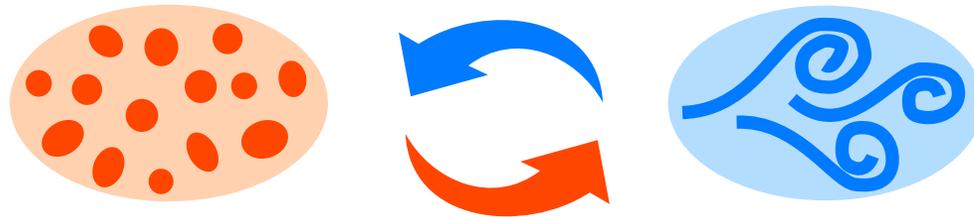


# PHYSICS OF MORPHOGENESIS

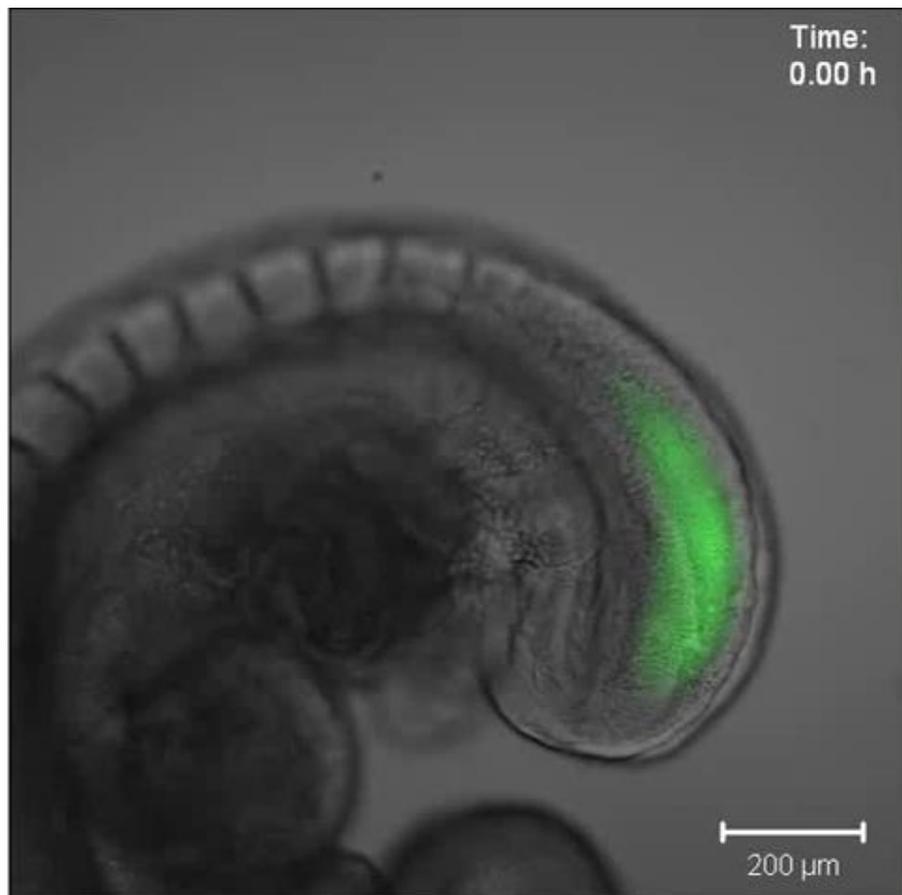
## VIA

### MECHANO-CHEMICAL COUPLINGS



Nicolas Lobato-Dauzier

# Mimicking embryogenesis to create life-like materials



## Mouse embryo morphogenesis

*Travelling wave of gene expression during segmentation*

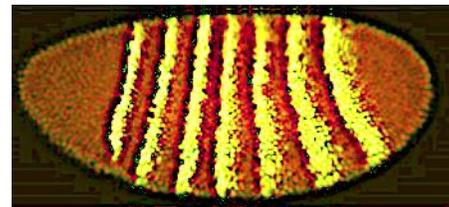
Aulehla et al., 2008. Nat Cell Biol

Complex **chemical reactions** lead to **large-scale motion**, patterning, differentiation, growth...

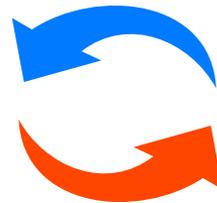
# MORPHOGENESIS VIA MECHANO-CHEMICAL COUPLINGS

**MORPHOGENESIS:**  
*Acquiring size and shape*

*Chemical  
motive*



*Credit: D Kong.*



*Mechanical  
behavior*



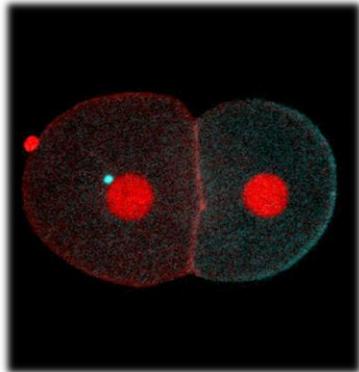
*Credit: D Tautz*

# MORPHOGENESIS VIA MECHANO-CHEMICAL COUPLINGS

## MORPHOGENESIS:

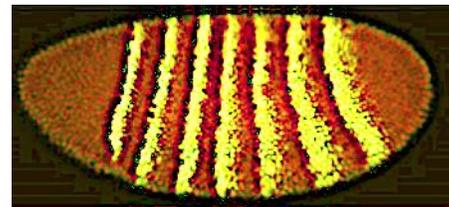
Acquiring *size and shape*

*in vivo*



Credit: N. Goehring

Chemical  
motive

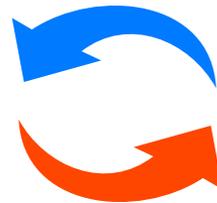


Credit: D Kong.

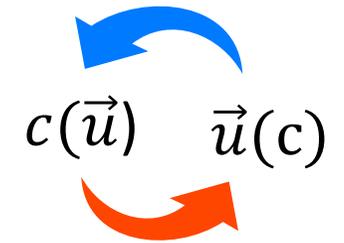
Mechanical  
behavior



Credit: D Tautz



*in silico*

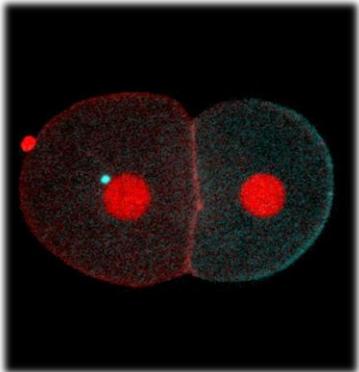


- How to build a **minimal system** allowing to program **mechano-chemical** couplings ?

# MORPHOGENESIS VIA MECHANO-CHEMICAL COUPLINGS

Target

*in vivo*

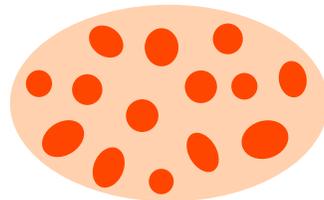


Credit: N. Goehring

✗ Independent control of parameters

*in vitro*

Chemical  
motive

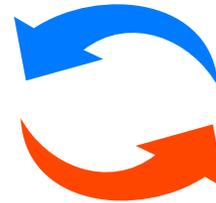


DNA

Mechanical  
behavior

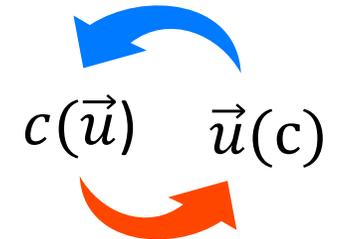


Active Gel



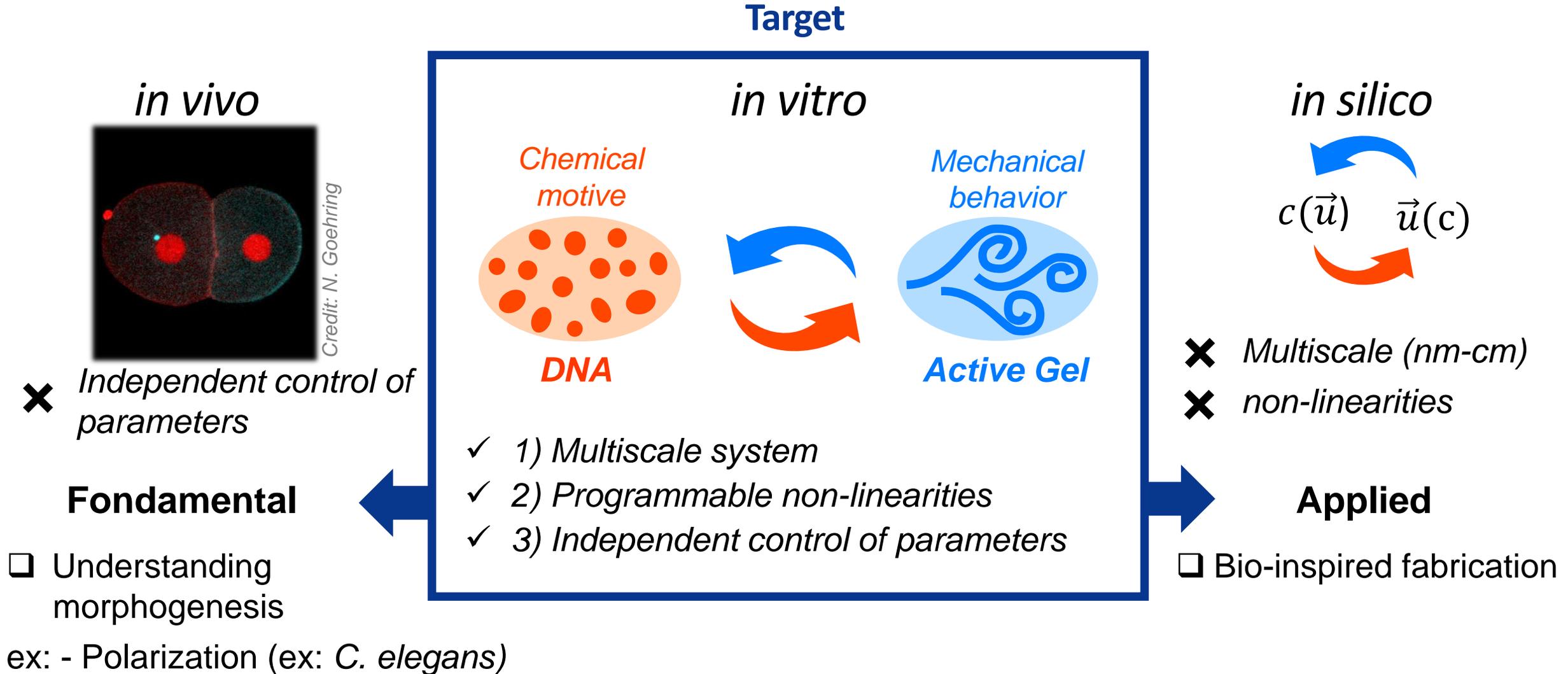
- ✓ 1) Multiscale system
- ✓ 2) Programmable non-linearities
- ✓ 3) Independent control of parameters

*in silico*



- ✗ Multiscale (nm-cm)
- ✗ non-linearities

# MORPHOGENESIS VIA MECHANO-CHEMICAL COUPLINGS



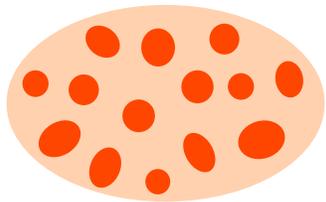
How do **mechano-chemical** couplings  
generate **robust self-organization** ?

