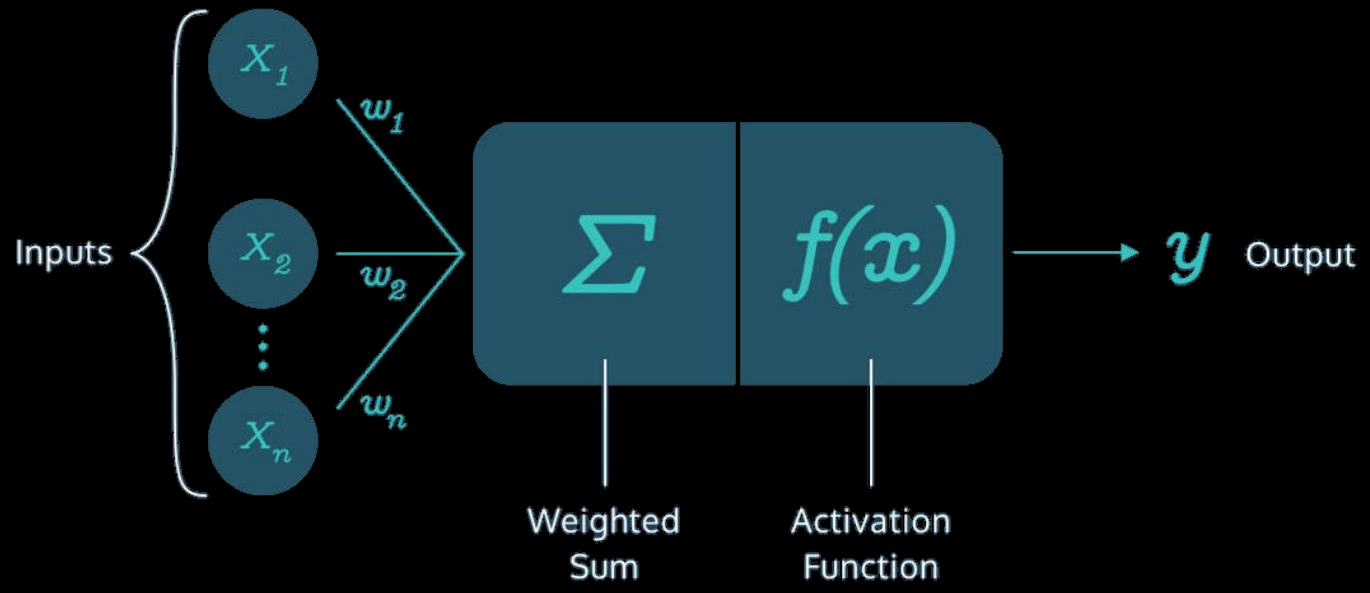
?

welke regels gelden er dan?

How can Chemical Reaction Networks compute?



Start with autocatalysis (**A -> 2A**)

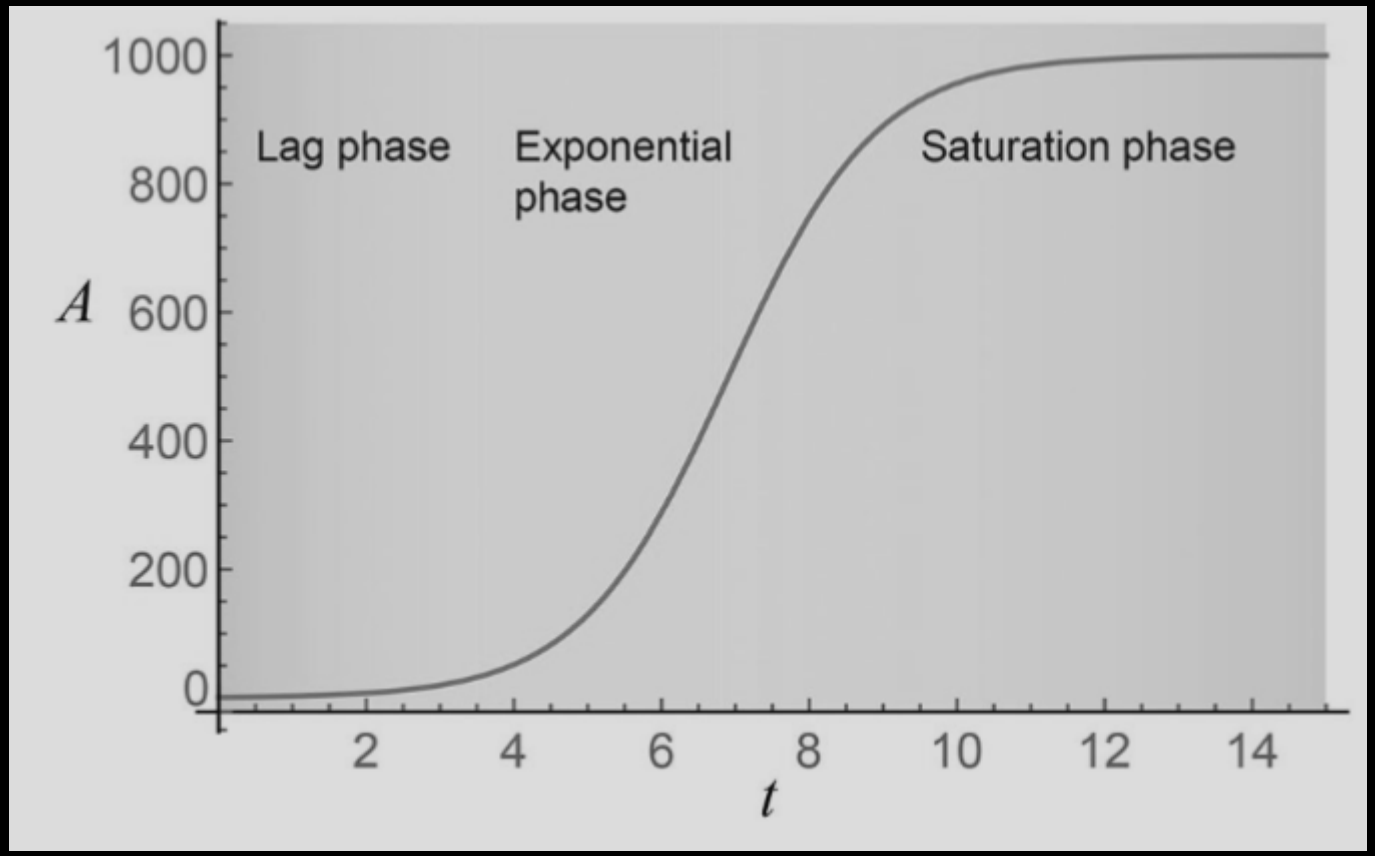


$f(x)$ must be a reaction that yields a product, which can catalyze its own formation

Question 1: How does a “response curve” for the reaction **A --> 2A** look like?

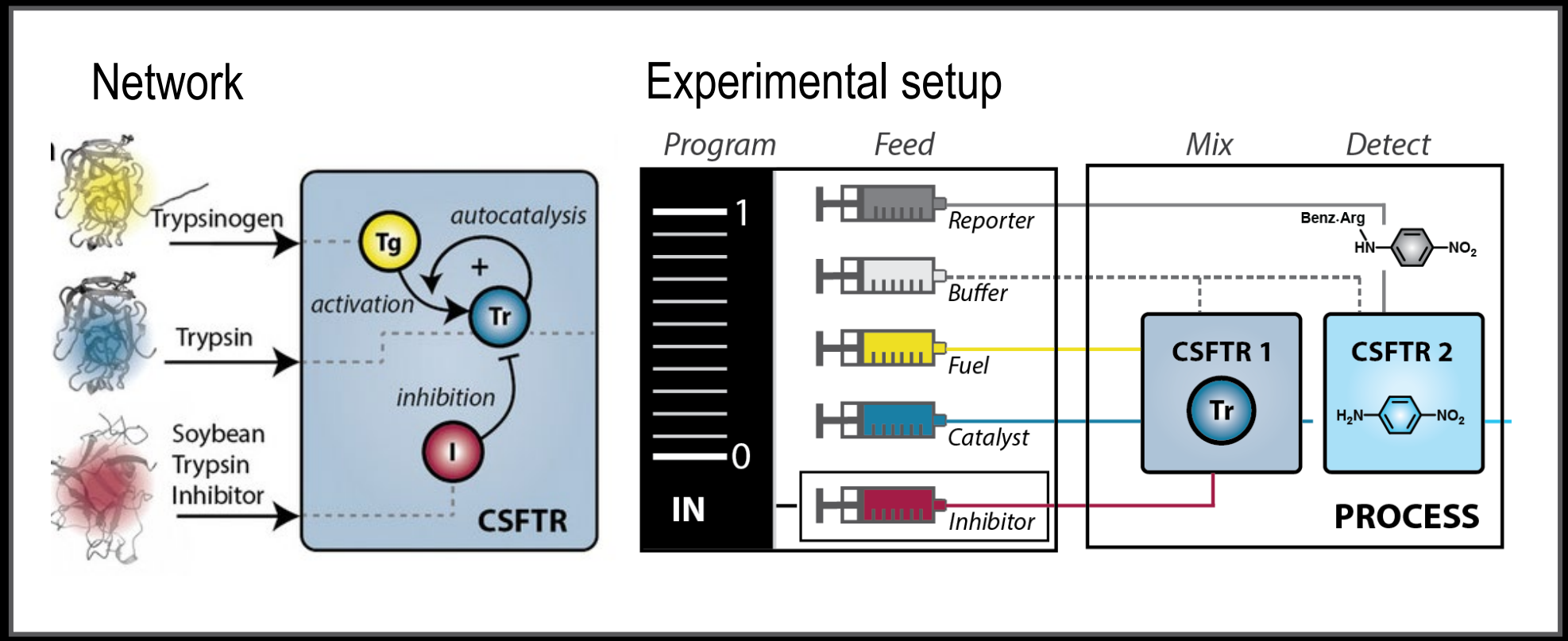
Question 1: How does a “response curve” for the reaction **A --> 2A** look like?

Answer:



Hanopolskyi, A. I. *et. al. ChemSystemsChem* **2021**

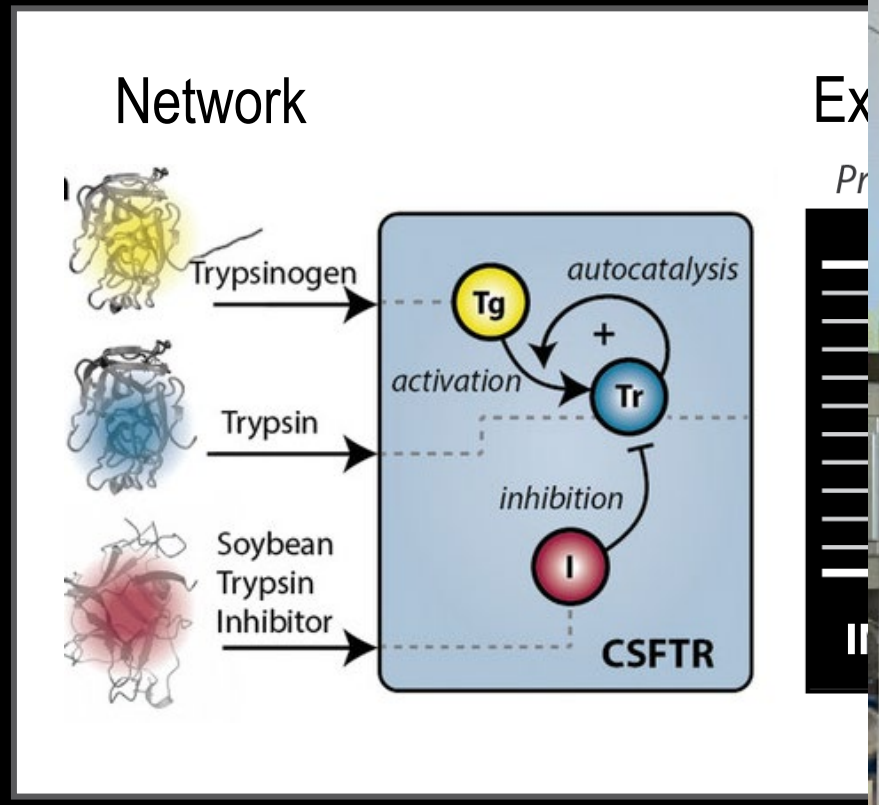
Creating an autocatalytic curve under out-of-equilibrium conditions

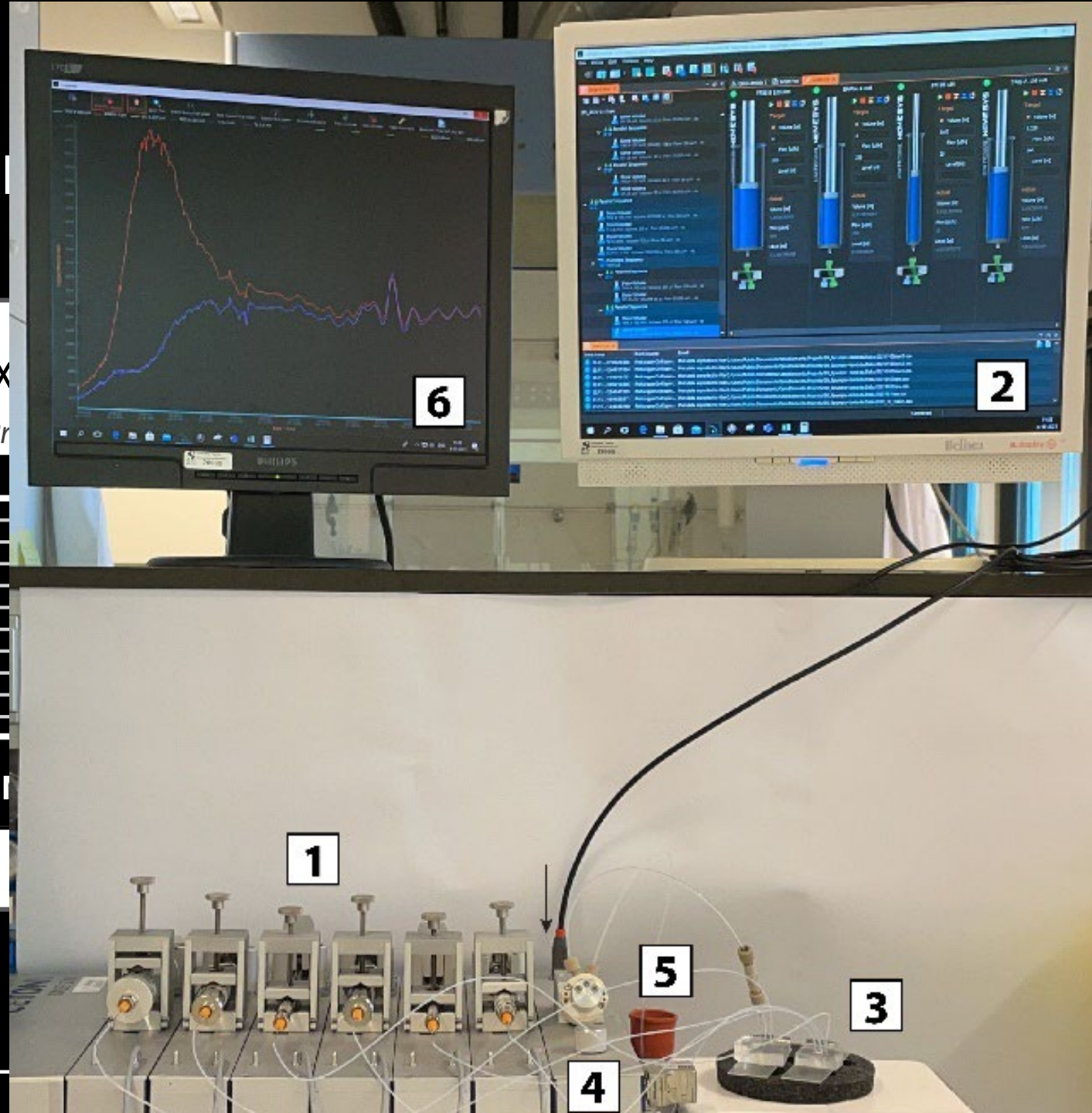




Kriukov, D. V.; Koyuncu, A. H.; Wong, A. S. Y. *Small* **2022**

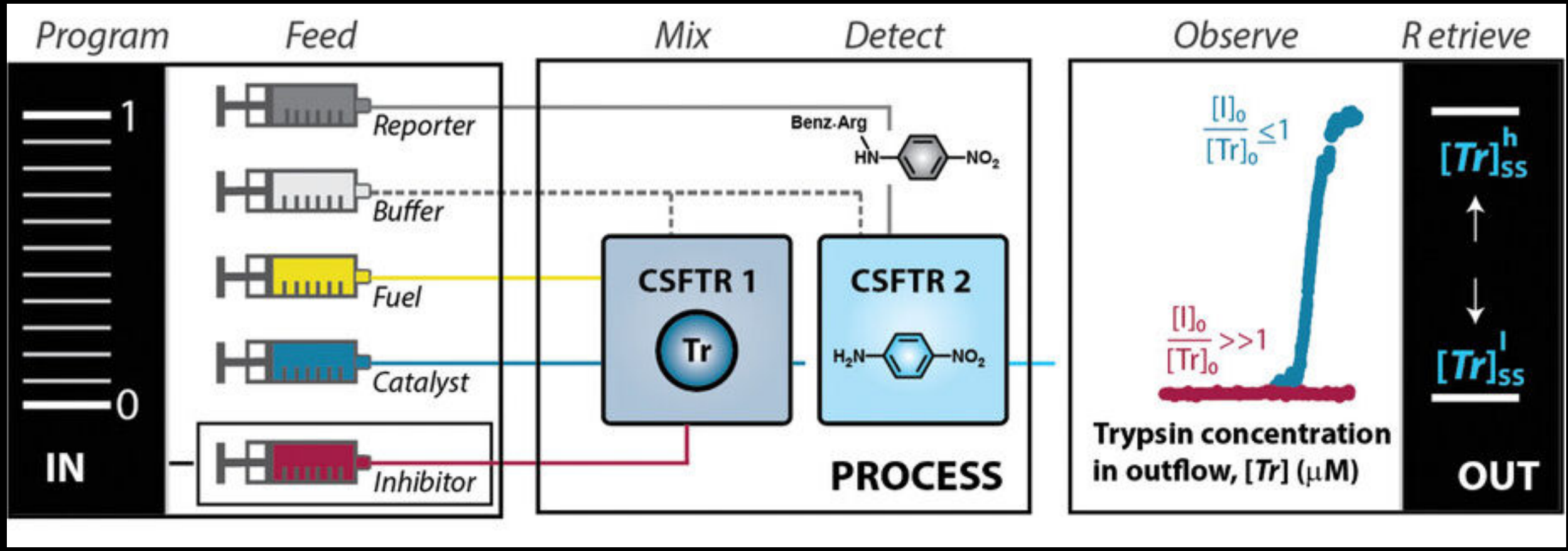
Creating an autocatalytic cu



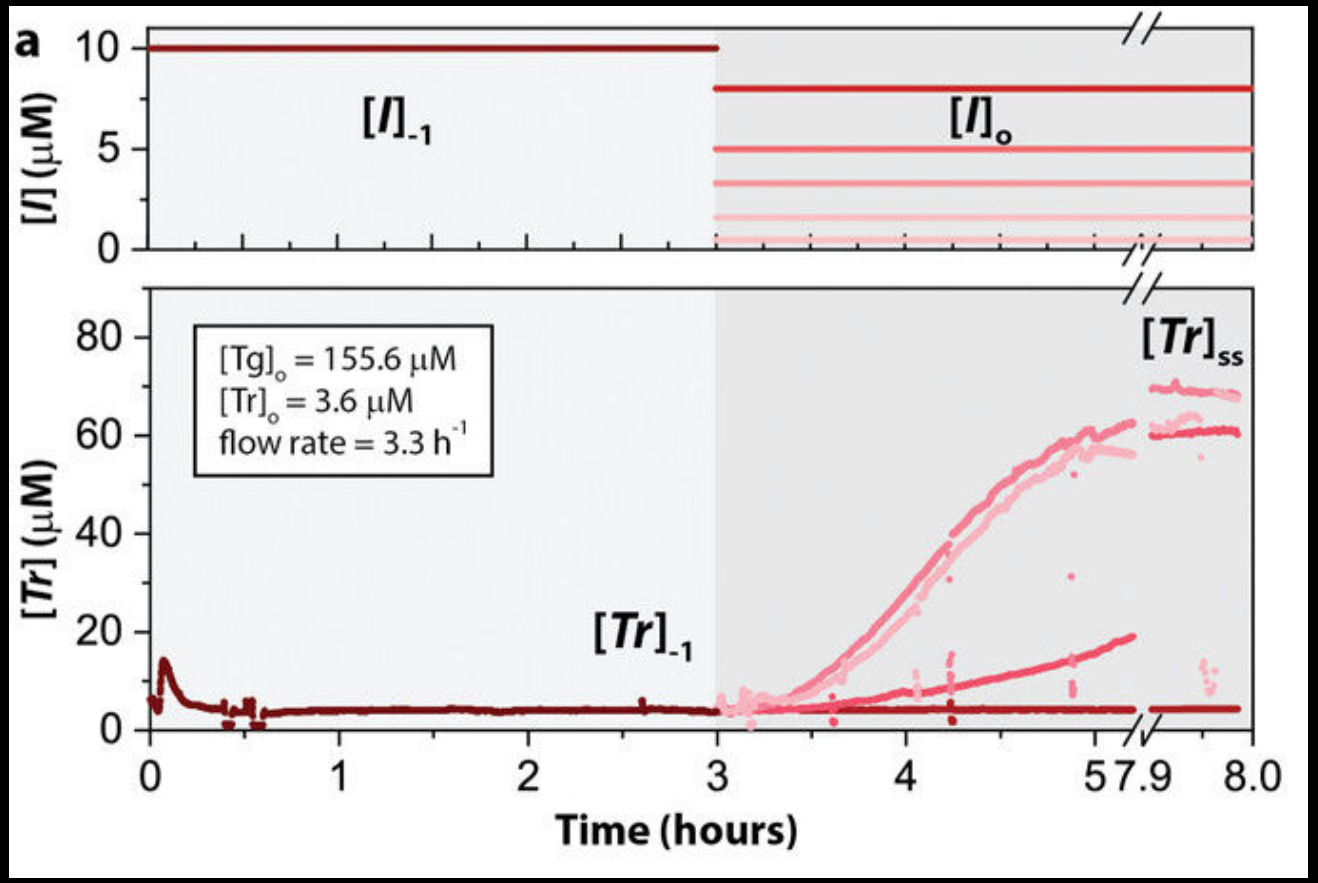


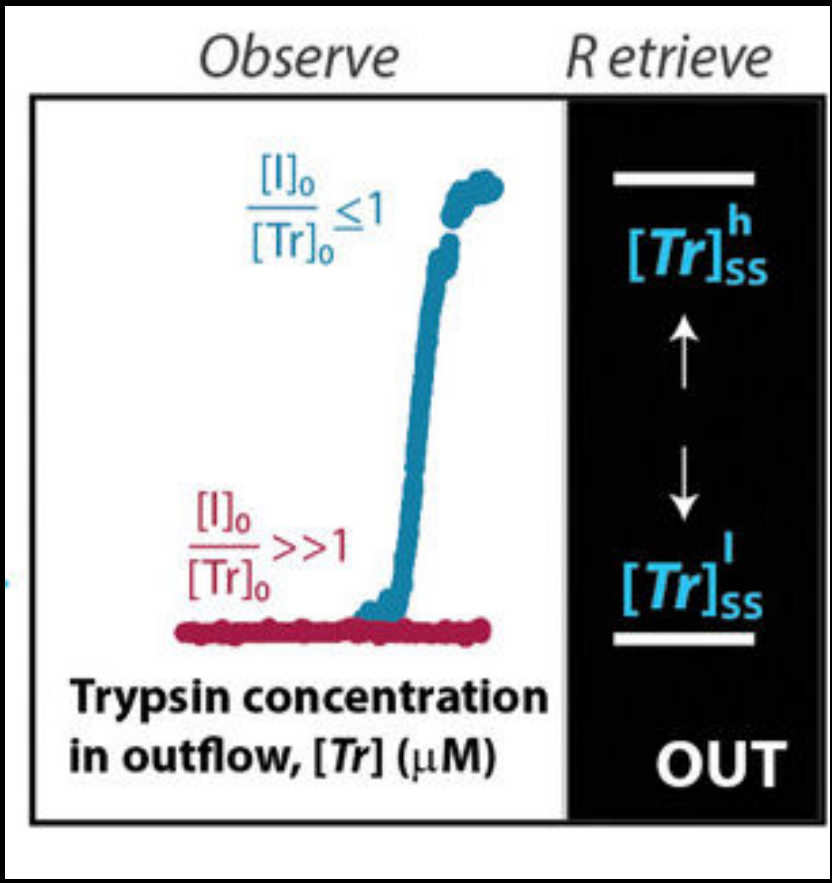
Kriukov, D. V.; Koyuncu, A. H

Creating an autocatalytic curve under out-of-equilibrium conditions



What happens when $[I]_{-1}$ was changed to $[I]_o$ from a high to low $[I]_o$?



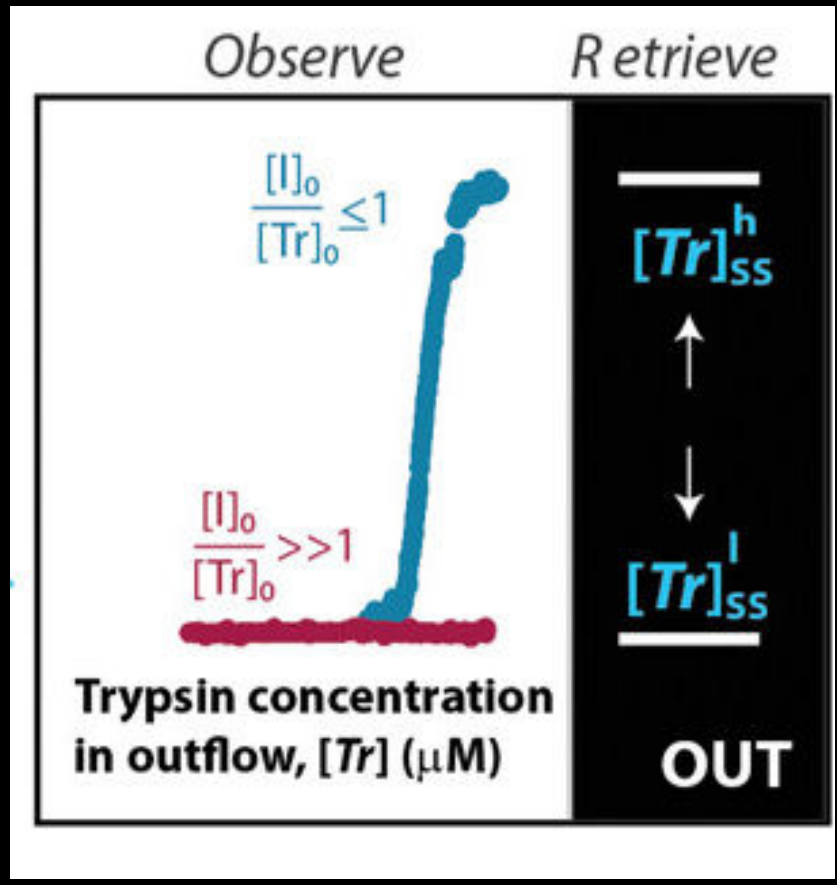


Question 2:

What happens when $[I]_{-1}$ was changed to $[I]_o$ from a <u>low to high</u> $[I]_o$?

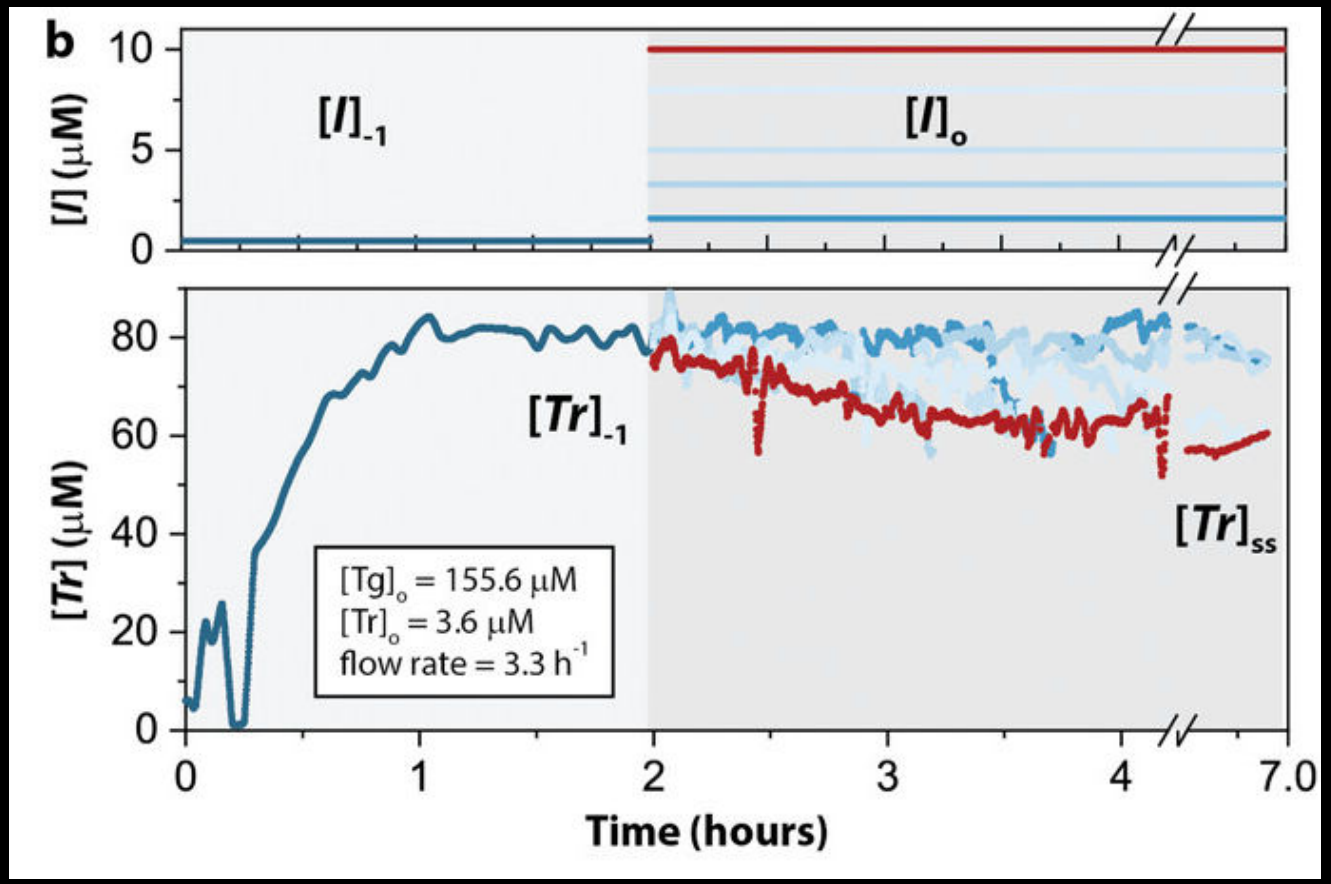
A) Same as before but reversed

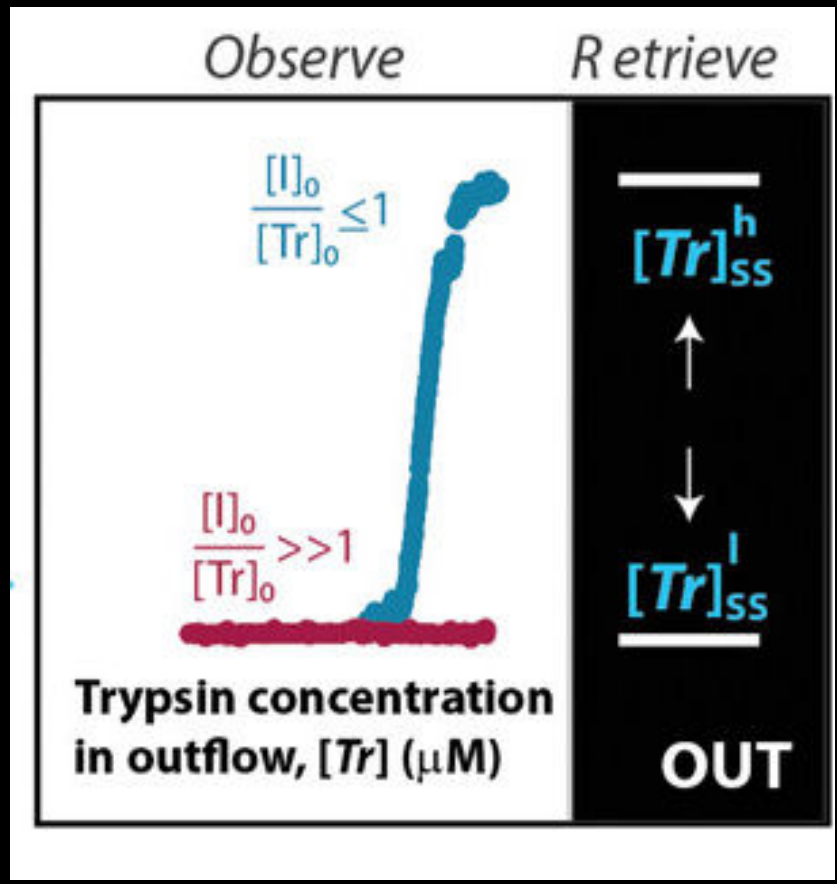
B) Not same as before



Question 2:

What happens when $[I]_{-1}$ was changed to $[I]_o$ from a <u>low to high</u> $[I]_o$?

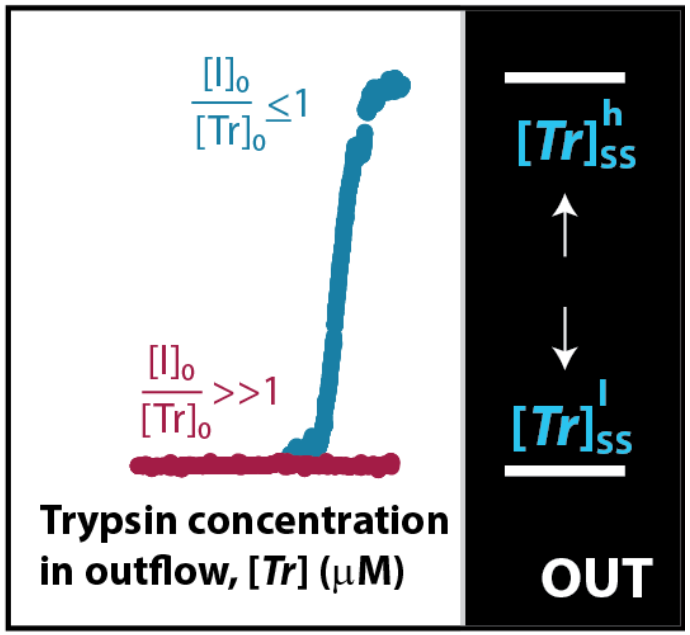




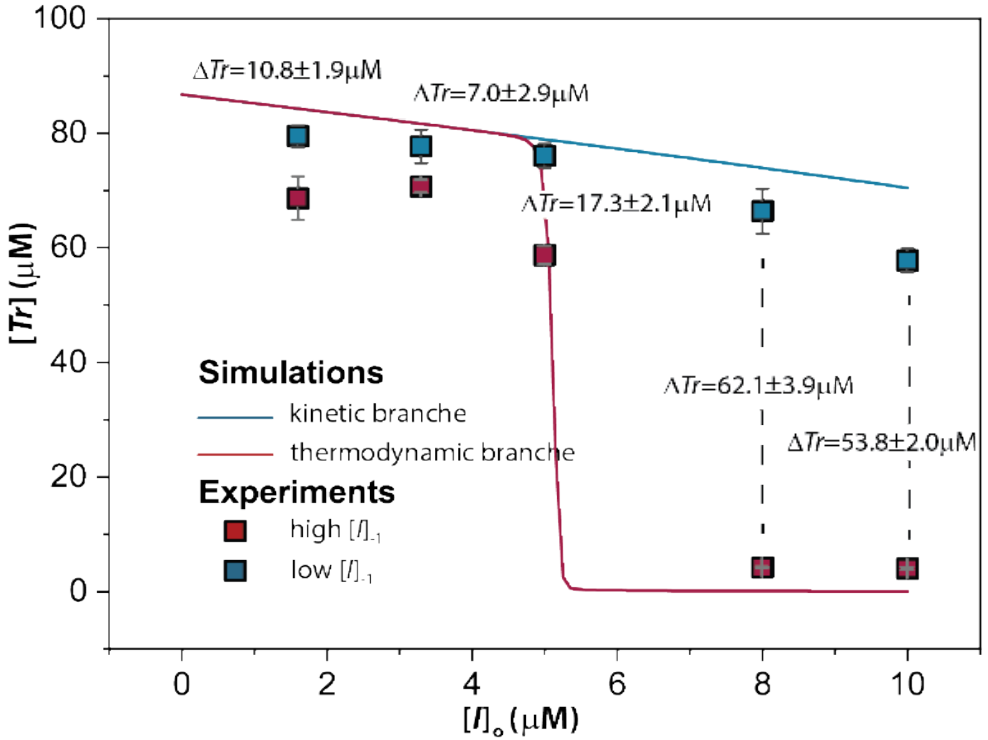
Answer: B) Not same as before

Thus, what we observed is that the autocatalytic network is essentially history-dependent