*(beyond what **chemistry** or **mechanics** can produce alone)*

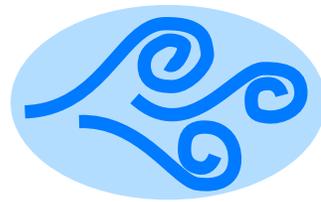
# MORPHOGENESIS VIA MECHANO-CHEMICAL COUPLINGS

## 1. State of the art

**Mechanical & Chemical**  
systems (separately)



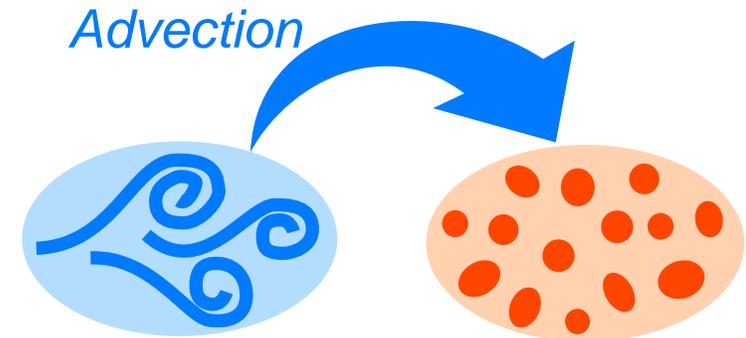
*DNA Nanotech.*



*Active gels*

## 2. Latest work

**Mechanics affect Chemistry**



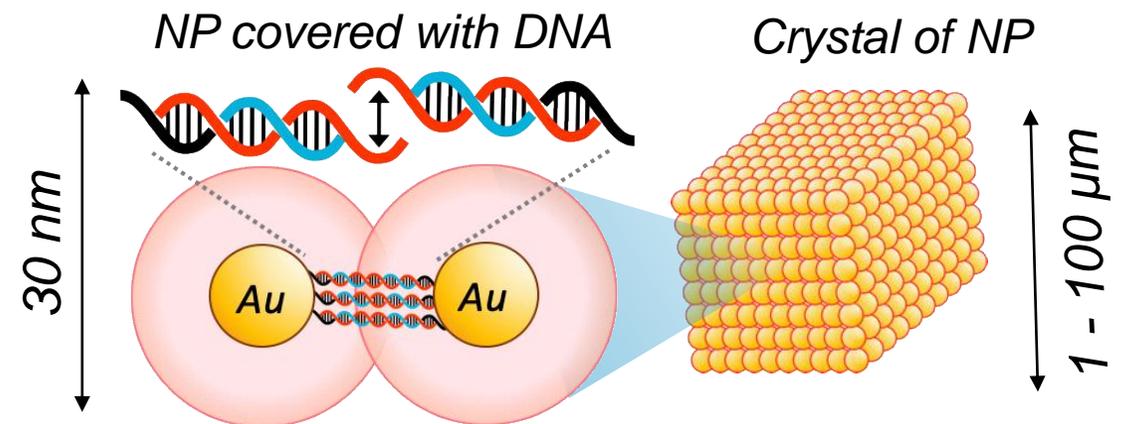
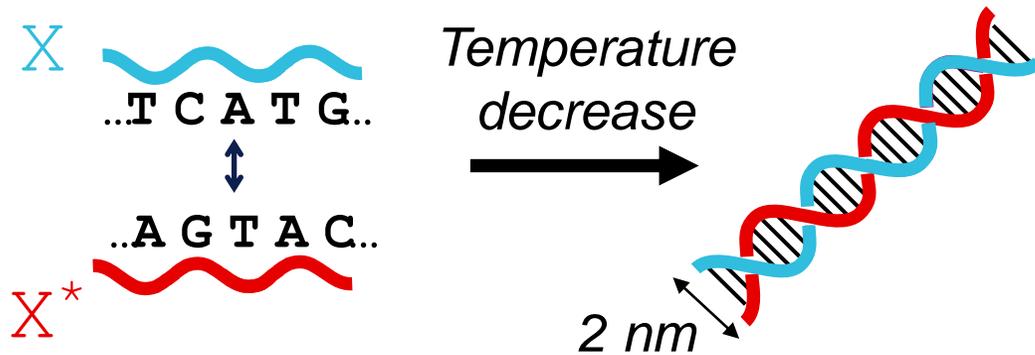
# DNA NANOTECHNOLOGY

*DNA is an information polymer enabling the formation nanostructures & reactions networks*

## 1. Pairing of complementary DNA



## Self-assembly of **basic bricks**

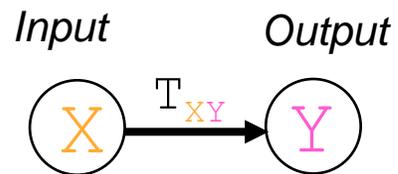
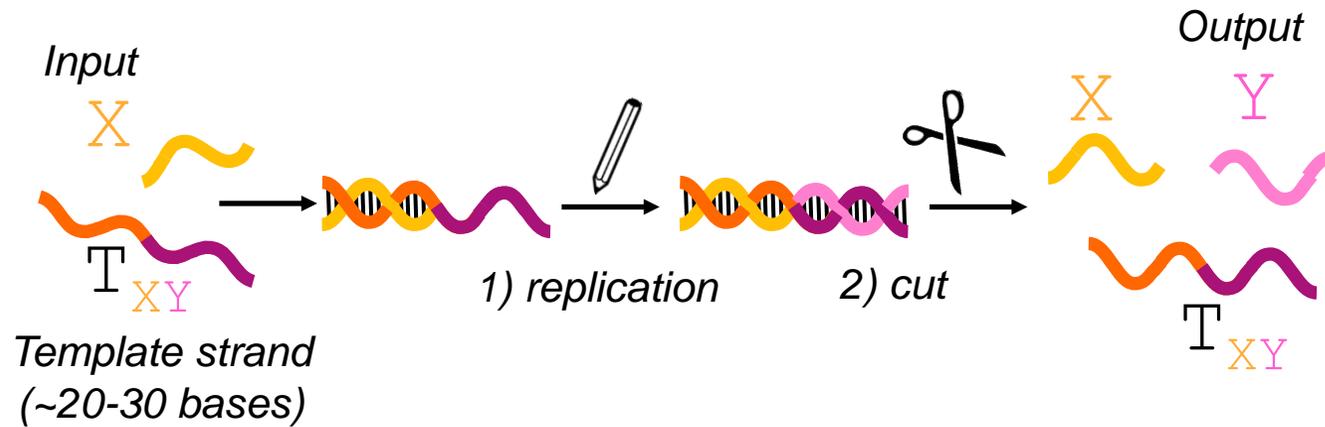


RJ Macfarlane, et al. (2011)

# DNA NANOTECHNOLOGY

*DNA is an informationnal polymer enabling the formation nanostructures & reactions networks*

## 2. Replication of DNA using a template

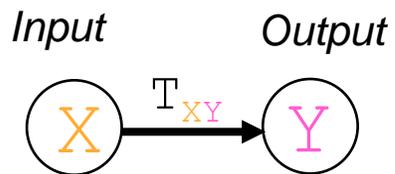
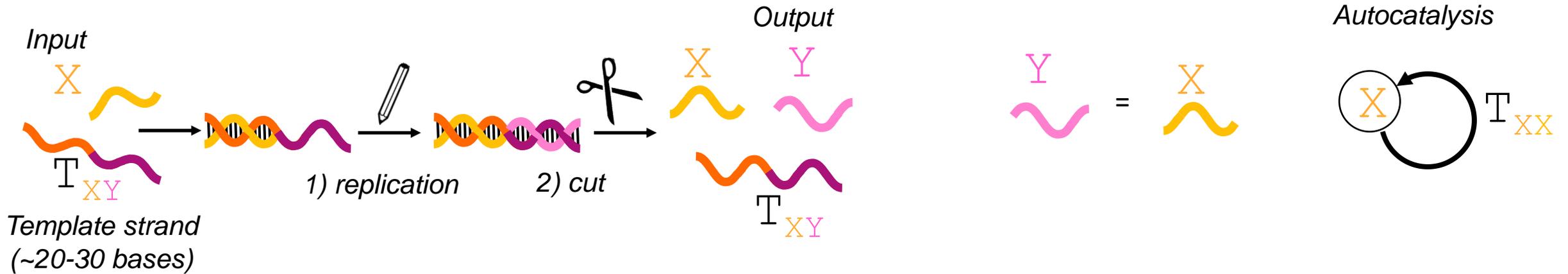


# DNA NANOTECHNOLOGY

*DNA is an informationnal polymer enabling the formation nanostructures & reactions networks*

## 2. Replication of DNA using a template

—————> Programming **reaction networks**

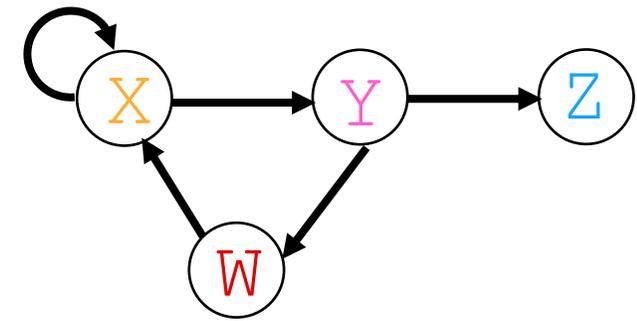
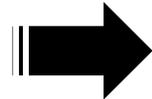
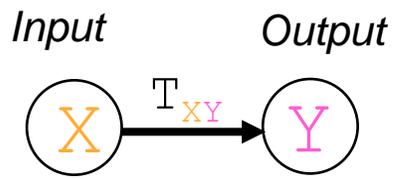
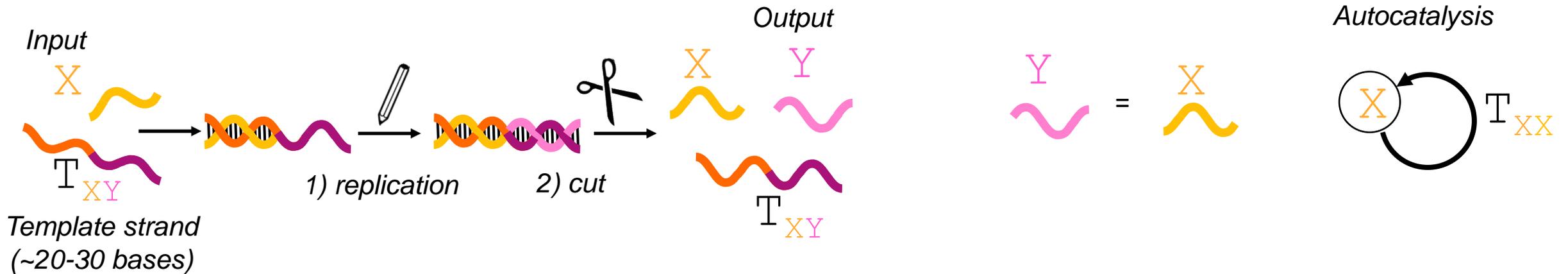


# DNA NANOTECHNOLOGY

*DNA is an informationnal polymer enabling the formation nanostructures & reactions networks*

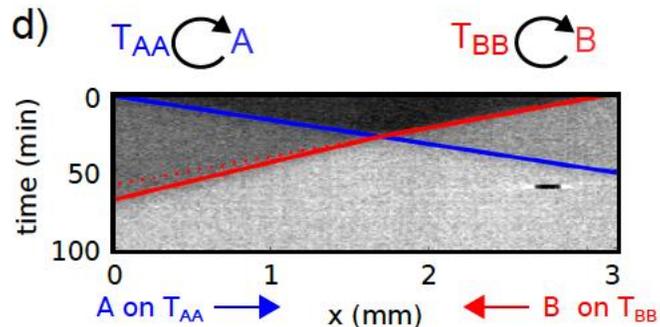
## 2. Replication of DNA using a template

→ Programming **reaction networks**



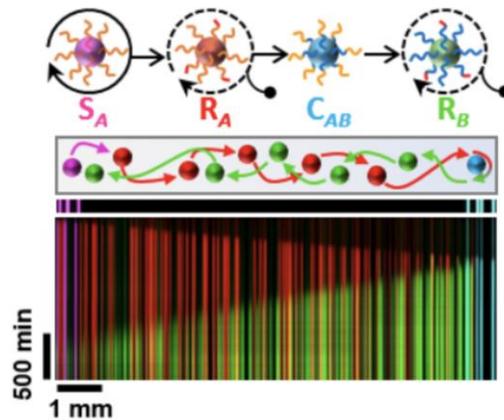
# DNA reaction networks produce a large variety of patterns

✓ *Traveling front*



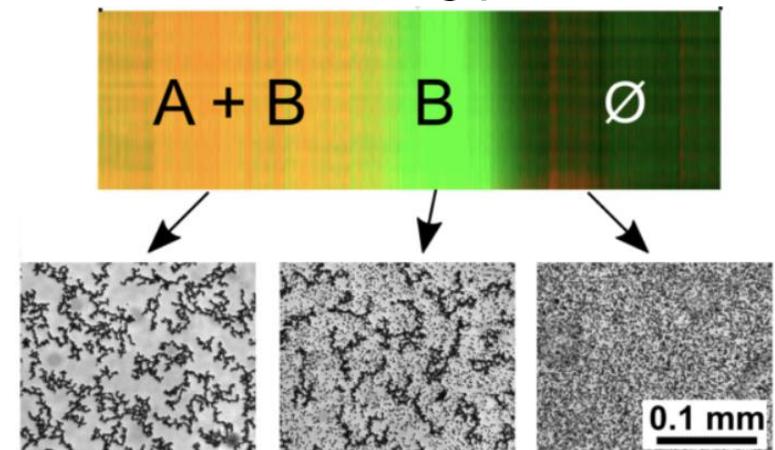
Zadorin, et al, *Physical review letters* (2015)

✓ *go-fetch front*



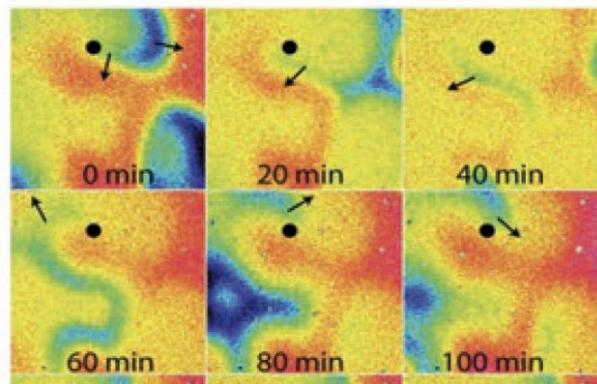
Gines, et al. *Nature nanotechnology* (2017)

✓ *french flag pattern*



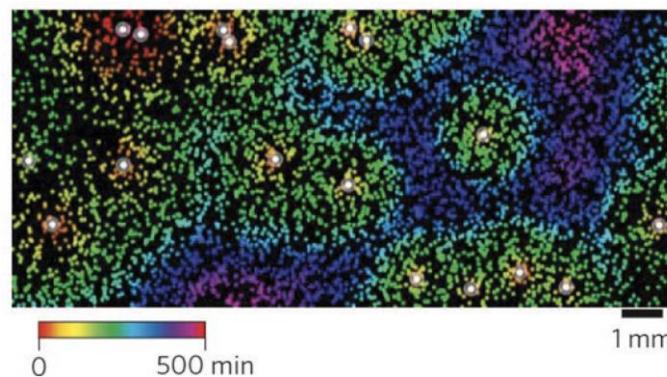
Zadorin, et al. *Nature chemistry* (2017)

✓ *wave and spiral*



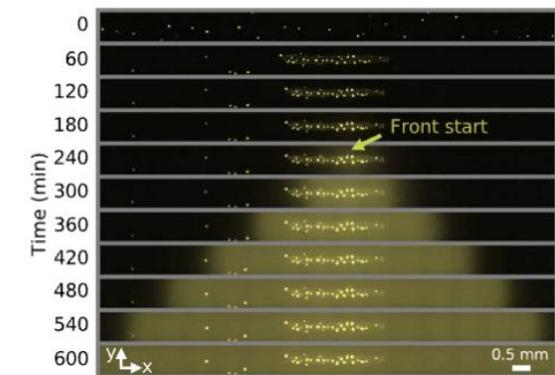
Padirac, et al. *JACS* (2013)

✓ *colony formation*



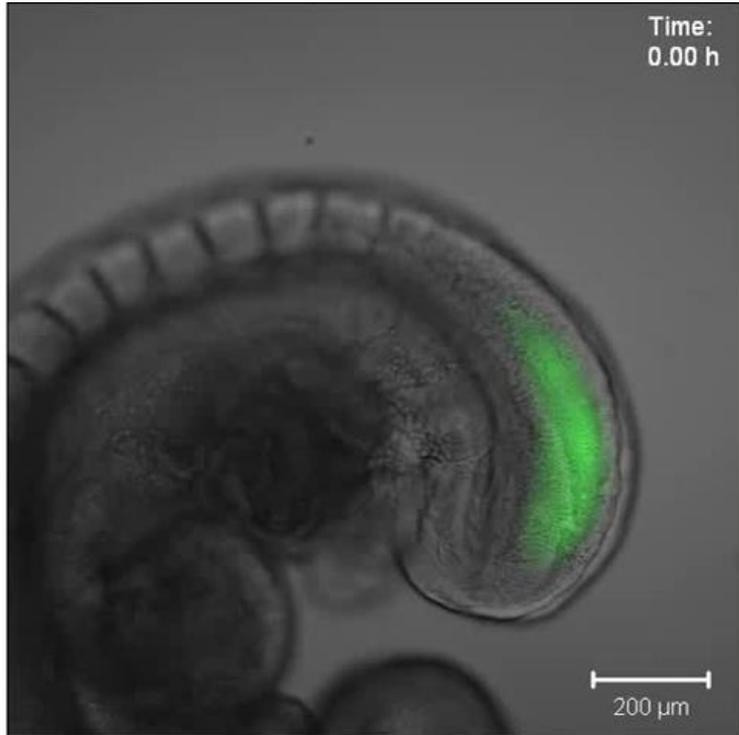
Gines, et al. *Nature nanotechnology* (2017)

✓ *Active gel triggered front*

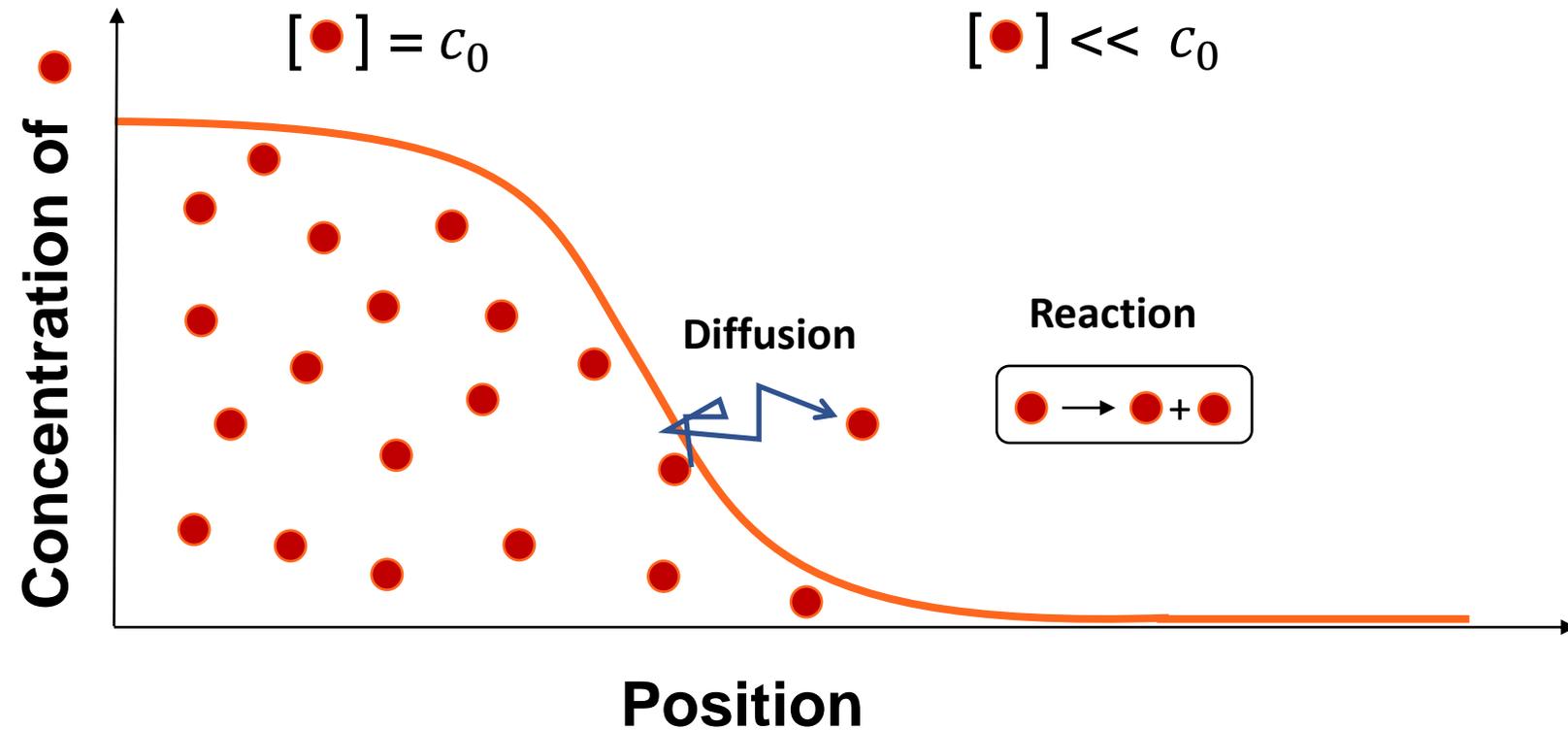


Senoussi, et al, *Science Advances* (2021).