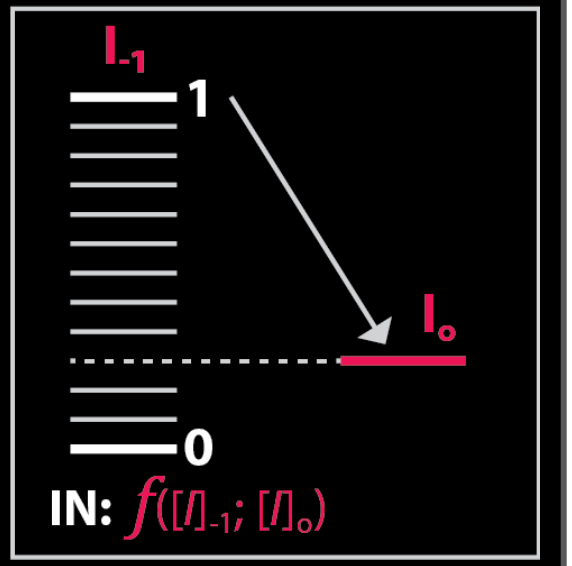
Bistability

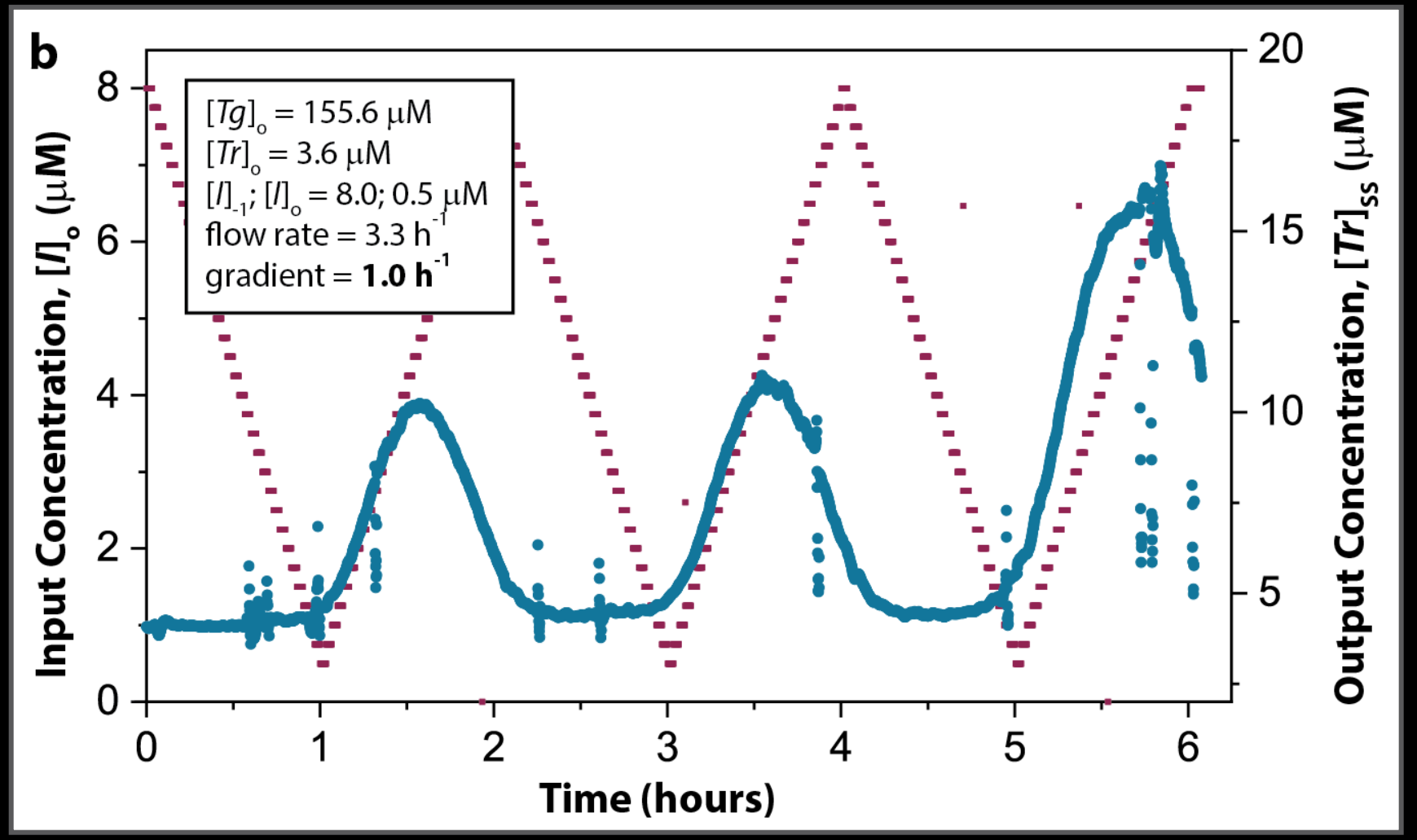


History dependency

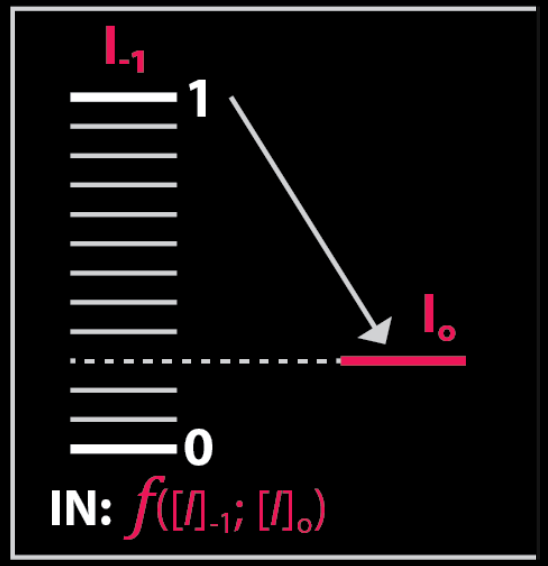


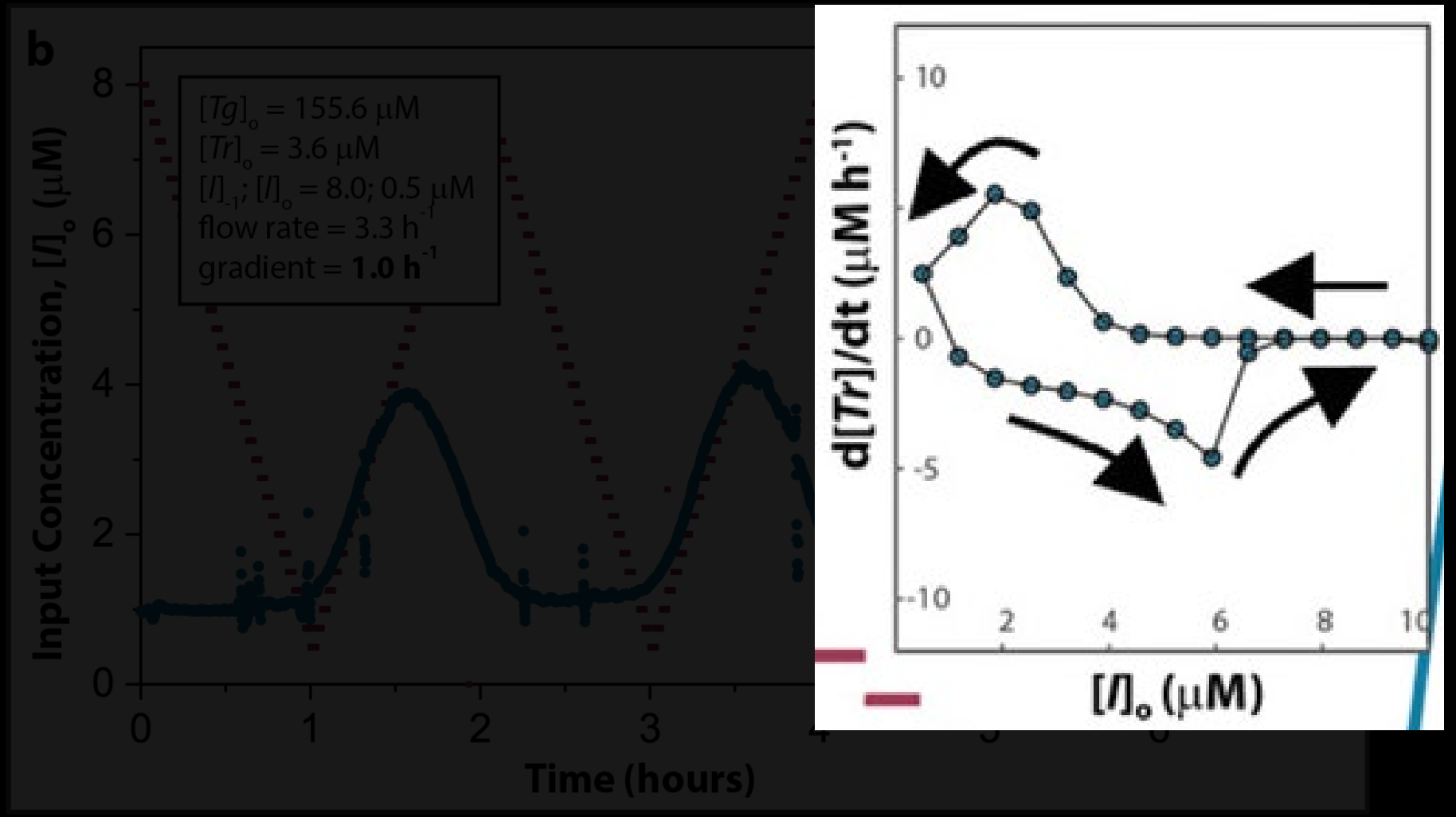
We can exploit this history-dependent behavior using gradients





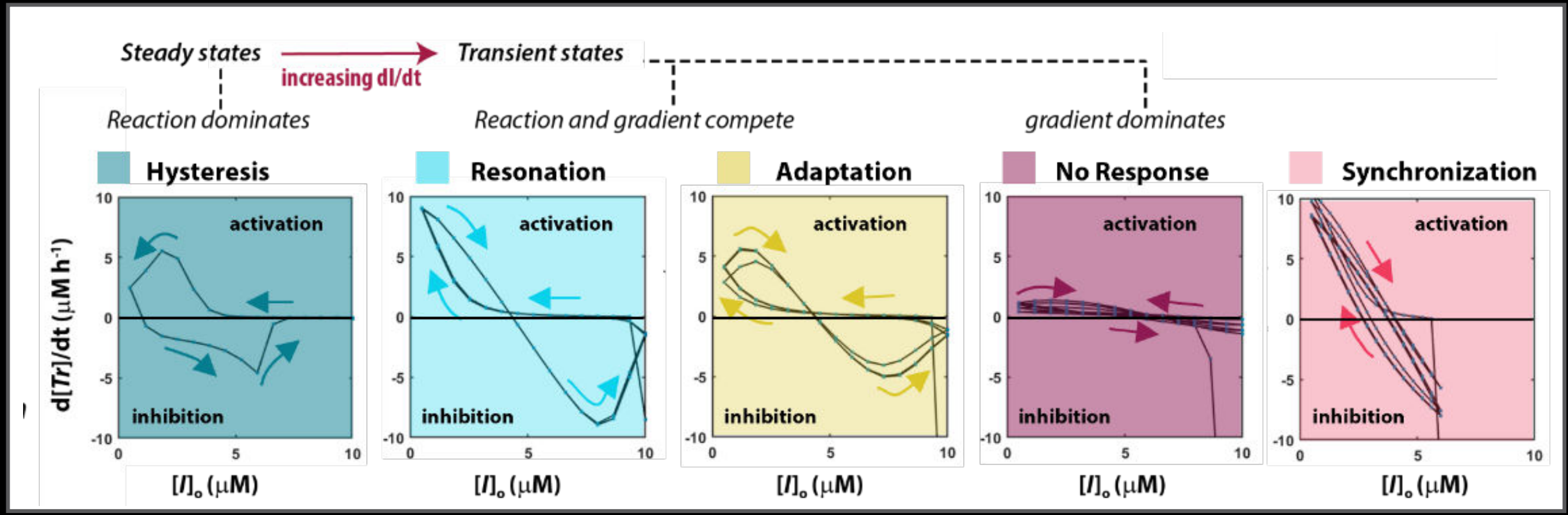
We can exploit this history-dependent behavior using gradients



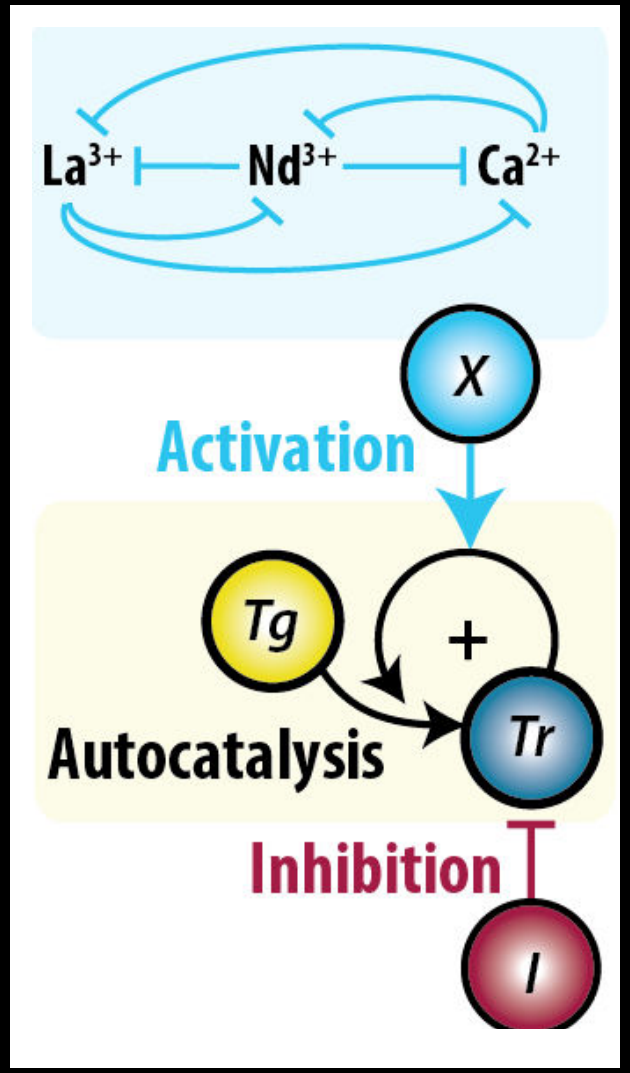


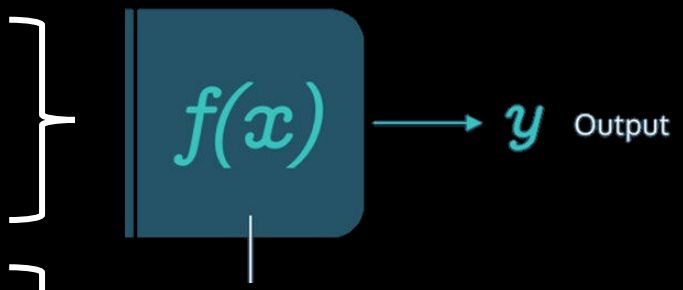
Two competing processes that enable history dependence:

- inhibition vs. autocatalysis
- intrinsic reaction rate vs. external gradients



Autocatalytic Networks are capable of basic computation

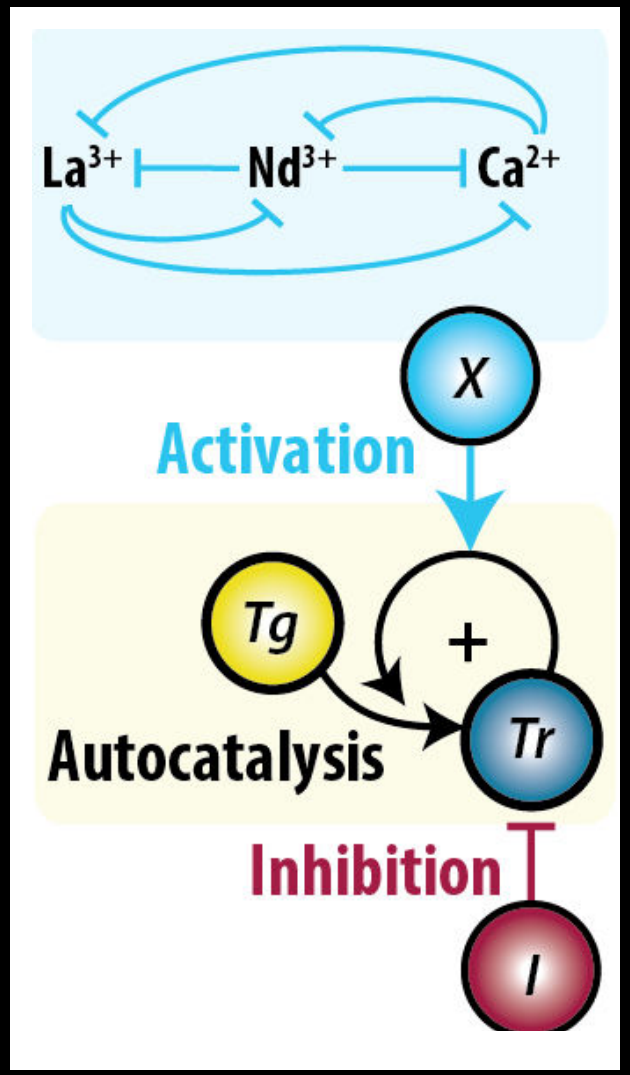




Inhibitor: strengthening and weakening
history dependency in logic

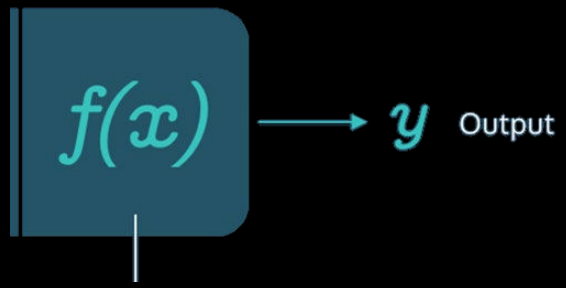
D. Kriukov *Small* **2022**

Autocatalytic Networks are capable of basic computation



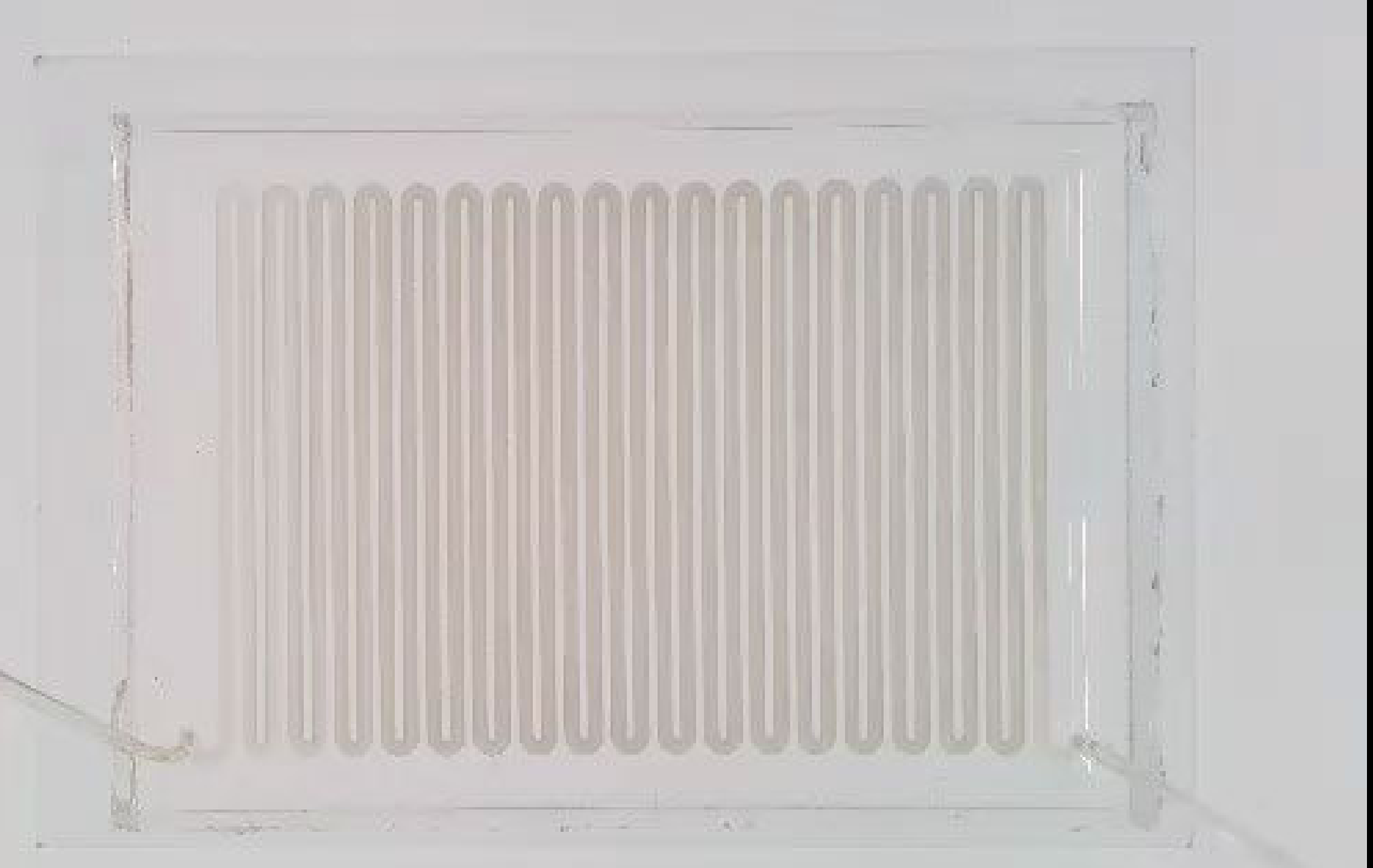
Accelerator: **tuning and switching** of the logic operation

D. Kriukov *Nat. Commun.* **2024**

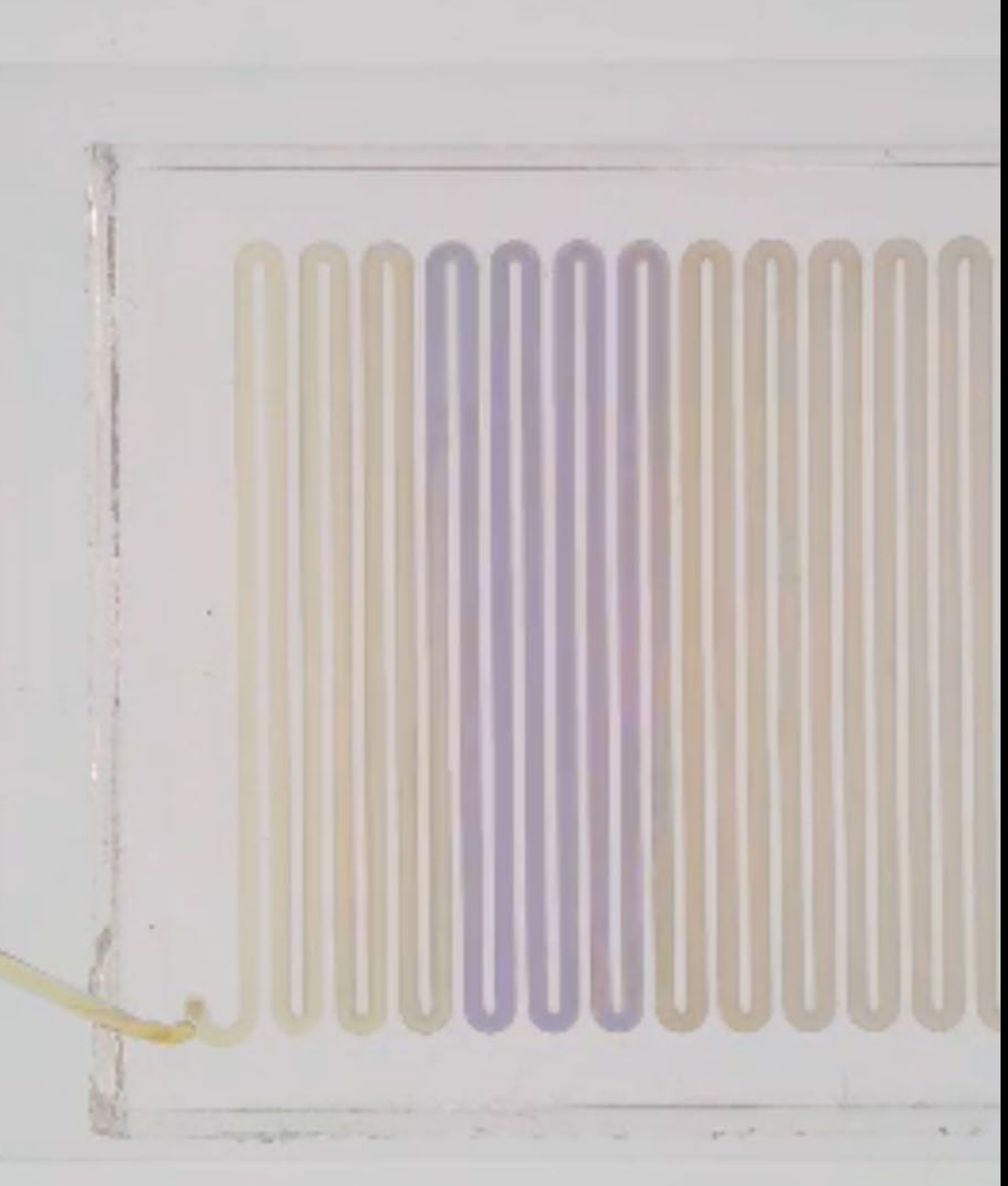


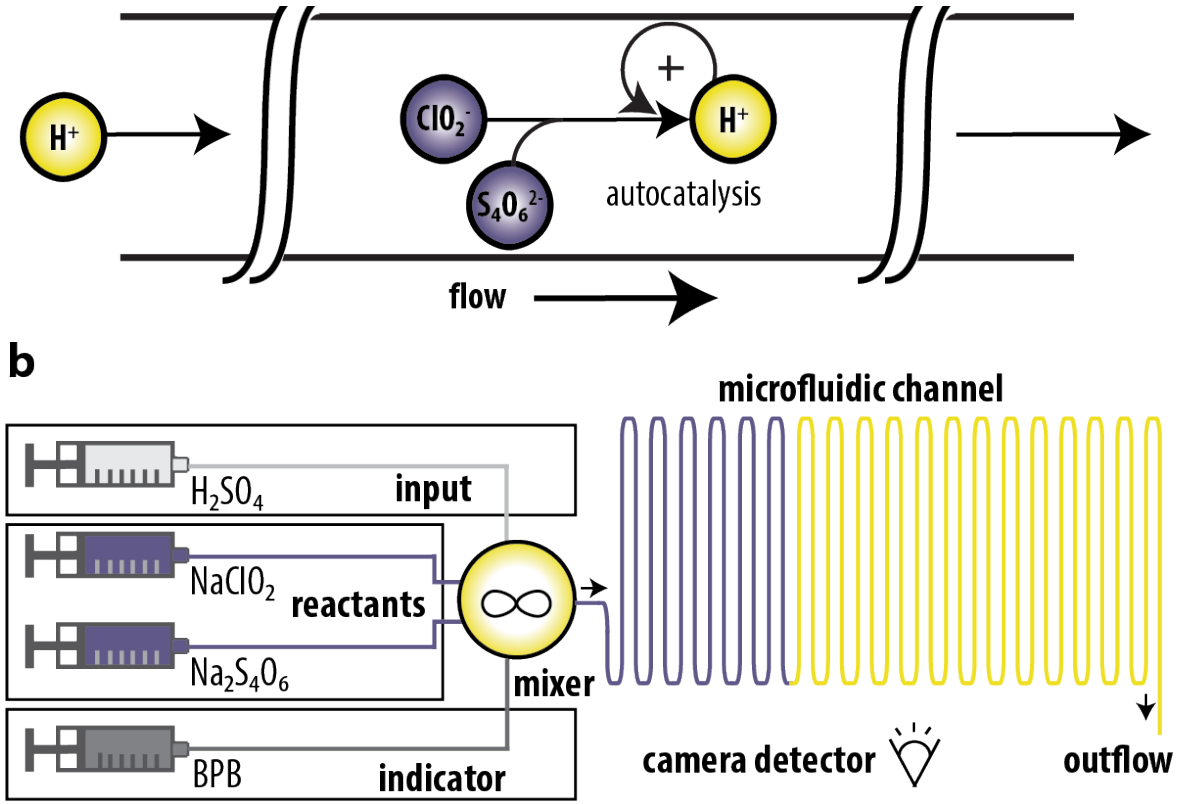
Inhibitor: **strengthening and weakening**
history dependency in logic

D. Kriukov *Small* **2022**

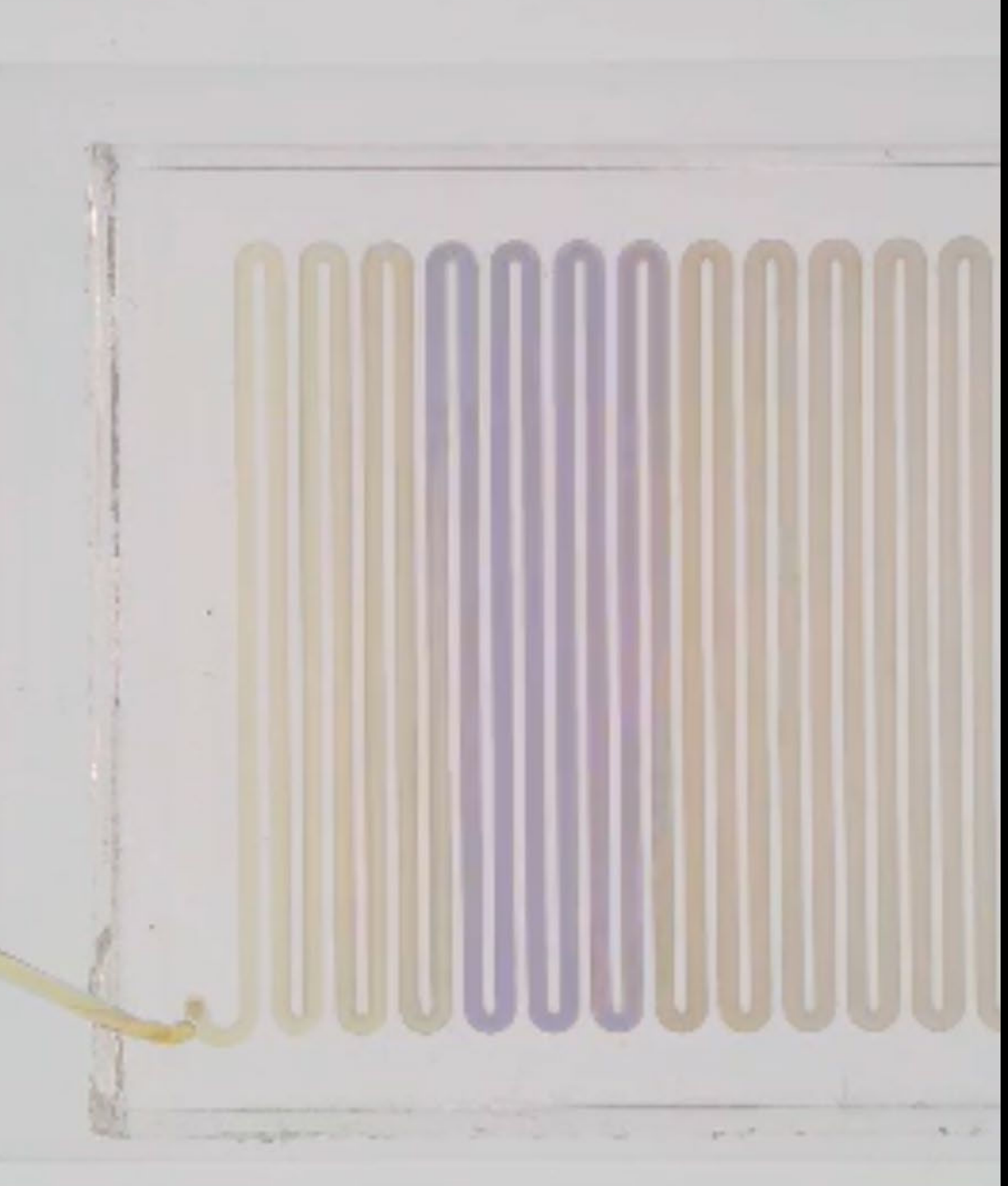


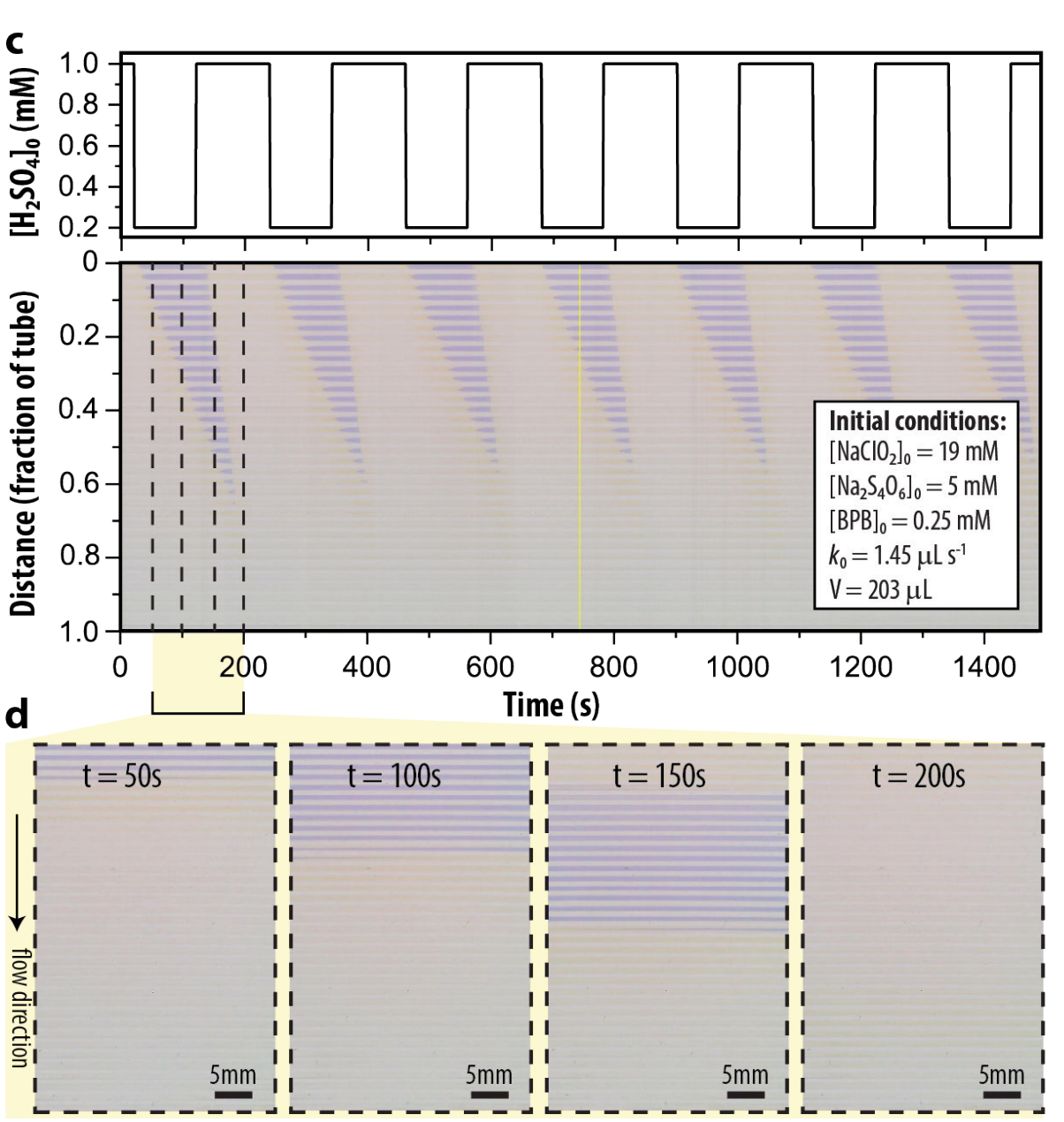
UNIVERSITY
OF TWENTE.