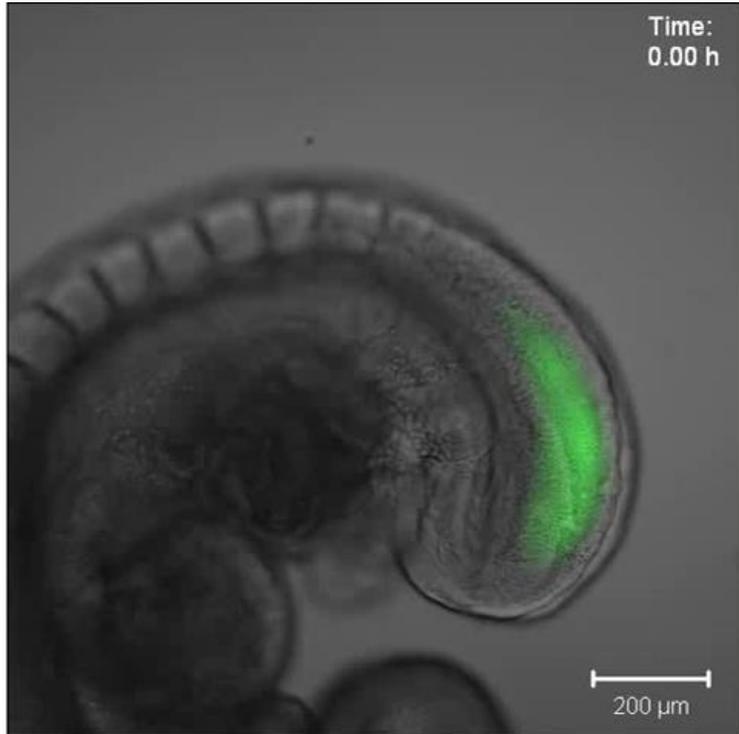
# RD fronts = simple but rich spatio-temporal pattern



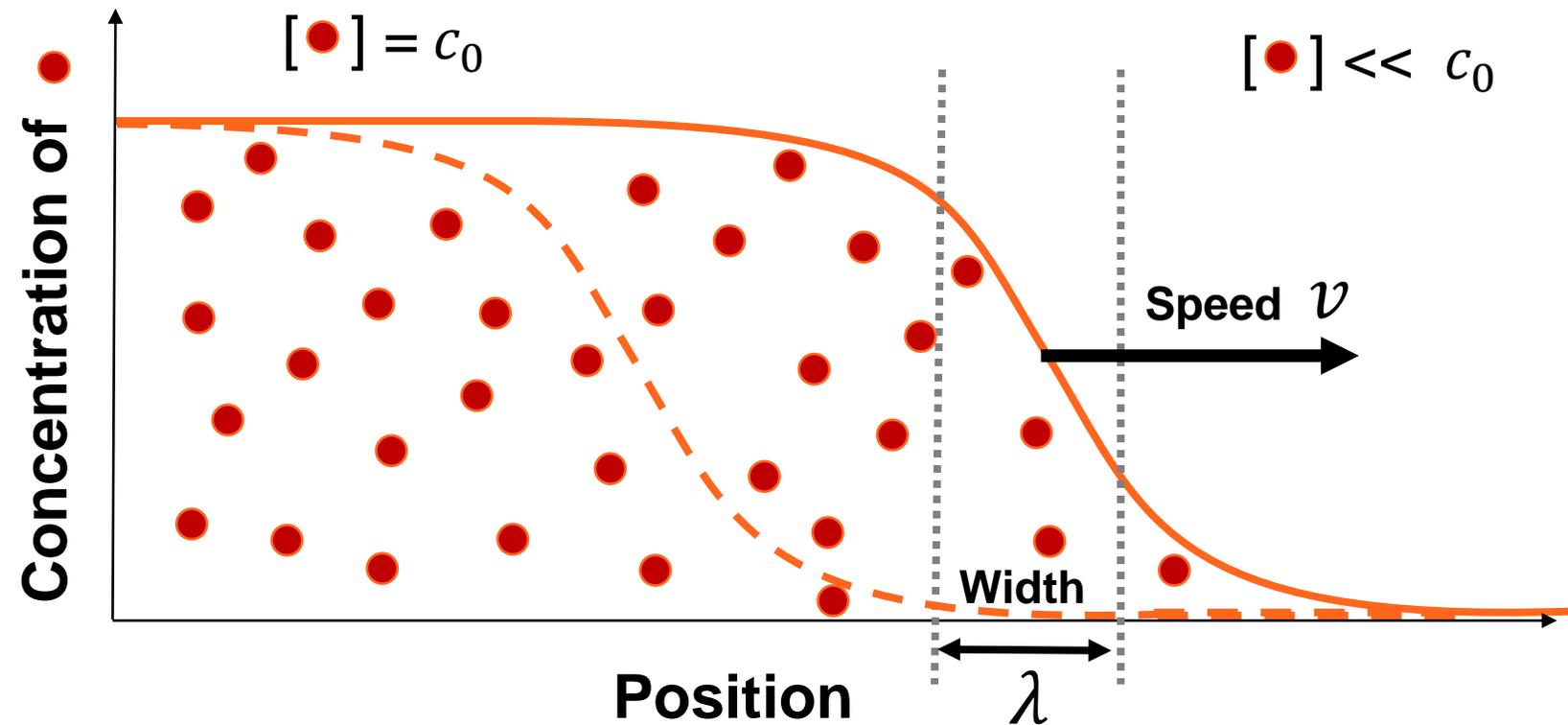
Aulehla et al., 2008. Nat Cell Biol



# RD fronts = simple but rich spatio-temporal pattern



Aulehla et al., 2008. Nat Cell Biol



*Size and sharpness of the pattern depend on  $v$  and  $\lambda$*

How to **enhance speed** ( $v_{RD}$ ) while maximizing **sharpness** ( $1/\lambda_{RD}$ ) ?

**How to overcome the limitations of  
Reaction-Diffusion kinetics ?**

*(Add advection)*

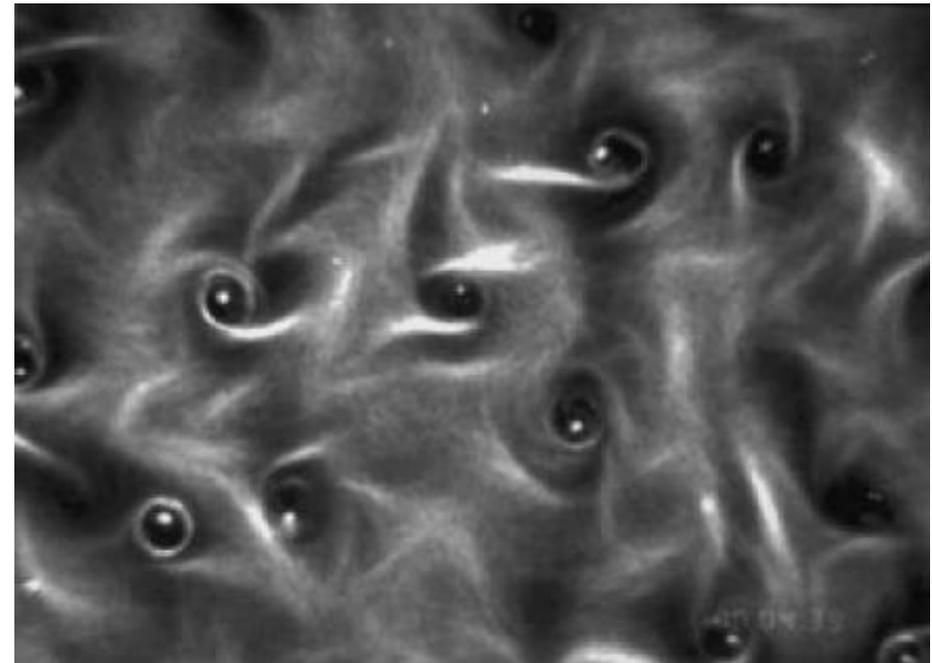
# Active matter:



*a large number of **active "agents"**  
which **consume energy**  
in order to **move** or exert **mechanical forces***



**A flock of birds.** (*credit: Owen Humphreys*)



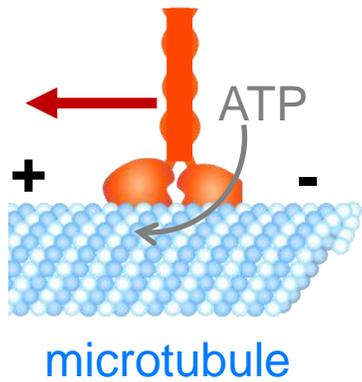
**Cytoskeletal filaments and molecular motors**  
Nédélec et al., Nature (1997)

# MECHANICS OF ACTIVE GELS

*How do microscopic forces lead to macroscopic behaviors ?*

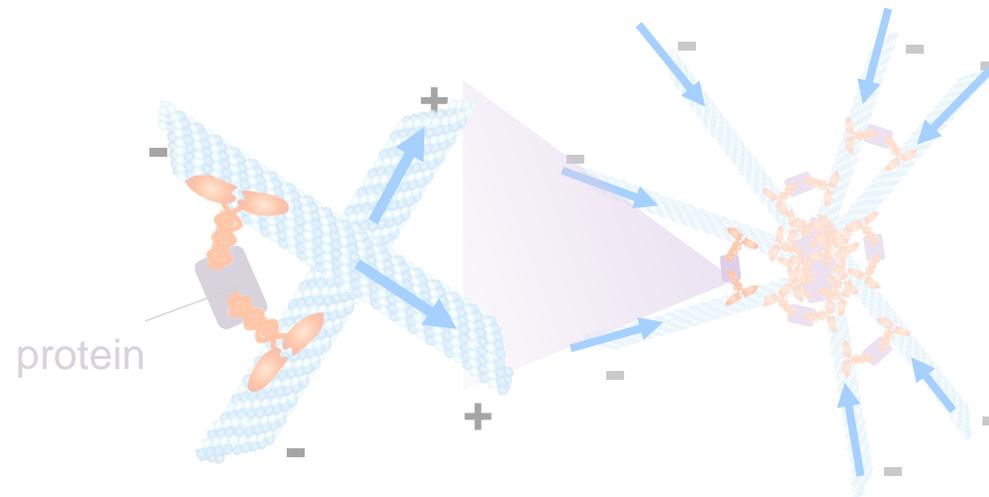
## 1. Kinesin + microtubules

Kinesin motor



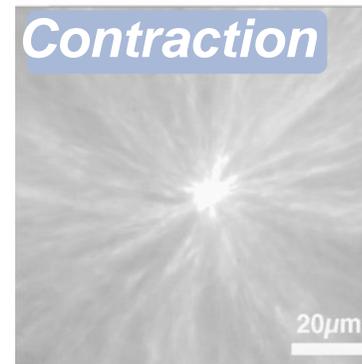
↳ Motion of **kinesin motors**

## 2. Connecting motors

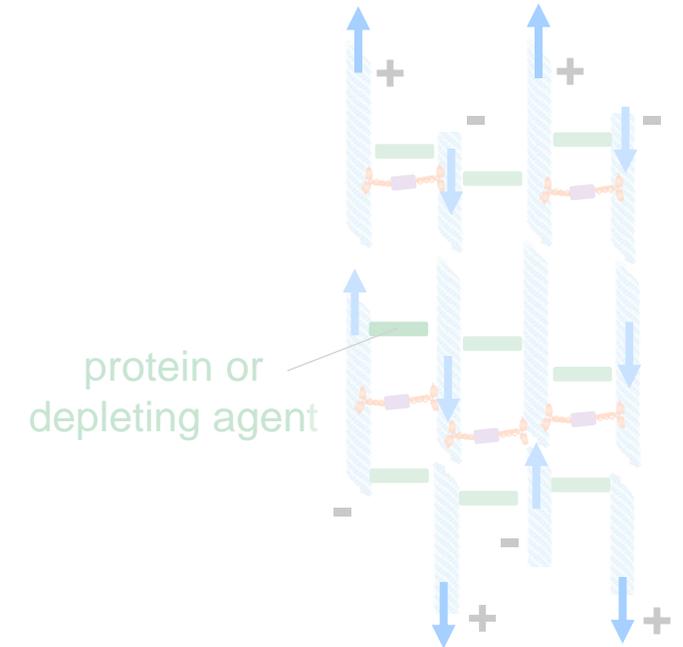


↳ Motion of **microtubules**

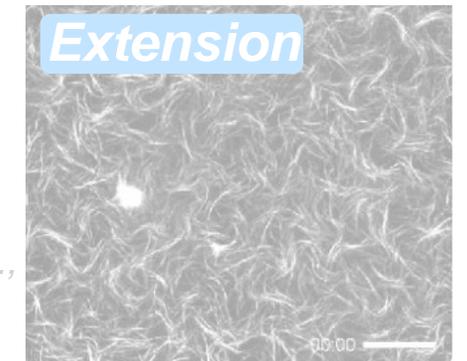
Nédélec *et al.*,  
(1997)



## 3. Bundles of microtubules



Sanchez *et al.*,  
(2012)

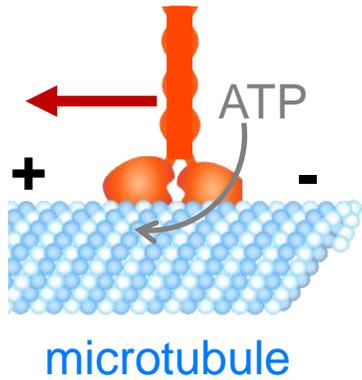


# MECHANICS OF ACTIVE GELS

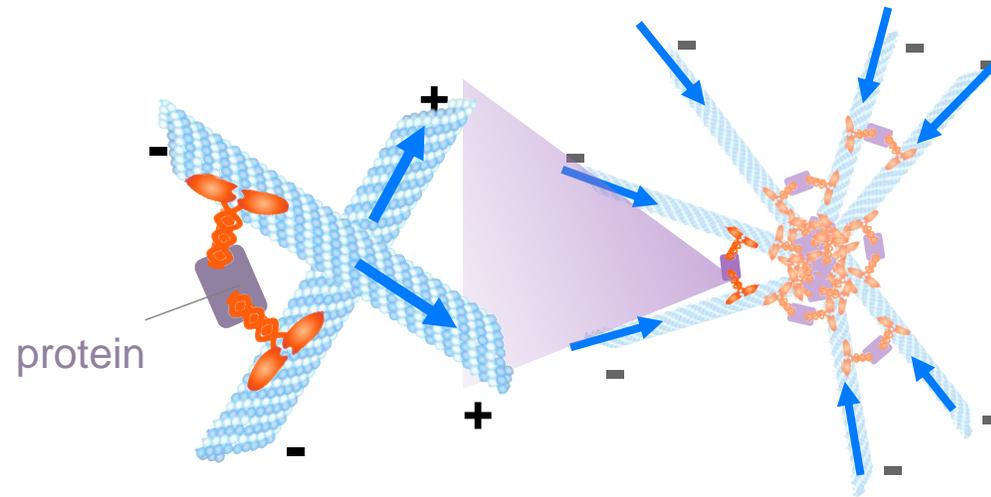
*How do microscopic forces lead to macroscopic behaviors ?*

## 1. Kinesin + microtubules

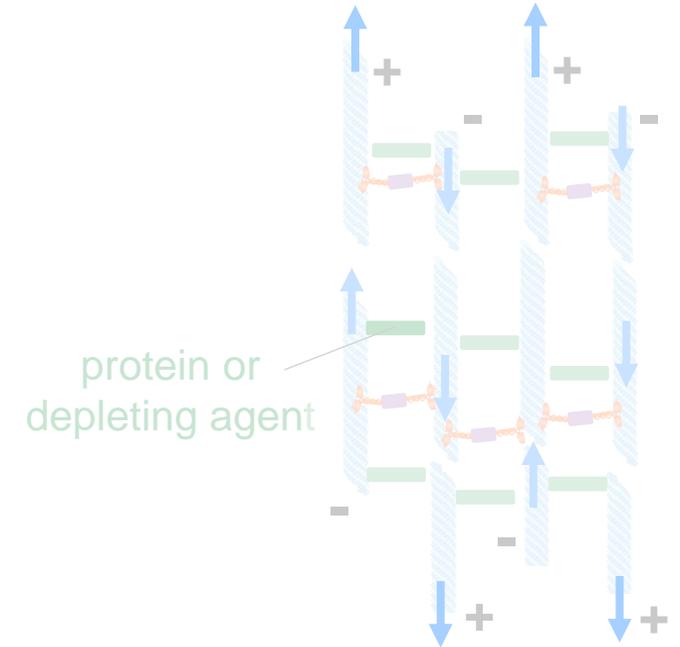
Kinesin motor



## 2. Connecting motors



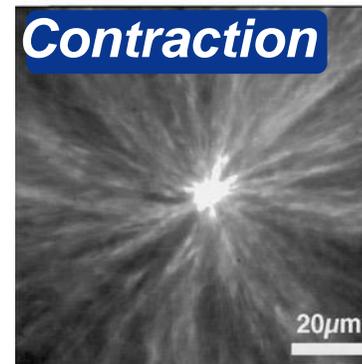
## 3. Bundles of microtubules



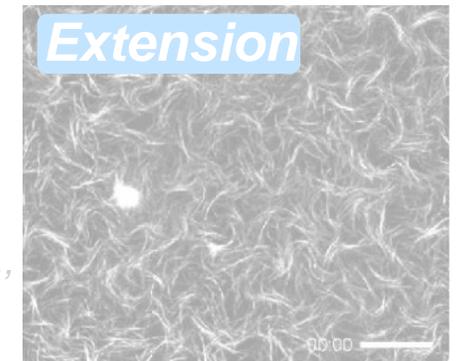
↳ Motion of **kinesin motors**

↳ Motion of **microtubules**

Nédélec *et al.*,  
(1997)



Sanchez *et al.*,  
(2012)

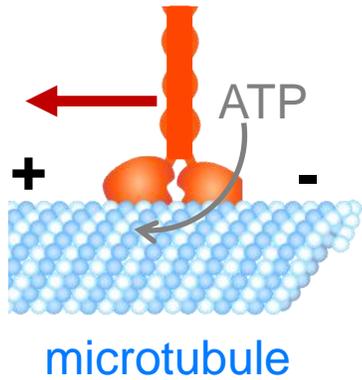


# MECHANICS OF ACTIVE GELS

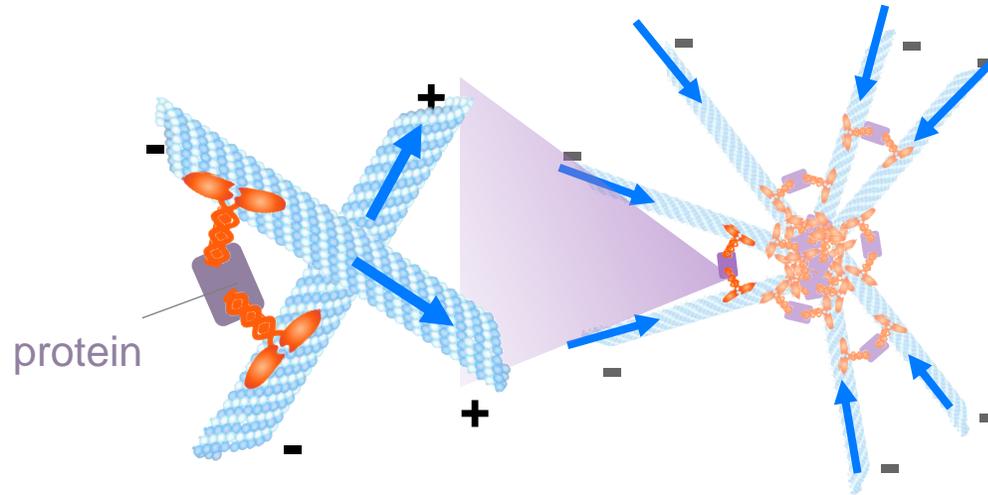
*How do microscopic forces lead to macroscopic behaviors ?*

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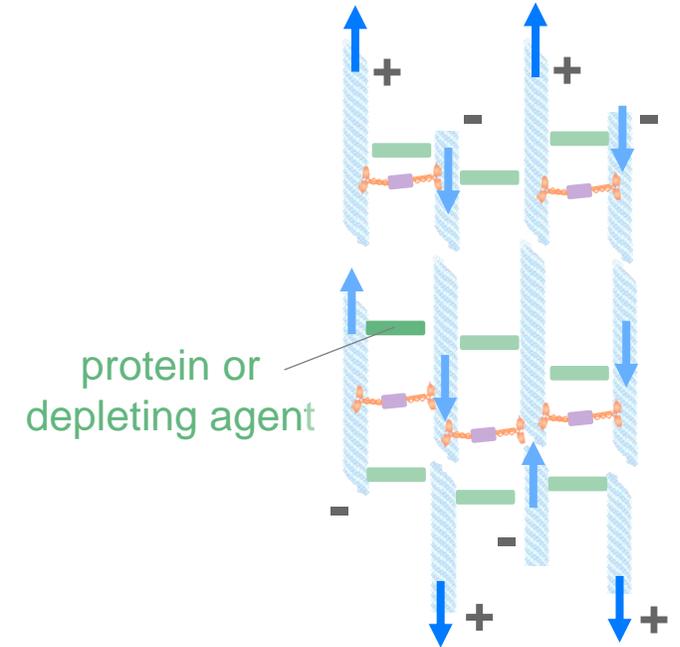
Kinesin motor