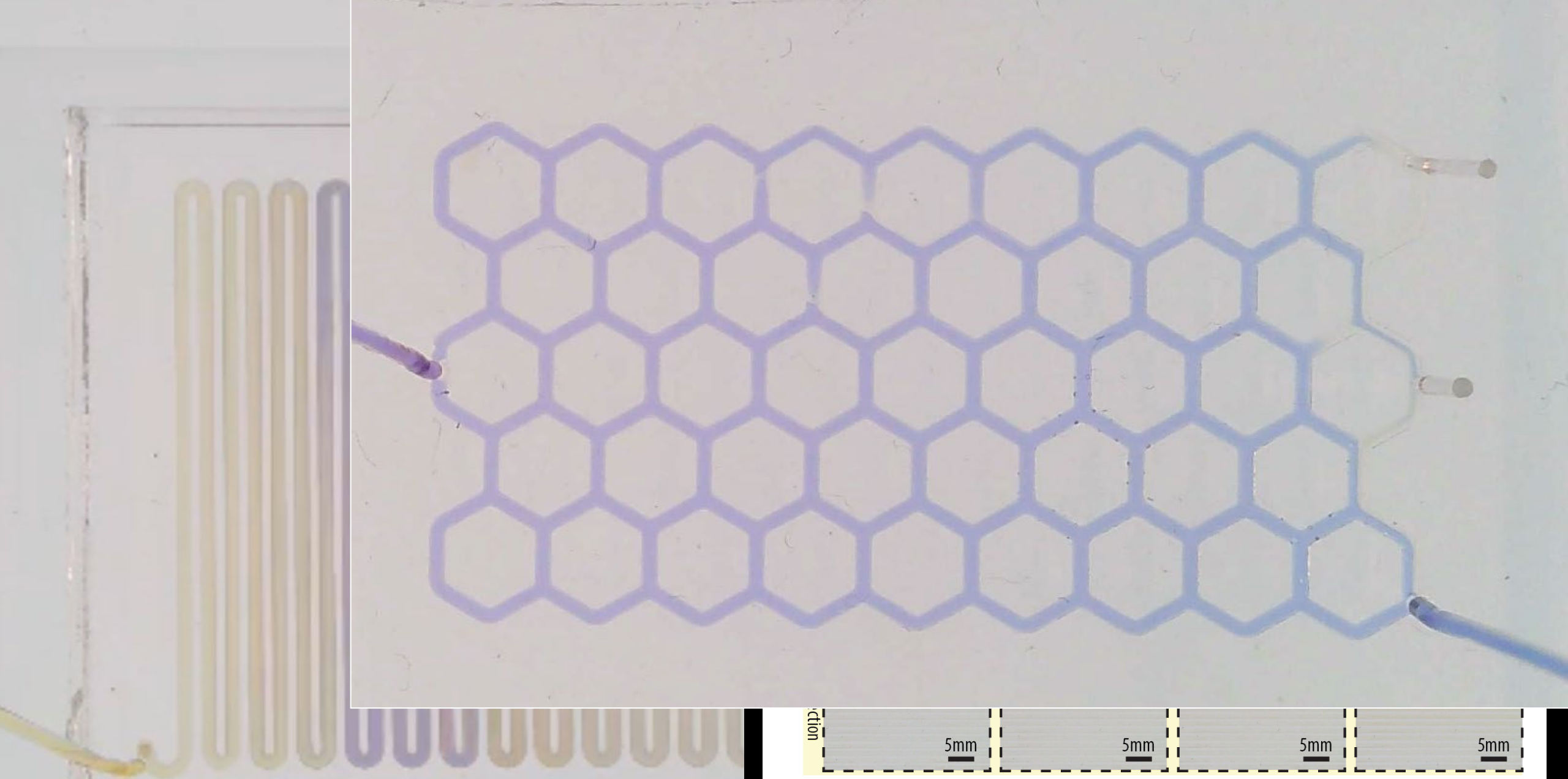


Kriukov, D. V.; Szalai, I.; Wong, A. S. Y. *under review*

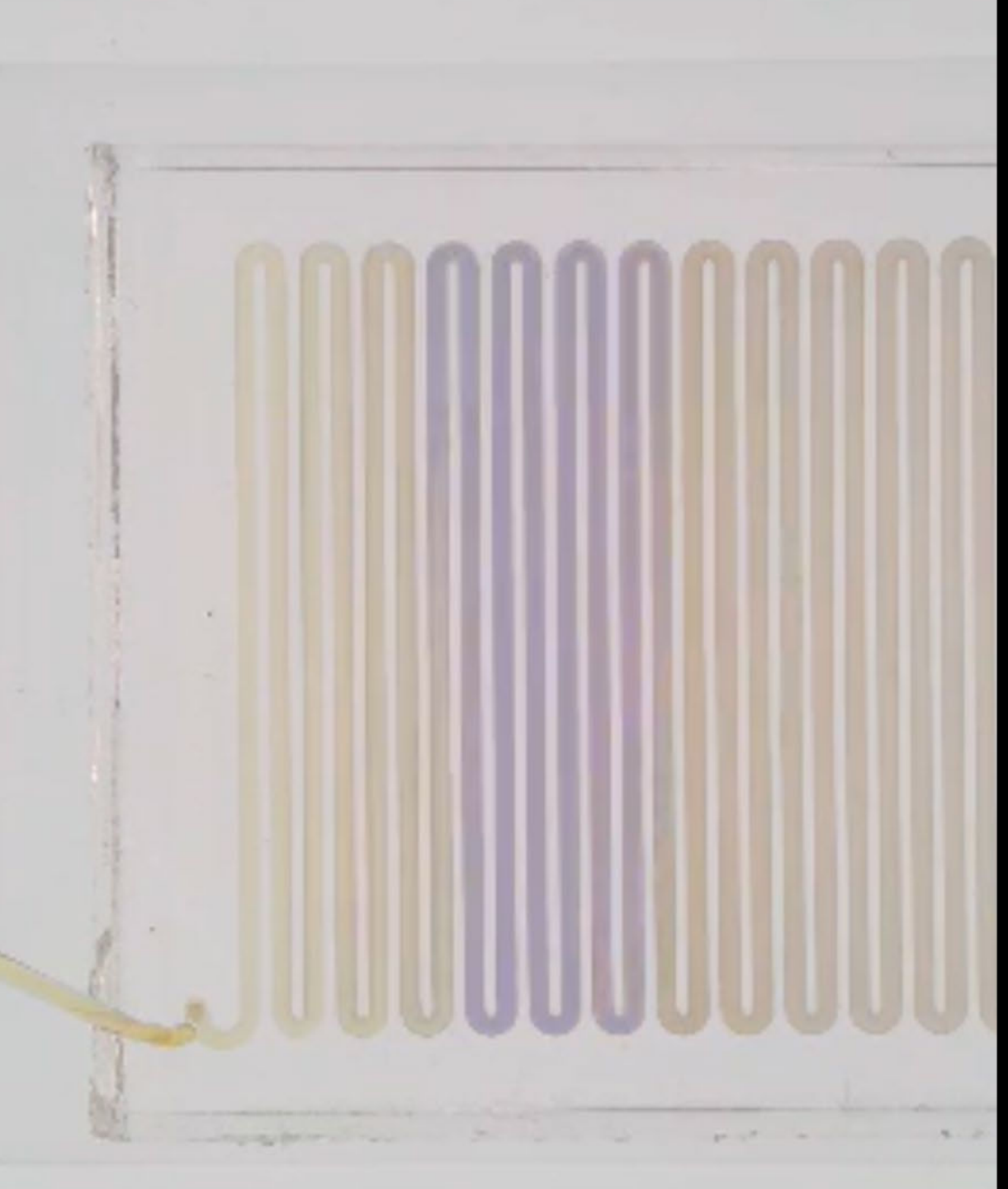


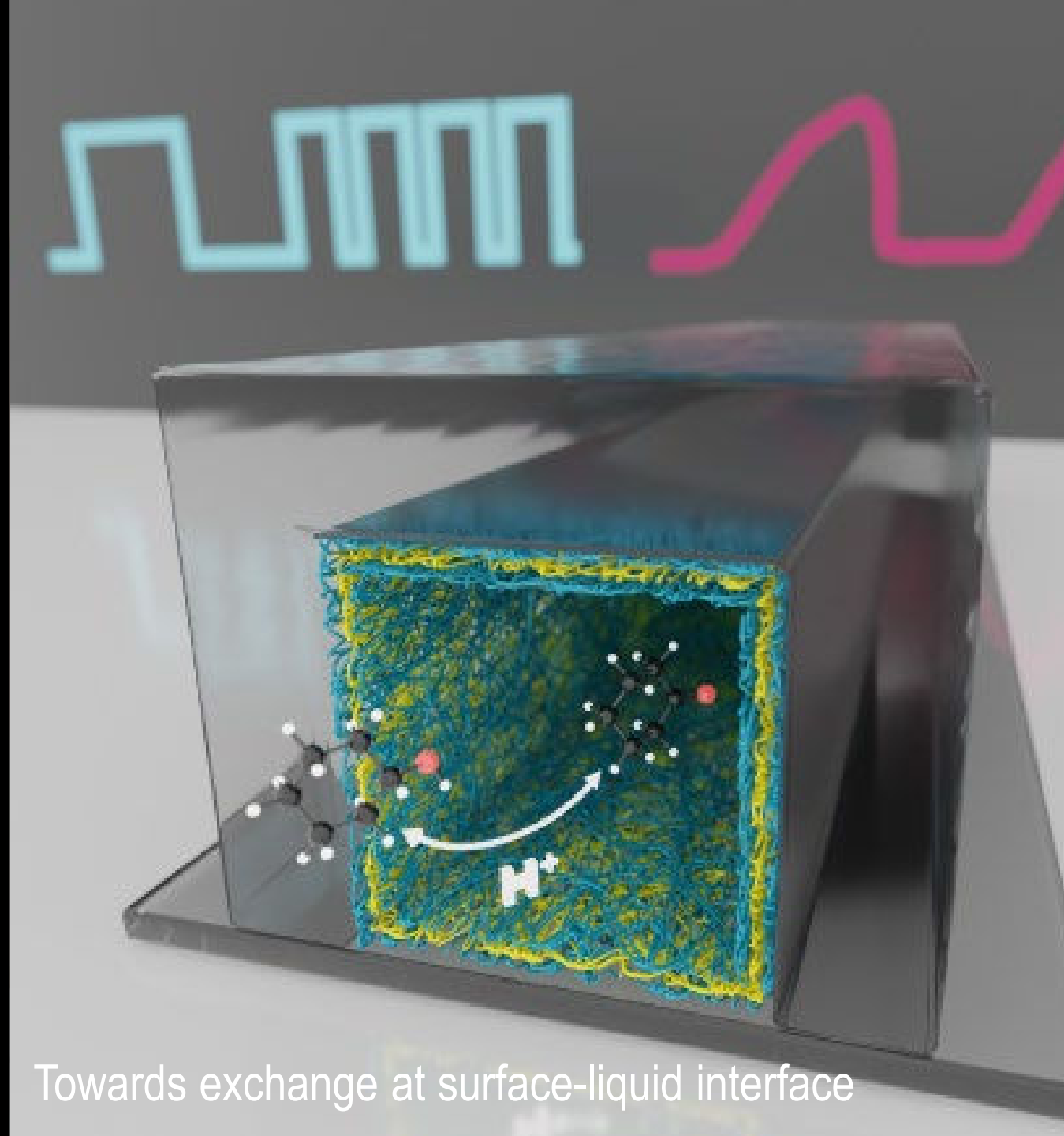


Kriukov, D. V.; Szalai, I.; Wong, A. S. Y. *under review*



Kriukov, D. V.; Szalai, I.; Wong, A. S. Y. *under review*



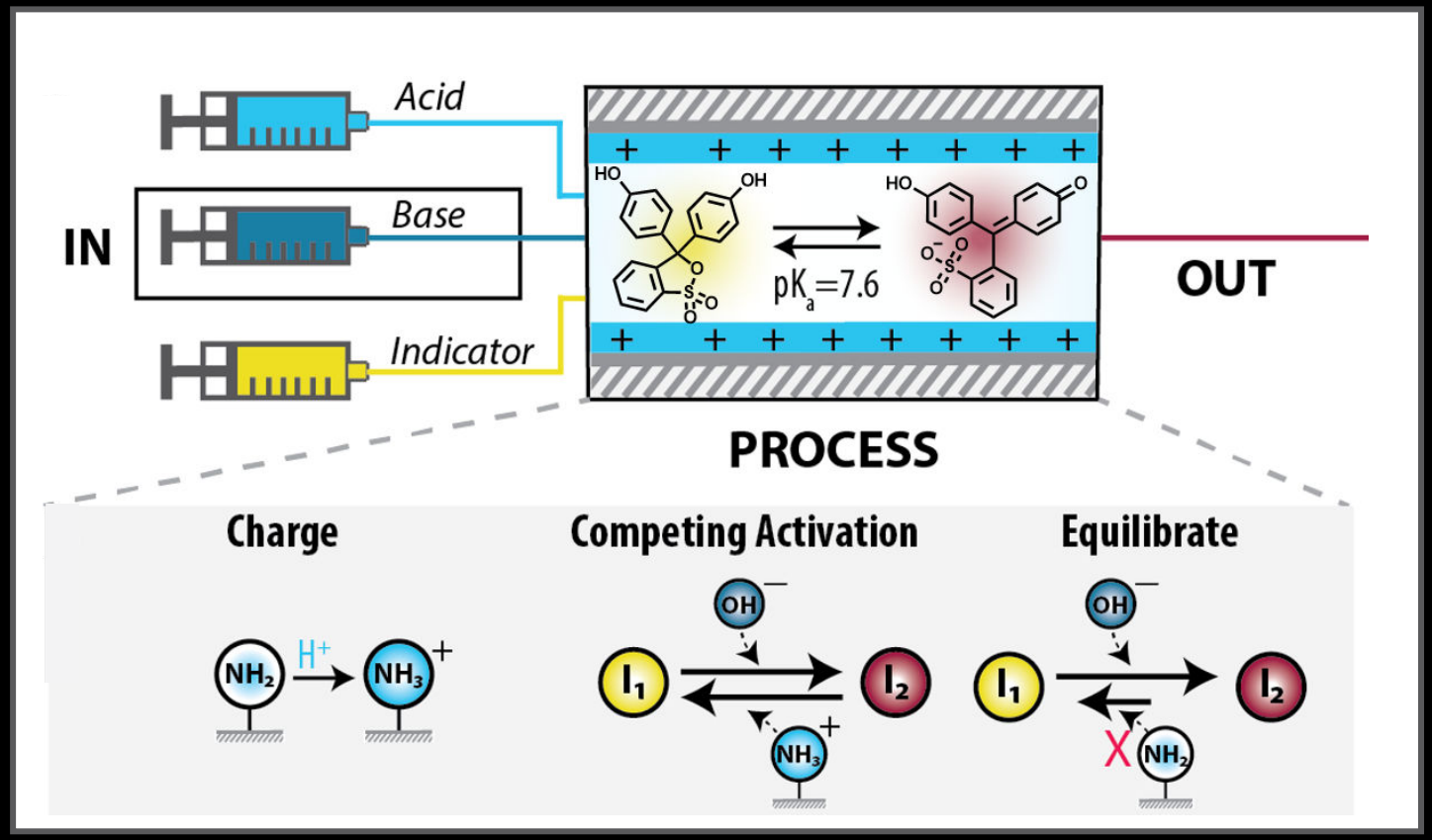


Towards exchange at surface-liquid interface

Leverage small scales in microfluidics

with the purpose to disrupt equilibrium reactions



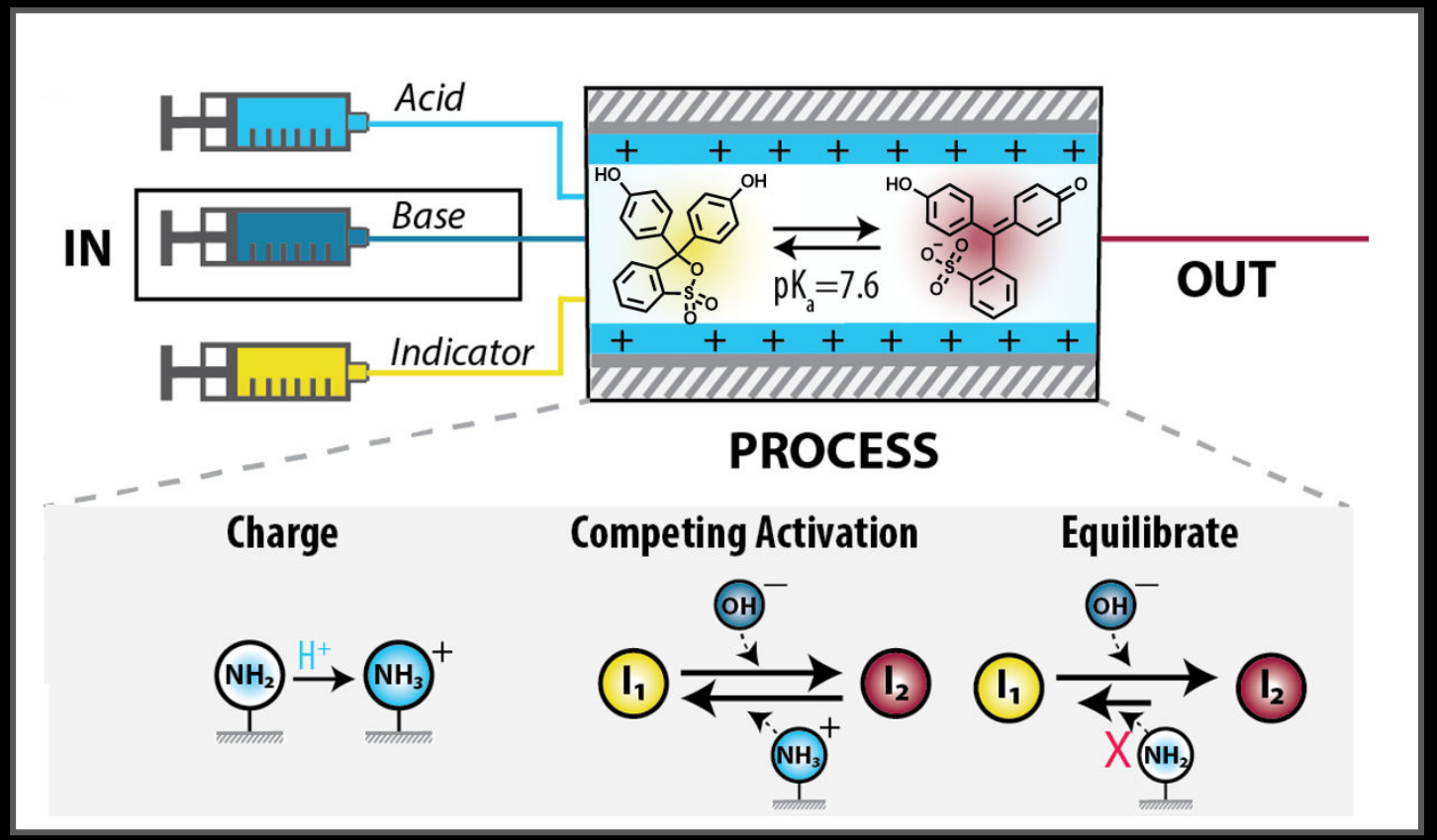


Koyuncu, A. H. ; Movilli, J.; Sahin, S.; Kriukov, D. V.; Huskens, J.; Wong, A. S. Y. *ChemSystemsChem* **2023**

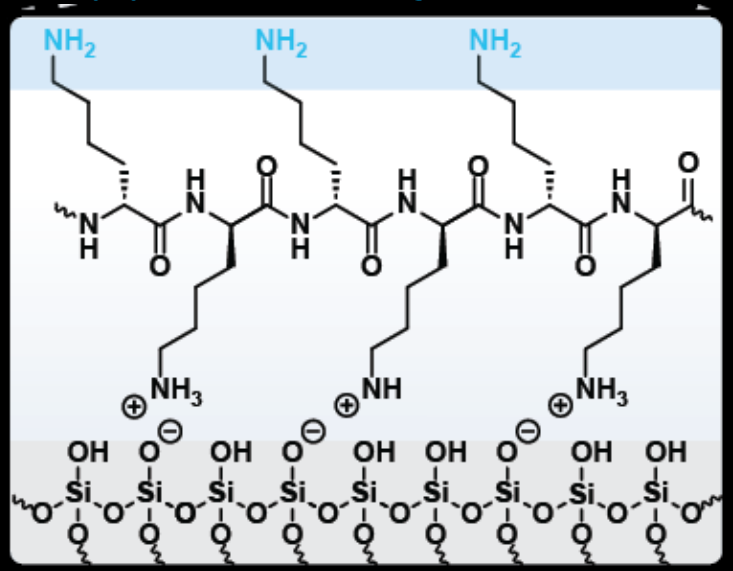
Leverage small scales in microfluidics

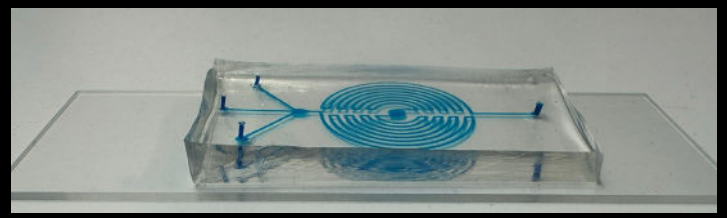
with the purpose to disrupt equilibrium reactions





Polylysine coating

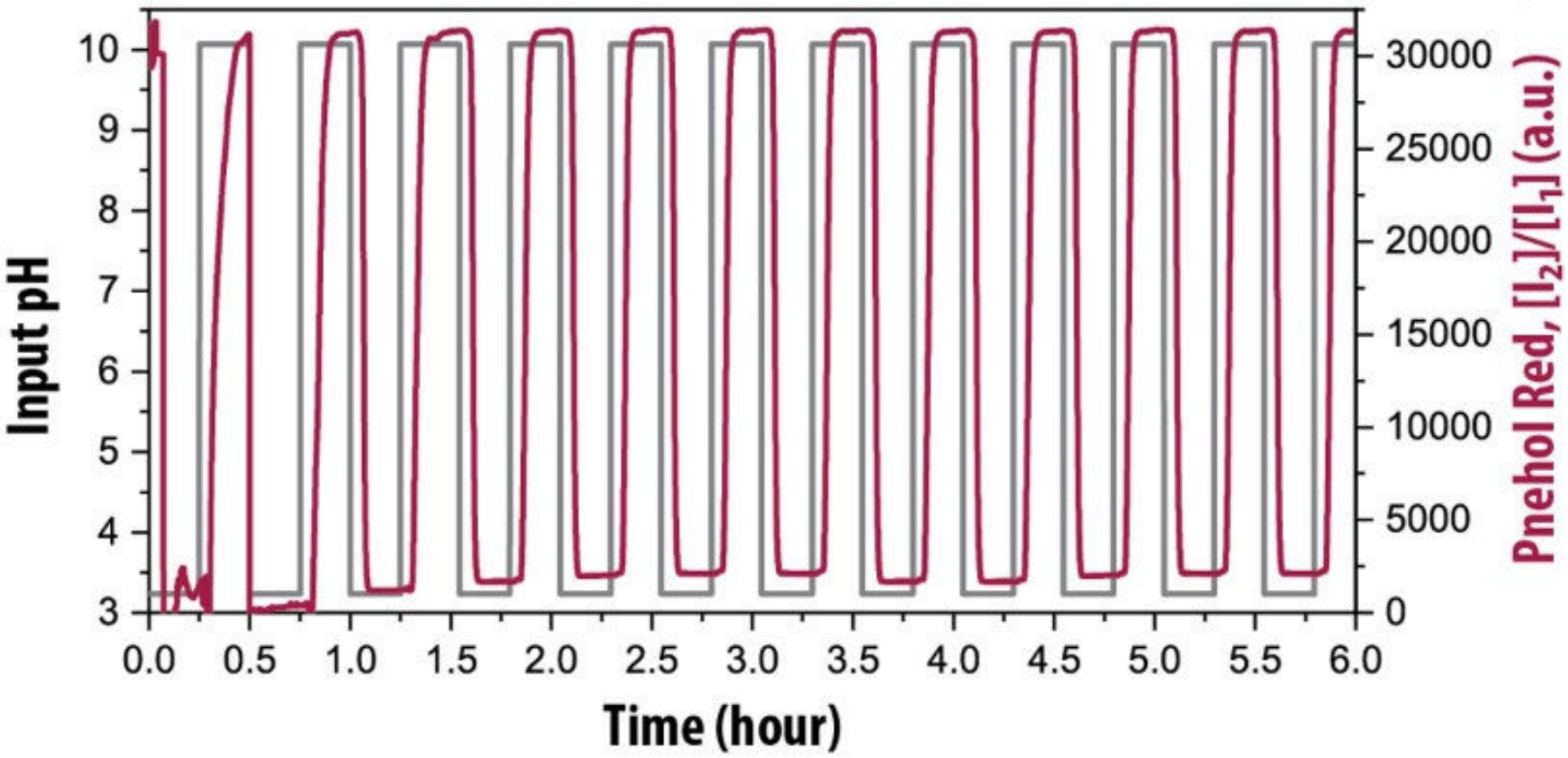




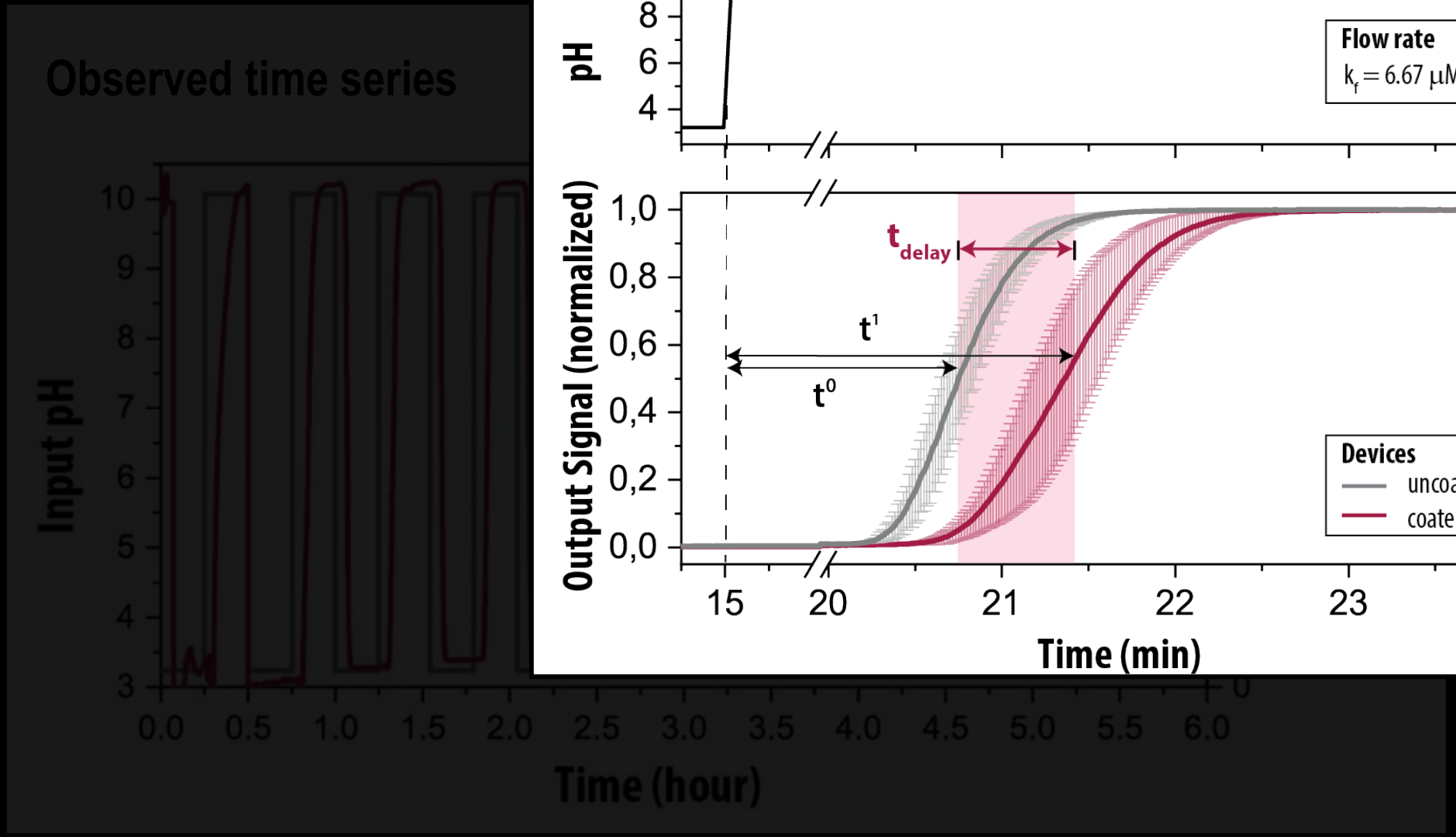
Koyuncu, A. H. ; Movilli, J.; Sahin, S.; Kriukov, D. V.; Huskens, J.; Wong, A. S. Y. *ChemSystemsChem* **2023**

Polylysine coating effectively delays the signal

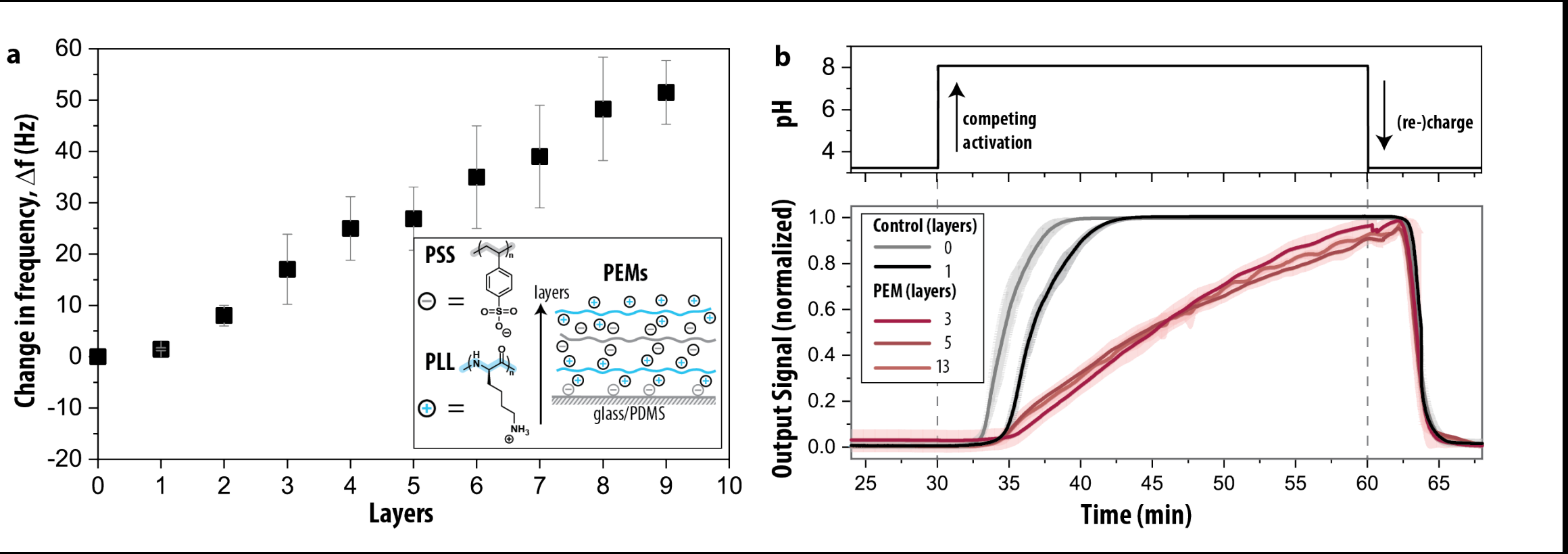
Observed time series



Polylysine coating effectively delays the signal



Increase the capacity of local activation



Observation: Significant decrease in the rate of activation.

How can we exploit this effect?

PEMs = polyelectrolyte multilayers

Our attempts to process molecular information

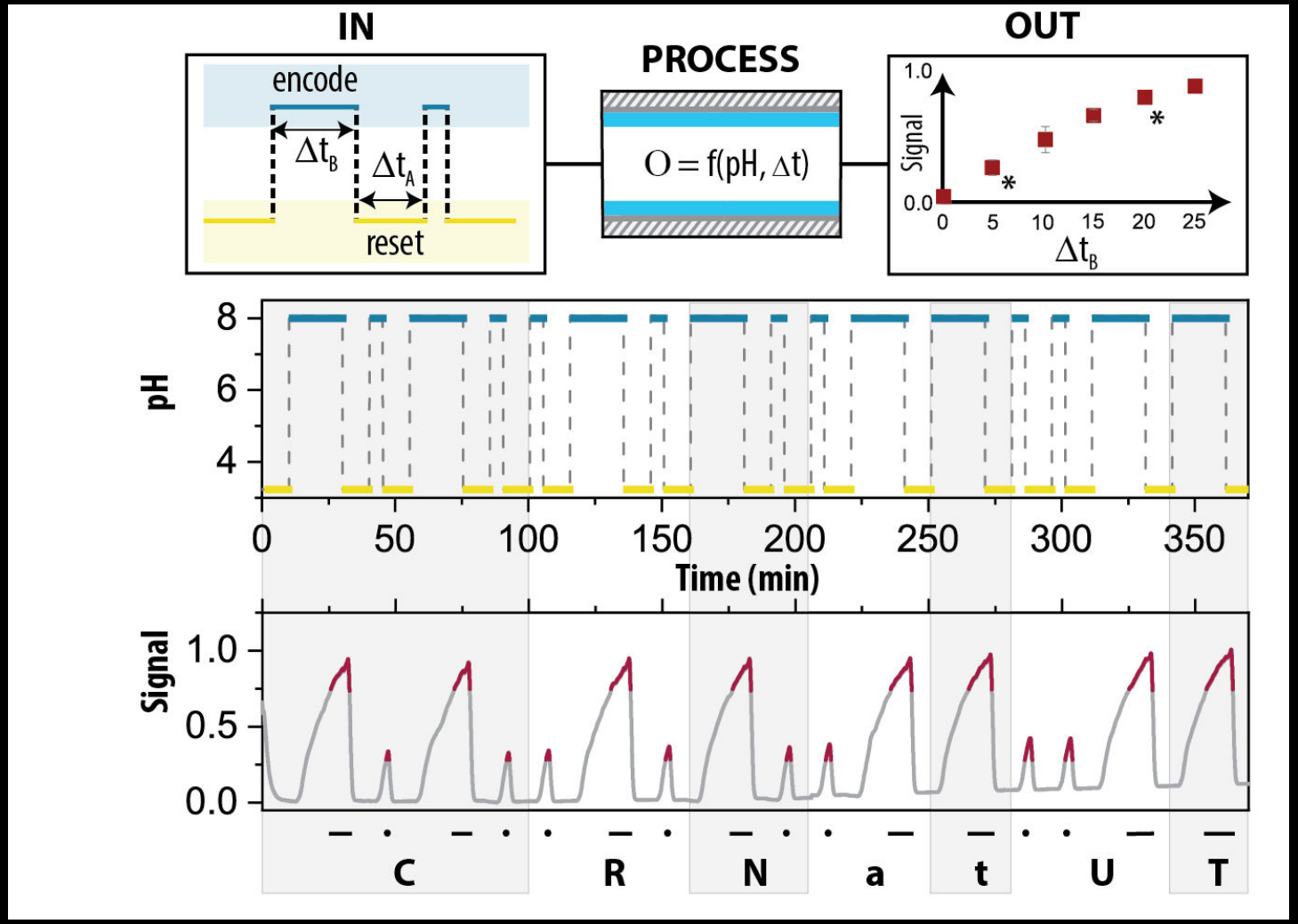
Introduce perturbations:

- **base = encode**
- **acid = reset**

Define decoding function:

(1) a '**dash**', 0.75 < l.m. < 1.0

(2) a '**dot**', 0.25 < l.m. < 0.5



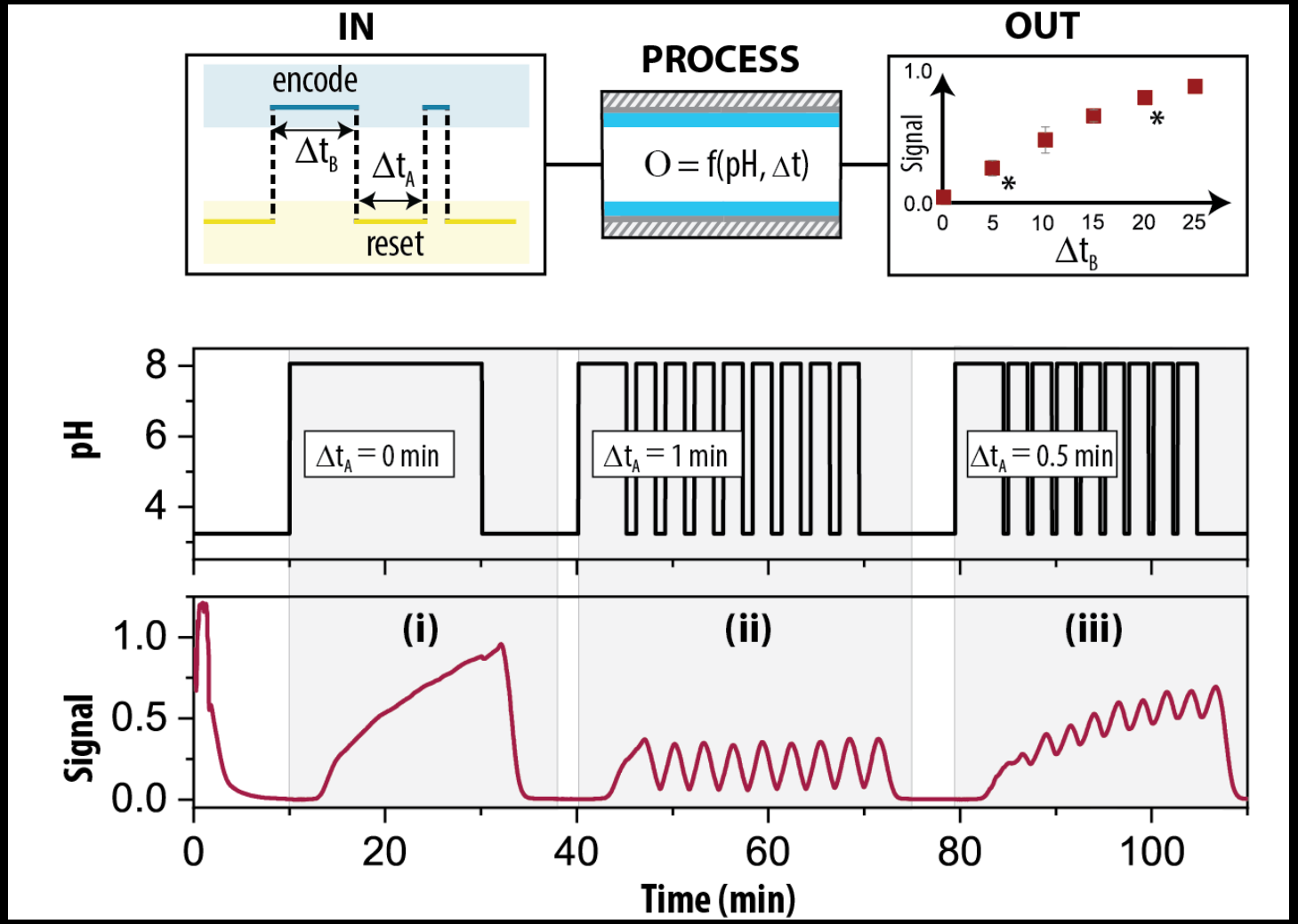
l.m. = local maxima

Our attempts to process molecular information

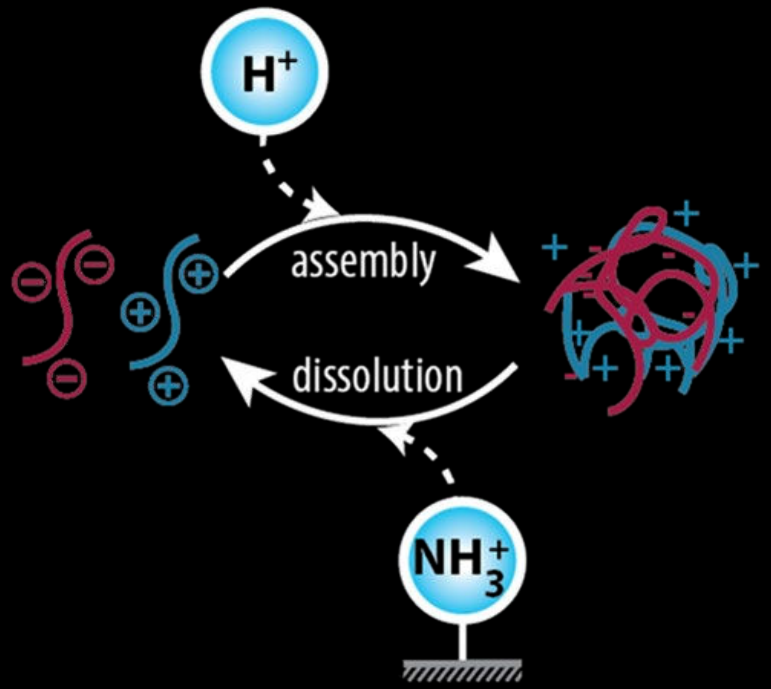
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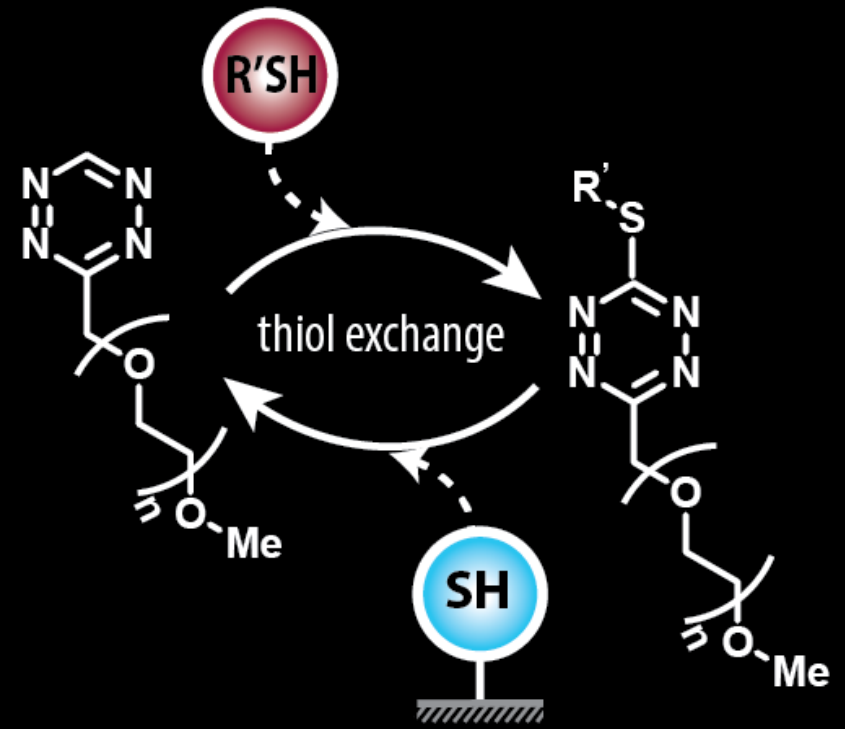
Other signal transformation:



Other types of networks based on this concept:

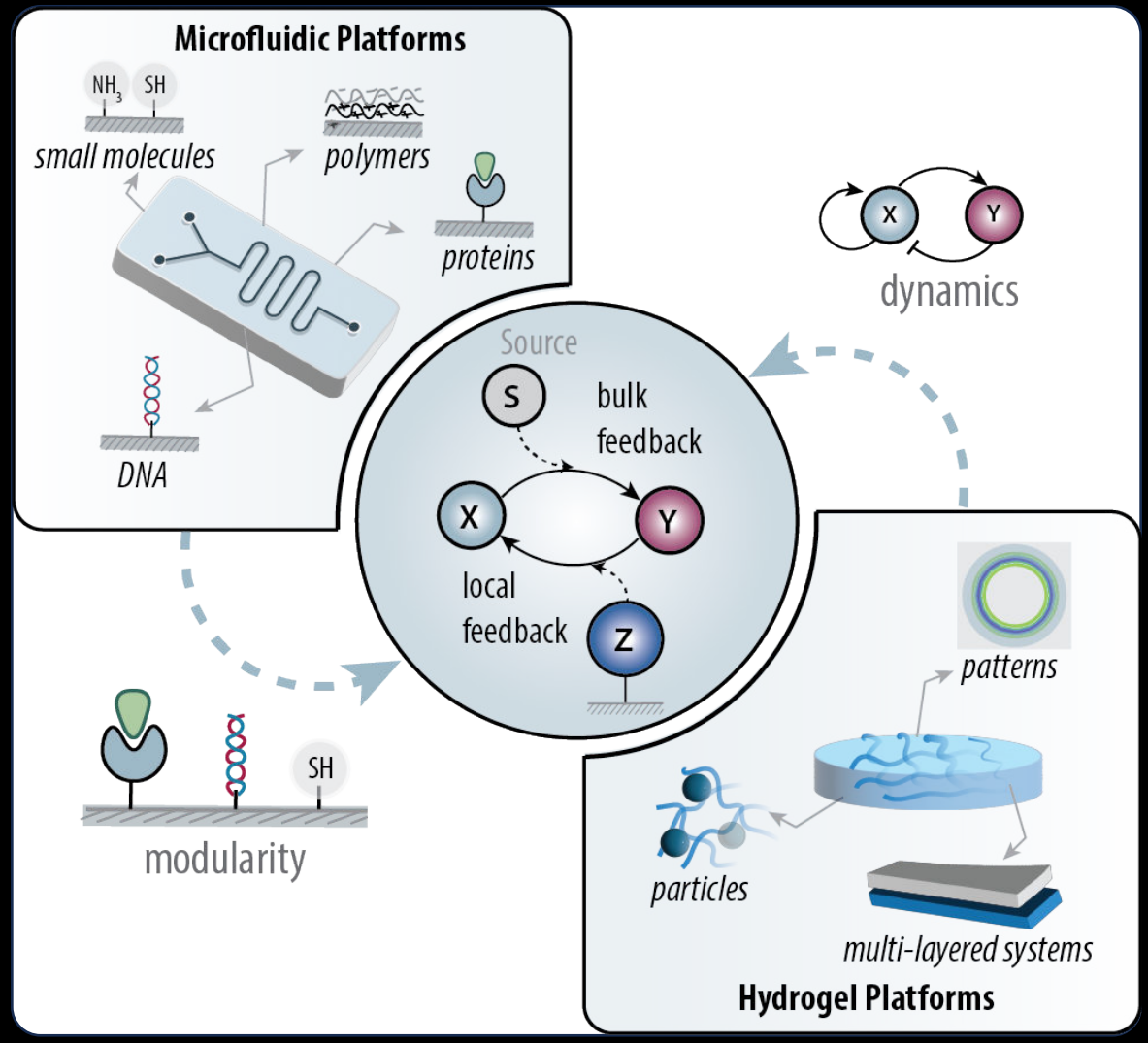


Koyuncu, A. H. *et al. ChemSystemsChem* **2024**



Tyumina, A.# & **Vasylkiv, I.#** *et al. JACS* **2026**

Towards Chemical Information Processing in CRN-based circuits



Koyuncu, A. H.; Wong, A. S. Y.
Under review

Rekenen met molekulen alleen mogelijk, indien

1. Er geen evenwicht optreedt
2. Netwerken gevormd

Continue vorming en afbraak is essentieel

- **Geheugen**, welke tijdelijk is en afhankelijk van verleden
- **Rekenen**, welke tijdelijk van niet-lineare versnelling in autocatalyse
- **Informatieverwerking**, welke chemoselectief is en werkt op oppervlakte
- **…**

Rekenen met molekulen alleen mogelijk, indien

1. Er geen evenwicht optreedt
2. Netwerken gevormd

Continue vorming en afbraak is essentieel



Zelfde condities als oscillerende reacties!

- **Geheugen**, welke tijdelijk is en afhankelijk van verleden
- **Rekenen**, welke tijdelijk van niet-lineare versnelling in autocatalyse
- **Informatieverwerking**, welke chemoselectief is en werkt op oppervlakte
- …

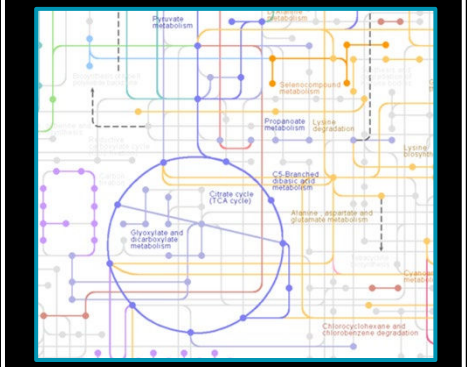
Inleiding



Focus:

Rekenen zonder brein

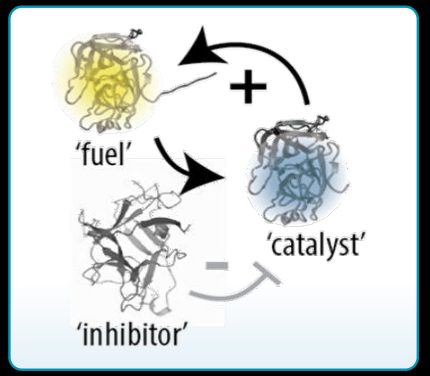
Kern 1

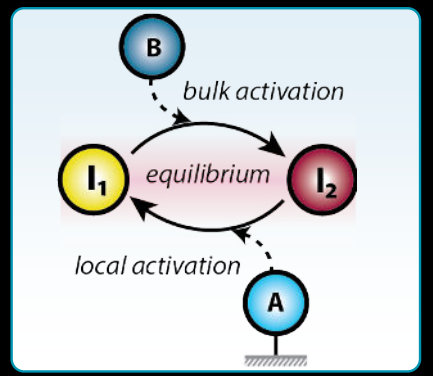


Focus:

Systeem chemie

Kern 2





Focus:

Rekenen met chemische netwerken

Kern 3

?

Focus:

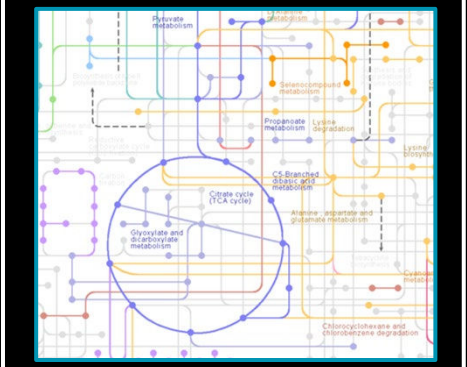
Inleiding



Focus:

Rekenen zonder brein

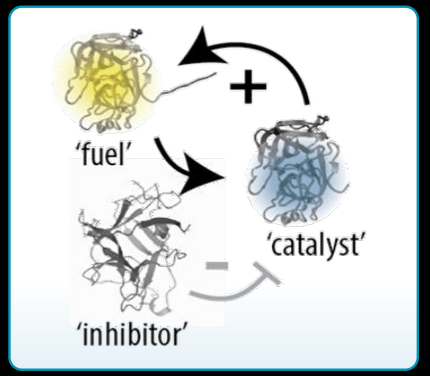
Kern 1

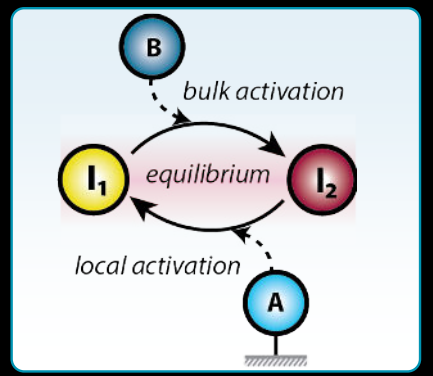


Focus:

Systeem chemie

Kern 2

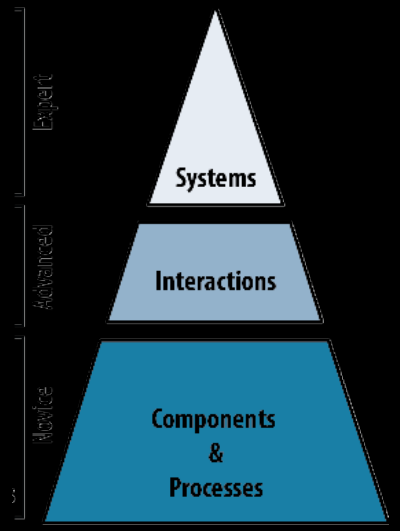




Focus:

Rekenen met chemische netwerken

Kern 3

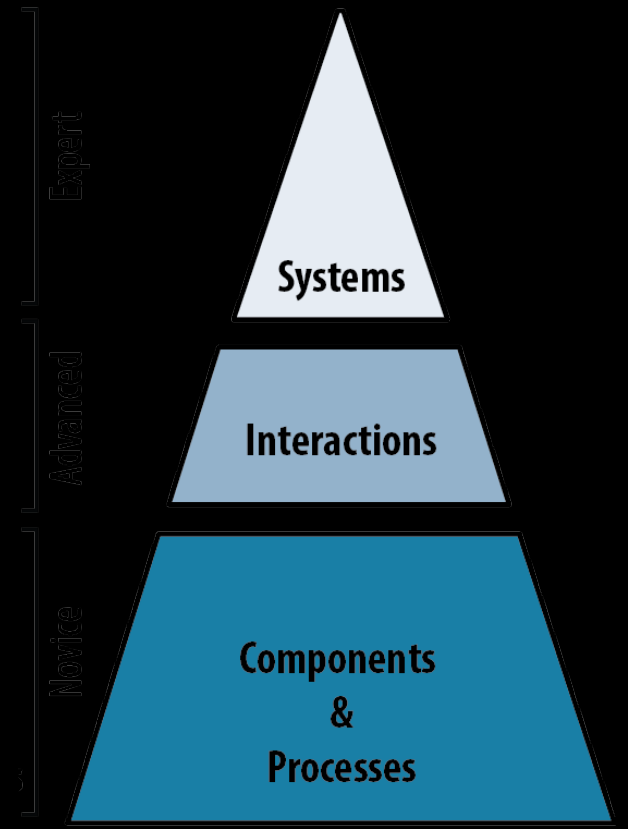


Focus:

Systeem denken

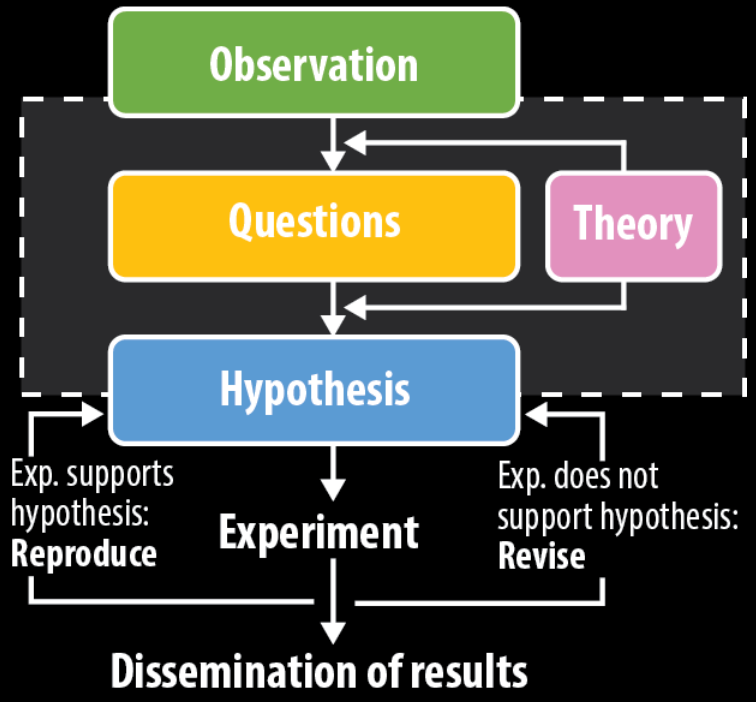
How can we educate Systems Thinking?

Systems Thinking



?

Design chemistry experiments

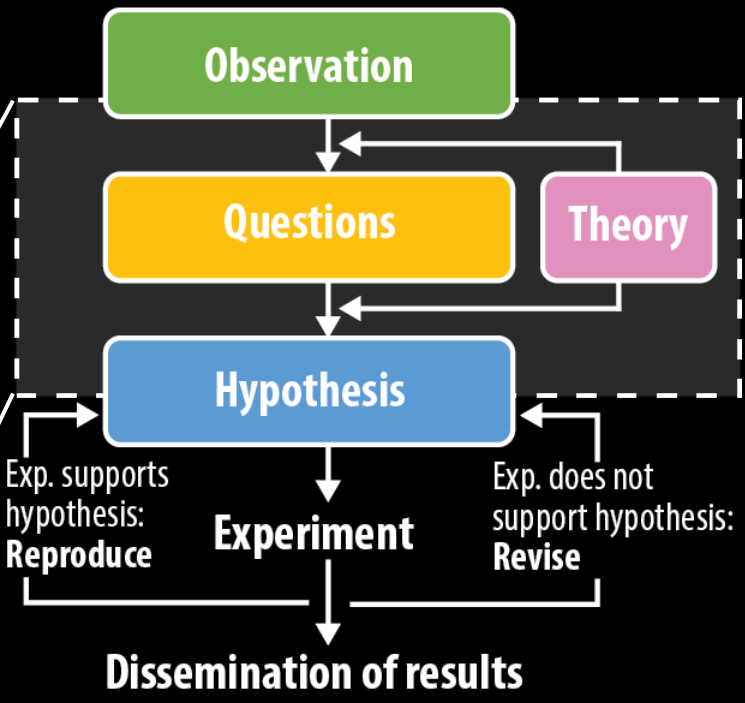


How can we educate Systems Thinking?