## 2. Connecting motors



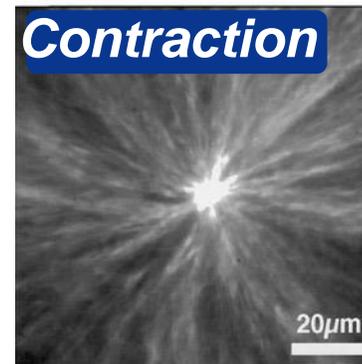
## 3. Bundles of microtubules



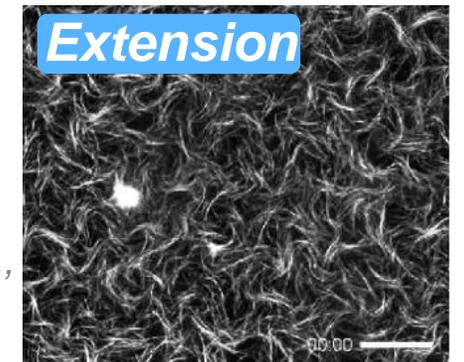
↳ Motion of **kinesin motors**

↳ Motion of **microtubules**

Nédélec *et al.*,  
(1997)

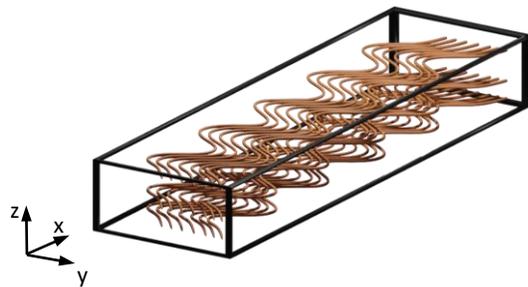
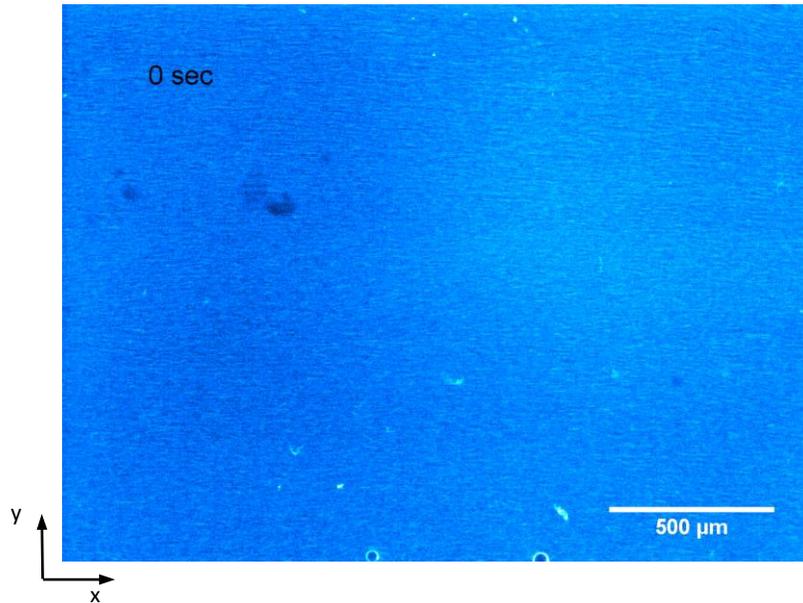


Sanchez *et al.*,  
(2012)



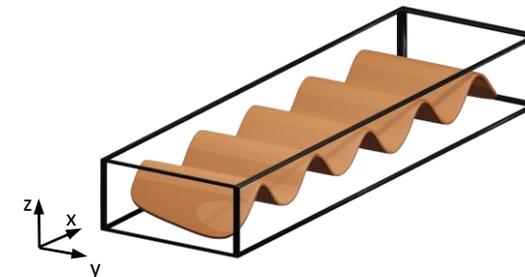
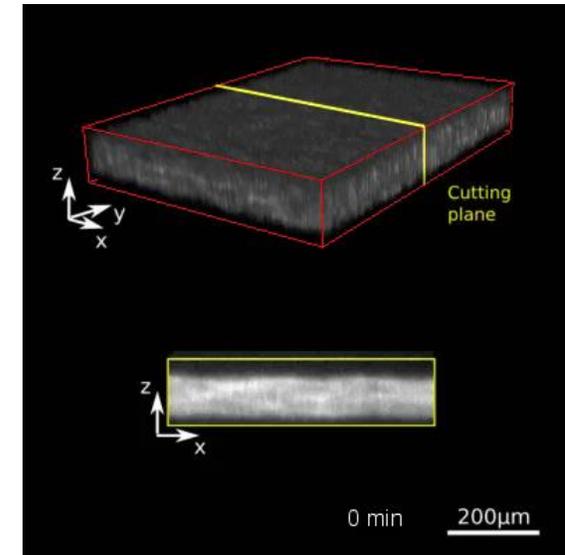
# A wide variety of self-organizations can be observed

## *Bending*



Chandrakar et al. PRL 2020  
In 2D geometry: Martínez-Prat et al. Nat. Phys. 2020

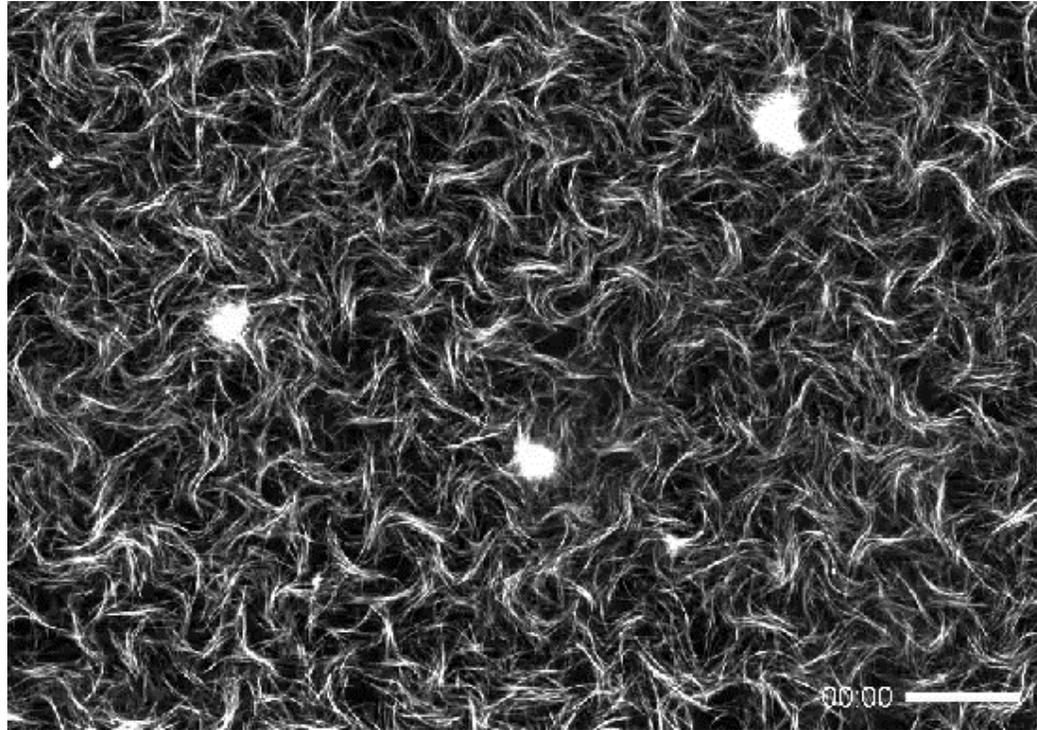
## *Buckling (out-of-plane bending)*



Senoussi et al. PNAS 2019  
Strubing et al. Nano Lett. 2020

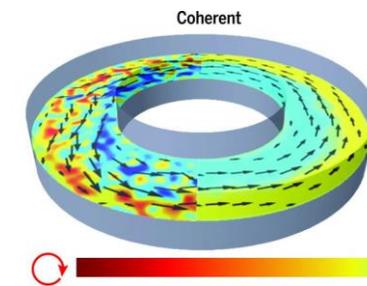
# A wide variety of self-organizations can be observed

Chaotic flow:



Sanchez et al. Nature 2012

150um



Wu et al. Science 2017

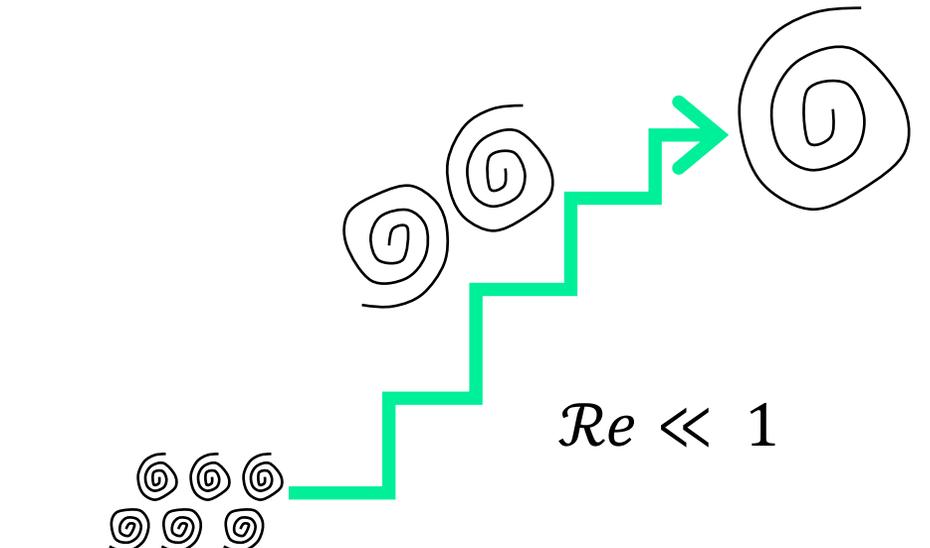
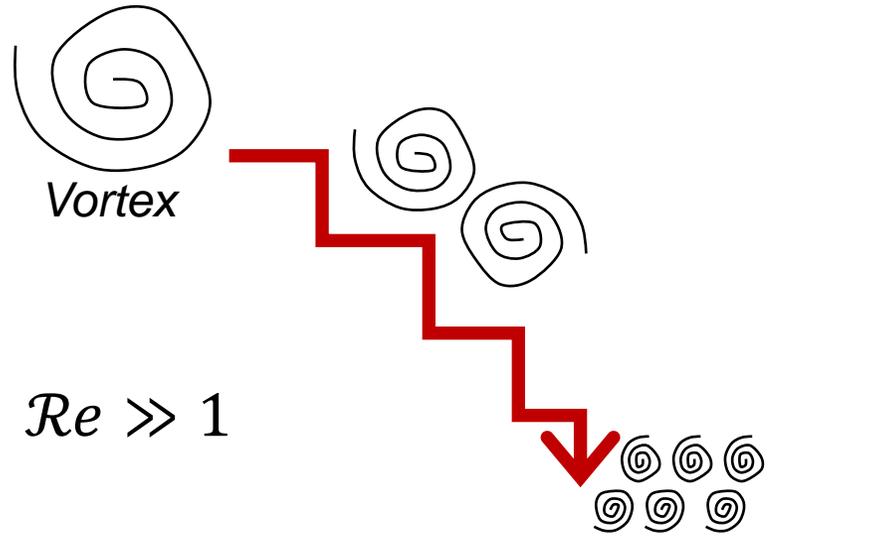
# Inertial turbulence

vs.