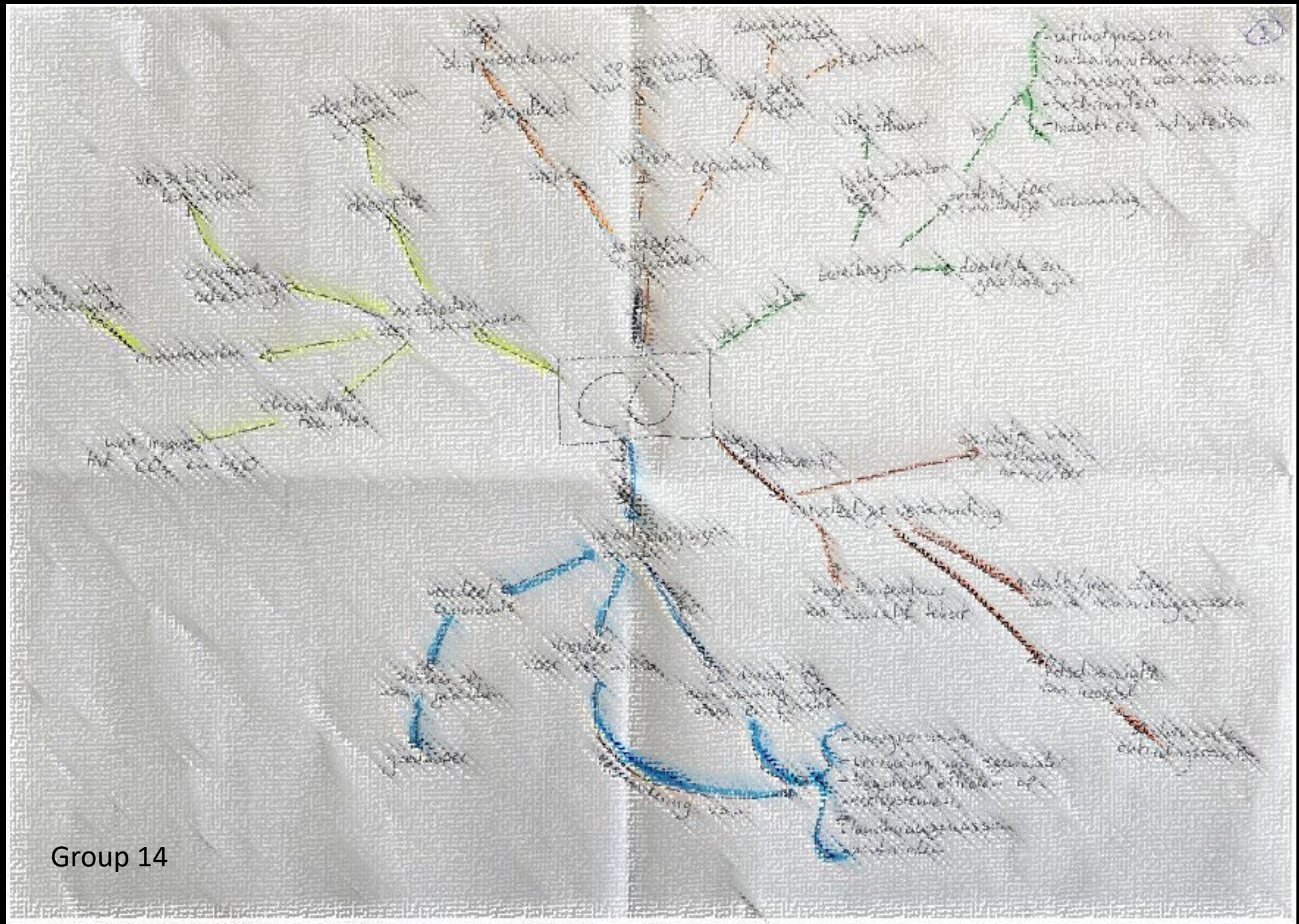
- Students should come up a hypothesis
- **But what grounds can they build a hypothesis?**

A Conceptual Model:

1. A tool for getting to a hypothesis
2. A tool to force iterations

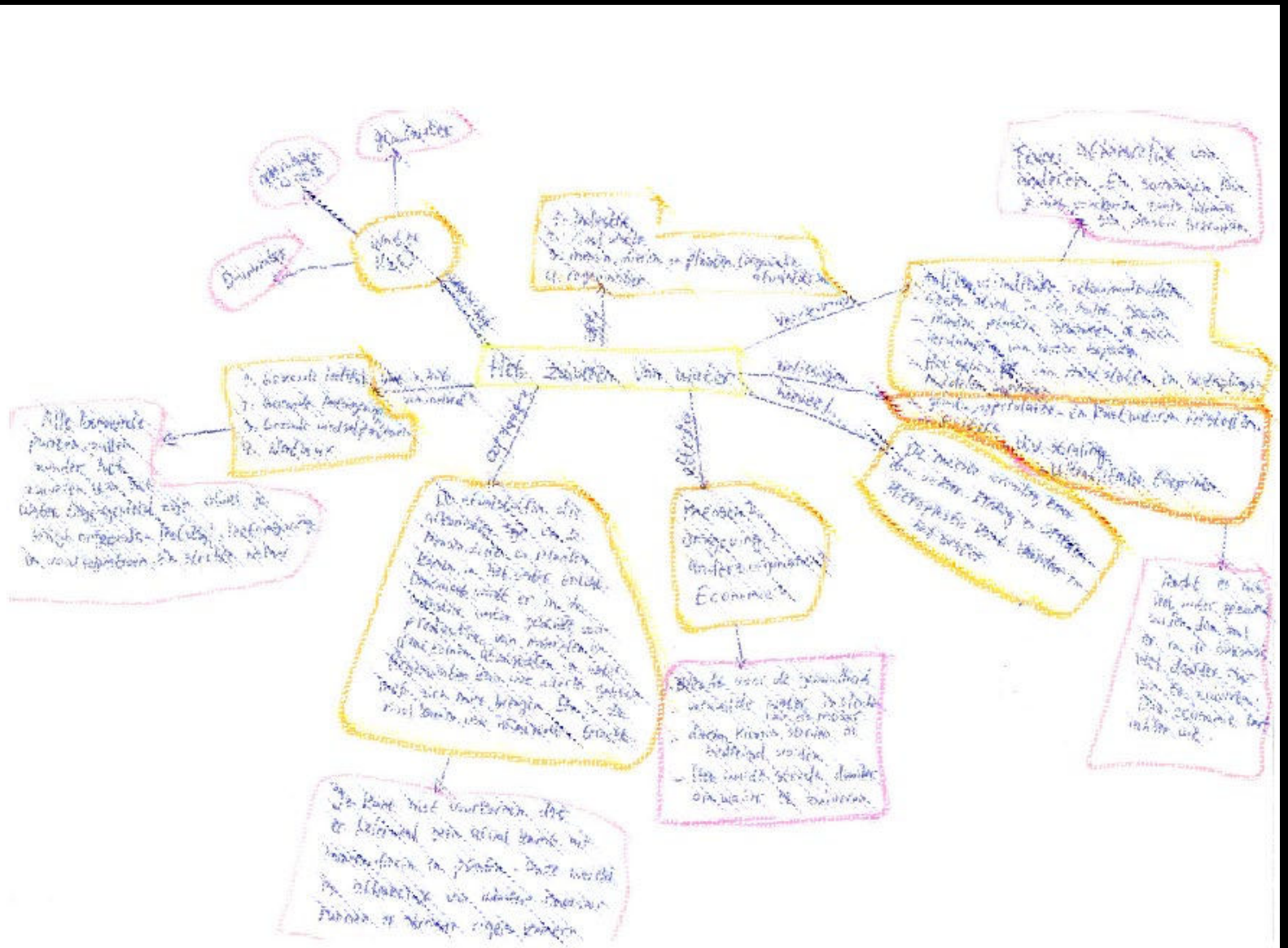


Krab-Hüsken,___, **Wong, A. S. Y.** *J. Chem. Educ.* **2023**



Group 14

UNIVERSITY
OF TWENTE.



Group 15

UNIVERSITY
OF TWENTE.

Can we also introduce conceptual modeling in highs school?

“First, we need new learning materials”



Lieke Pieters

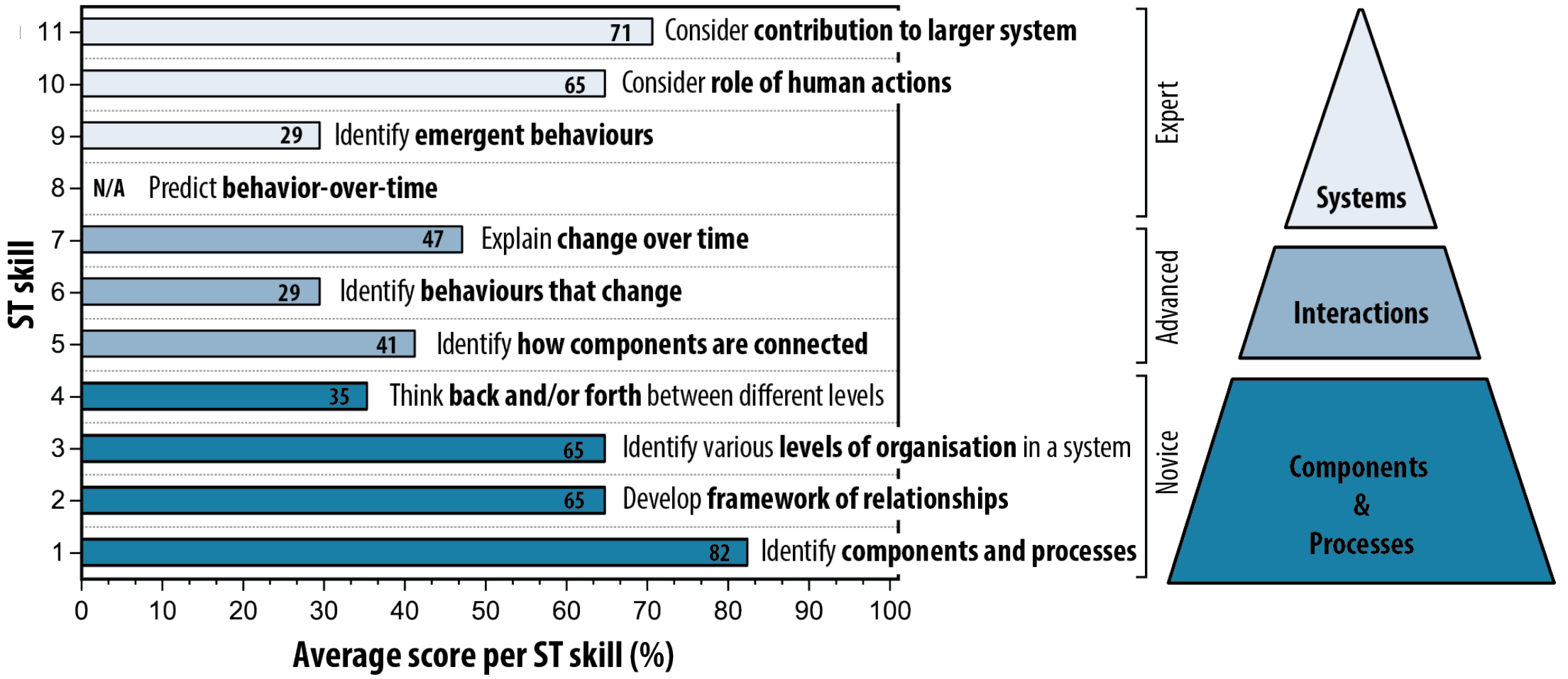
	School			
	1	2	3	4
Teacher (6)	A	B	C & D	E & F
Classes (8)	8th grade 9th grade	2x 9th grade	2x 9th grade	2x 8th grade
Lessons	5	4	5	4
Students (151)	8th grade: 20 9th grade: 19	20 & 22	21 & 15	20 & 14
Observations (4)	8th grade 9th grade	-	9th grade	8th grade
Questionnaire (128)	8th grade:17 9th grade:19	9th grade:36	9th grade:36	8th grade:20
Interview students (20)	8th grade:4 9th grade:4	-	9th grade(A):2 9th grade(B):5	8th grade:5
Number of submitted final Conceptual Models (27)	8th grade:4 9th grade:3	9th grade:10	9th grade:5	8th grade:5
Number of Conceptual Models assessed for evaluating systems thinking skills(17)	8th grade:3 9th grade:2	9th grade:5	9th grade:3	8th grade:4

Pieters, L.; Visser, T. C.*; **Wong, A. S. Y.*** *J. Chem. Educ.* **2026**

Identifying ST skills in conceptual models

ST Skill			Response (group)																	Average	
Category	#	Description	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	per skill	per level
Expert	11	Consider how the system under study might be a component of and/or contribute to the behaviours of a larger system	X	X	X		X	X	X	X		X				X	X	X	X	71%	42 ± 29%
	10	Consider the role of human actions on current and future systemlevel behaviours	X	X	X				X			X	X	X	X		X	X	X	65%	
	9	Identify, examine, and/or explain (to the extent possible) emergent system-level behaviours			X				X	X				X		X				29%	
	8	Use behavior-over-time trends under one set of conditions to make predictions about behavior-over-time trends under another set of conditions.																		0%	
Advanced	7	Explain and/or predict how a system has changed and will change over time	X	X				X	X		X		X				X		X	47%	39 ± 7%
	6	Identify behaviours that change over time		X											X	X	X		X	29%	
	5	Identify how components of a system are connected	X	X					X	X	X					X			X	41%	
Novice	4	Think back and/or forth between different levels of organisation in a system				X				X	X					X	x		X	35%	62 ± 17%
	3	Identify various levels of organisation in a system	X	X	X		X		X			X			X	X	X	X	X	65%	
	2	Organize components and place them within a framework of relationships	X	X	X		X		X			X			X	X	X	X	X	65%	
	1	Identify the individual components and processes within a system	X	X	X		X	X	X	X		X	X	X		X	X	X	X	82%	
Average number of ST skills applied per group			7	8	6	1	4	3	8	5	3	5	3	3	4	8	8	5	9	5.3	48%

Identifying ST skills in conceptual models



Pieters, L.; Visser, T. C.*; **Wong, A. S. Y.*** *J. Chem. Educ.* **(2026)**

Main Findings in *J. Chem. Educ.* **2023 & 2026**

CM skills can be developed at the start of a university curriculum & before

Assessment:

- Ability to search the relevant literature
- Ability to cooperate effectively with their group
- Ability to report a problem statement and the proposed solution(s)

Value of Conceptual Modeling:

- Deepen student learning experiences
- Alleviate student workload
- Improve student-teacher interaction



TOP RATED PROGRAMME KEUZEGIDS 2027

Ranglijst Scheikunde en scheikundige technologie

	Feiten				Prestatie		Oordelen					
	Voertaal	Opleidingsvorm(en)	Numerus fixus?	Instroom	Doorstroom naar jaar 2	Diploma na 4 jaar	Inhoud	Docenten	Toetsing	Voorbereiding loopbaan	Sfeer	TOTAALSCORE
	en	vt	nee	74	•	-	+	+	+	+	+	70
	nl	vt	nee	121	•	•	+	•	+	•	•	69
!	nl	vt	nee	52	•	•	+	•	+	+	•	67
!	nl	vt	nee	52	•	•	+	•	+	+	•	67
	en	vt	nee	36	•	--	-	-	•	+	•	55
Scheikundige technologie												
Enschede UT - chemical science and engineering	en	vt	nee	59	•	•	++	++	++	++	++	88
Groningen RUG	en	vt	nee	56	•	•	•	+	++	•	•	68
Eindhoven TU/e - De Engelstalige variant van de opleiding heet chemical science and engineering en heeft numerus fixus. De Nederlandstalige variant heeft geen numerus fixus.	nl/en	vt	ja	175	•	-	•	•	+	+	•	61
Molecular science and technology												
Delft TUD !	nl	vt	nee	160	•	•	•	•	+	+	•	66
Leiden UL !	nl	vt	nee	160	•	•	•	•	+	+	•	66
Food technology												
Wageningen WUR	en	vt	nee	103	+	+	•	•	+	+	•	72

Voor toelichting en bronnen zie de icoontjes bovenaan deze tabel, de leeswijzer, de verantwoording, of de methodi

- = ondergemiddeld, • = gemiddeld, + = bovengemiddeld



De toekomstige generatie chemici ontstaat niet op de universiteit, maar in het klaslokaal van de middelbare school!

TOP RATED PROGRAMME KEUZEGIDS 2027

Ranglijst Scheikunde en scheikundige technologie

	Feiten				Prestatie		Oordelen					
	Voertaal	Opleidingsvorm(en)	Numerus fixus?	Instroom	Doorstroom naar jaar 2	Diploma na 4 jaar	Inhoud	Docenten	Toetsing	Voorbereiding loopbaan	Sfeer	TOTAALSCORE
	en	vt	nee	74	•	-	+	+	+	+	+	70
	nl	vt	nee	121	•	•	+	•	+	•	•	69
	nl	vt	nee	52	•	•	+	•	+	+	•	67
	nl	vt	nee	52	•	•	+	•	+	+	•	67
	en	vt	nee	36	•	--	-	-	•	+	•	55
engineering	en	vt	nee	59	•	•	++	++	++	++	++	88
van de opleiding heet chemical science and engineering en heeft numerus fixus. De Nederlandstalige variant heeft geen numerus fixus.	nl/en	vt	ja	175	•	-	•	•	+	+	•	61
Molecular science and technology												
Delft TUD	nl	vt	nee	160	•	•	•	•	+	+	•	66
Leiden UL	nl	vt	nee	160	•	•	•	•	+	+	•	66
Food technology												
Wageningen WUR	en	vt	nee	103	+	+	•	•	+	+	•	72

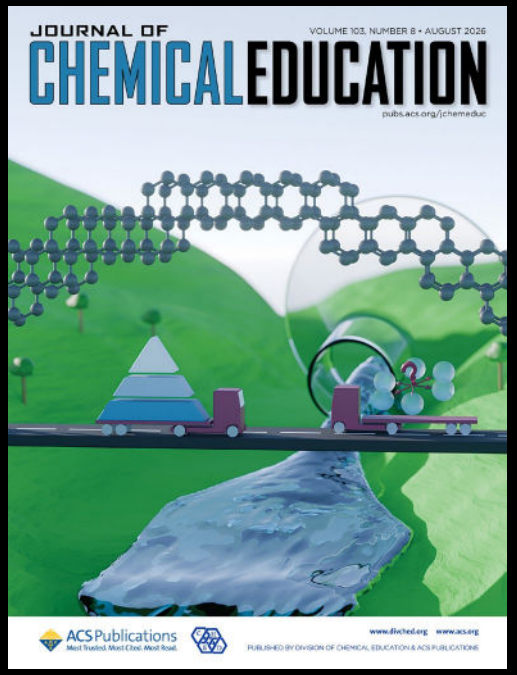
Voor toelichting en bronnen zie de icoontjes bovenaan deze tabel, de leeswijzer, de verantwoording, of de methodi

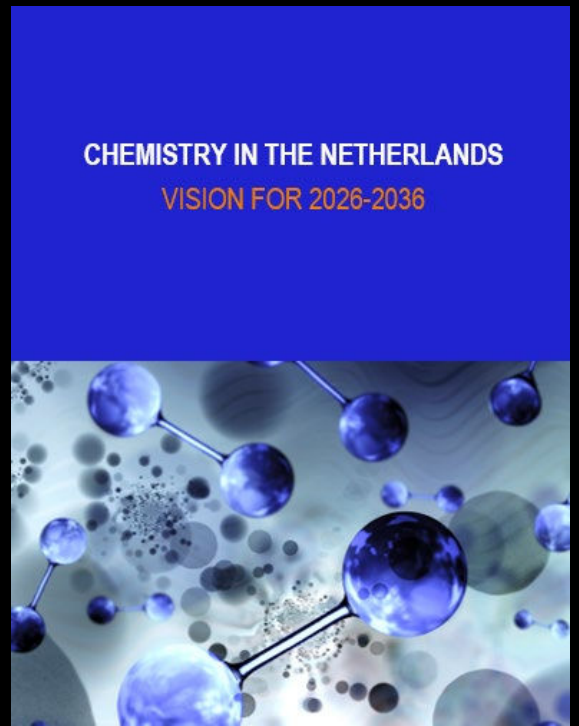
- = ondergemiddeld, • = gemiddeld, + = bovengemiddeld

Wat hebben we nodig voor een toekomst-bestending chemie?

Een brug slaan tussen middelbare scholen & universiteiten:

Pieters, L.; Visser, T. C.*; **Wong, A. S. Y.*** *J. Chem. Educ.* **2026**





o.a. een duurzaam behoud van docenten

Rutjes, F. P. J. T., Kamperman, M. M. G., Koper, M. T. M., Meijerink, A., **Wong, A. S. Y.**, Chemistry In the Netherlands, Vision for 2026-2036. Dutch Chemistry Council.

Stelling:

Chemie wordt niet alleen bepaald door wat we onderwijzen,
maar door hoe zichtbaar wij als ambassadeurs van ons vak zijn.

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