# Active turbulence

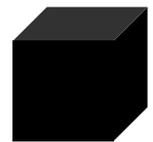
*Energy goes down*

*Energy goes up*



**Energy dissipation**  
(Mechanical → Thermal)

**Energy source**  
(Chemical → Mechanical)



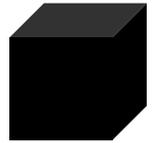
**Macro**



**micro**



**micro**



**Macro**

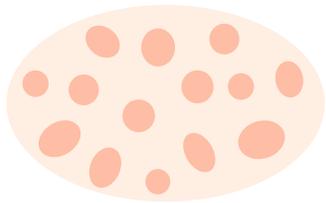


Can we **harness** active turbulence to **enhance** RD ?

# MORPHOGENESIS VIA **MECHANO-CHEMICAL** COUPLINGS

## 1. *State of the art*

**Mechanical & Chemical**  
systems (separately)



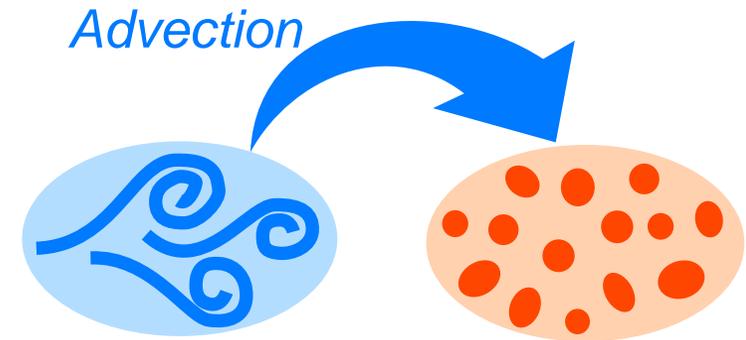
*DNA Nanotech.*



*Active gels*

## 2. *Latest work*

**Mechanics affect Chemistry**

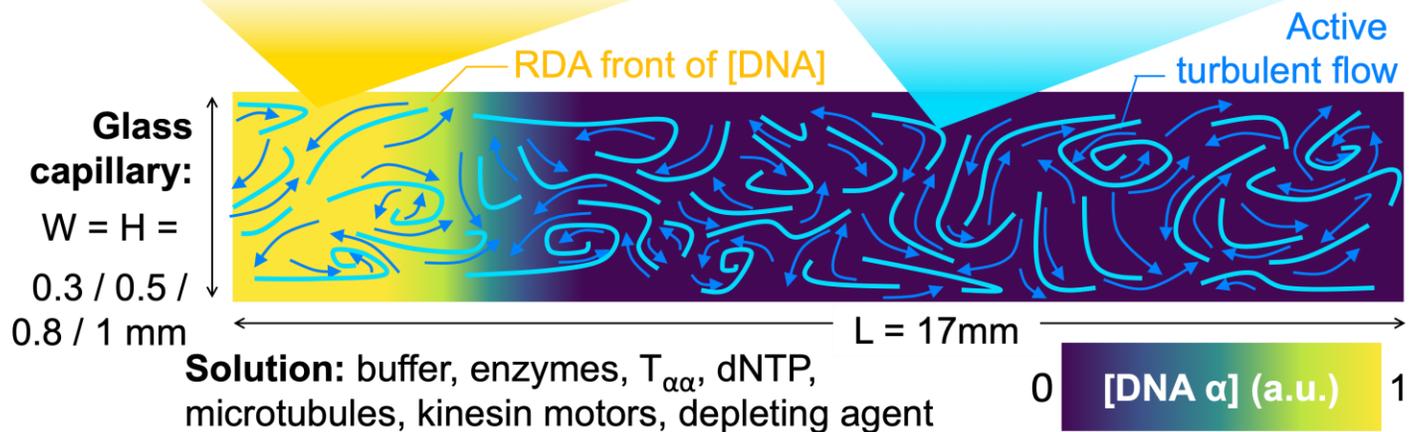
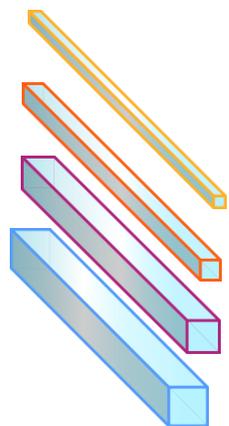
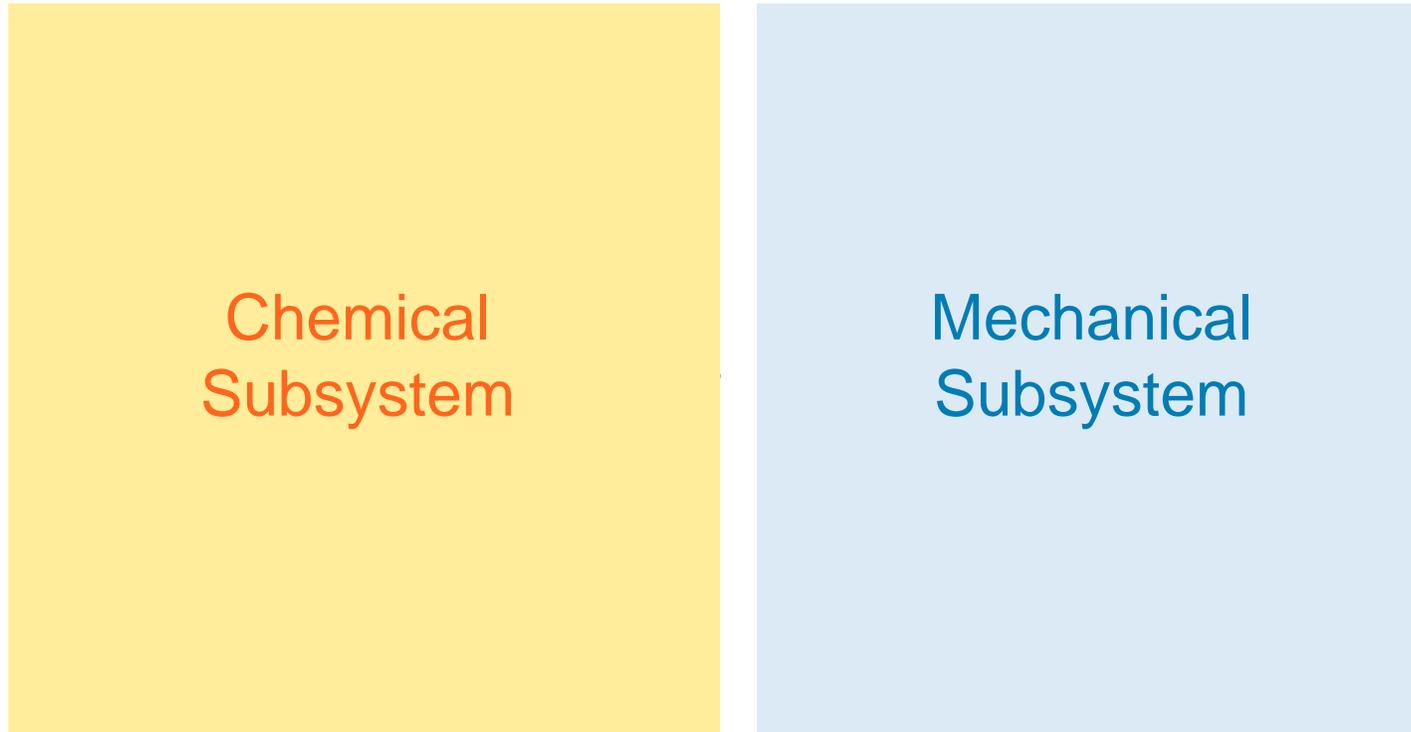


## Confinement Determines Transport of a Reaction-Diffusion Active Matter Front

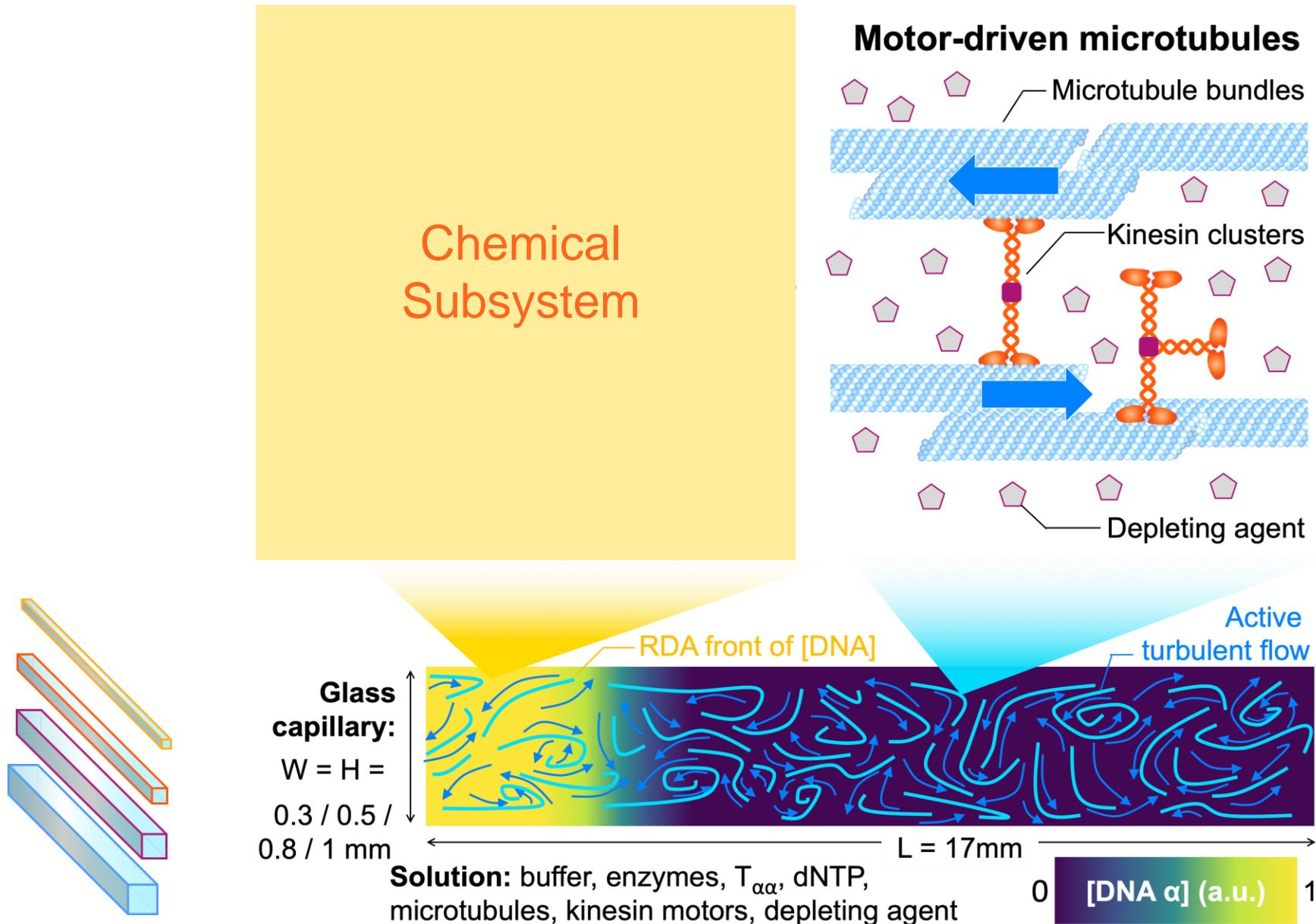
Nicolas Lobato-Dauzier,<sup>1,\*</sup> Ananyo Maitra<sup>1,2</sup> ,<sup>1,2</sup> André Estevez-Torres,<sup>1,3,†</sup> and Jean-Christophe Galas<sup>1,‡</sup>



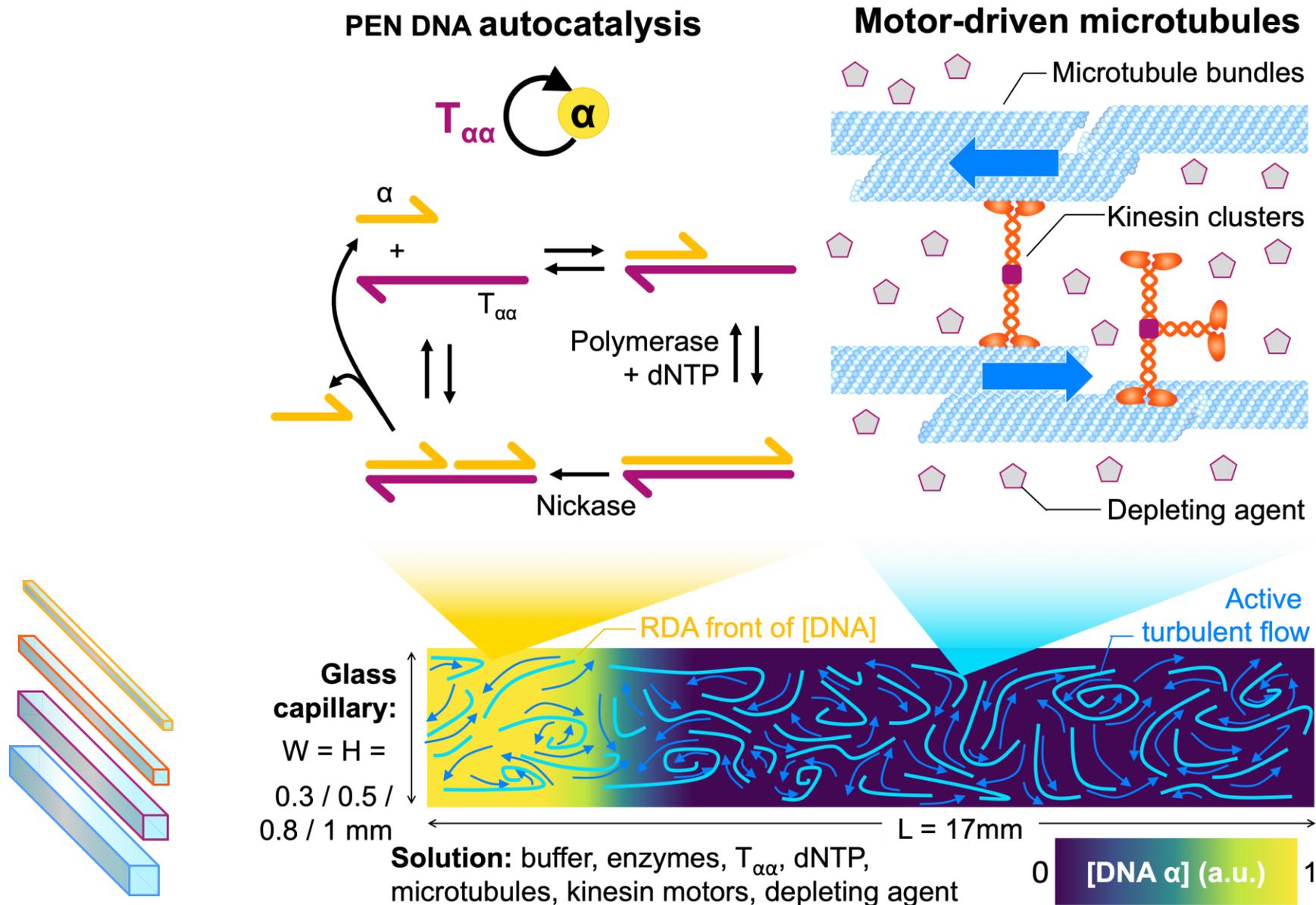
# Experimental setup and its building sub-systems



# Experimental setup and its building sub-systems



# Experimental setup and its building sub-systems



# Dissecting

## *Reaction-Diffusion-Advection*

$$\frac{\partial c}{\partial t} = k c + D \Delta c + \left( \vec{u}_{AM} \cdot \vec{\nabla} \right) c$$

# Active matter

Reaction

Polymerase

Kinesin

		( $\emptyset$ )	(+)
Reaction	( $\emptyset$ )	Diffusion $\frac{\partial c}{\partial t} = D\Delta c$	Diffusion Active matter $\frac{\partial c}{\partial t} = D\Delta c + \left(\vec{u}_{AM} \cdot \vec{\nabla}\right)c$
	(+)	Reaction Diffusion $\frac{\partial c}{\partial t} = k c + D\Delta c$	Reaction Diffusion Active Matter $\frac{\partial c}{\partial t} = k c + D\Delta c + \left(\vec{u}_{AM} \cdot \vec{\nabla}\right)c$

# Dissecting *Reaction-Diffusion-Advection*

Diffusion



Reaction-Diffusion



Diffusion-Active Matter



Reaction-Diffusion-Active Matter

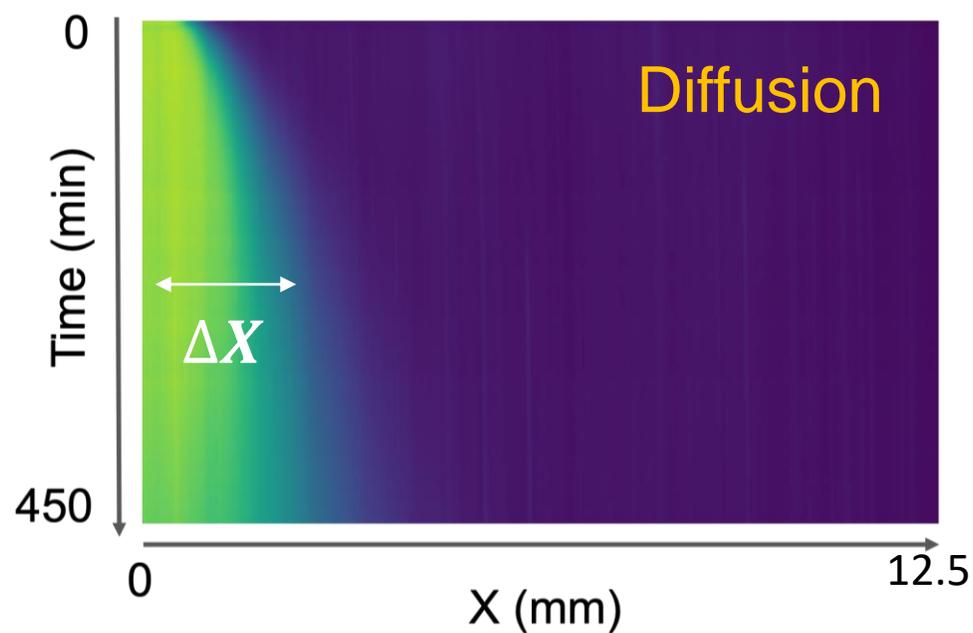


0 min.



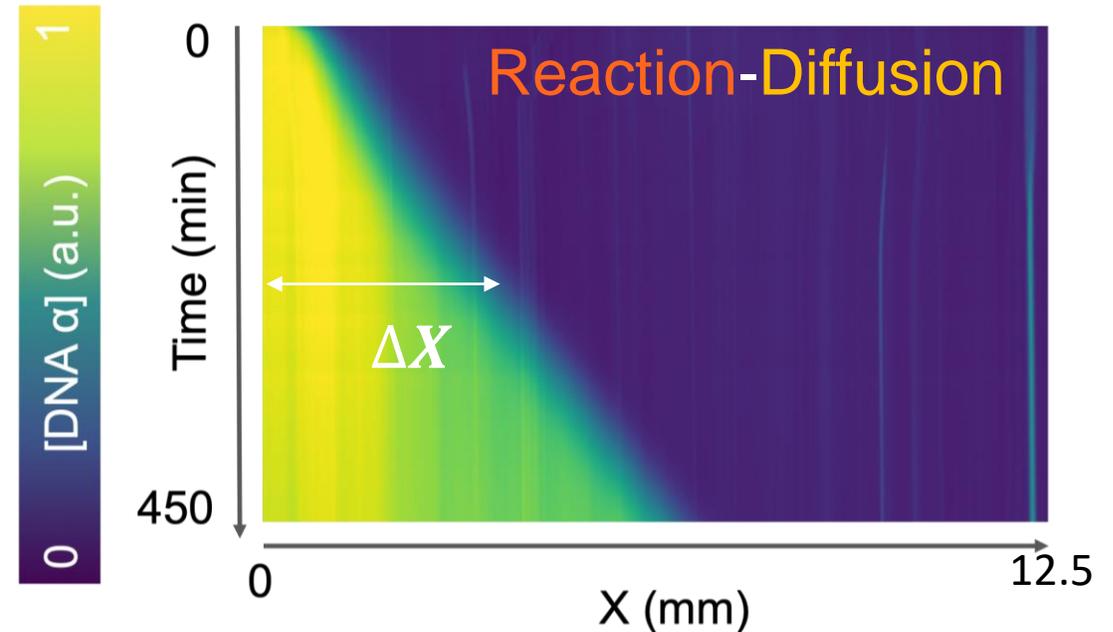
1mm

# No *Activity* : Reaction sustains RD front



$$\Delta X = \sqrt{Dt} \propto \sqrt{t}$$

$$(D = 2 \cdot 10^3 \mu\text{m}^2/\text{min})$$



$$\Delta X \propto t$$

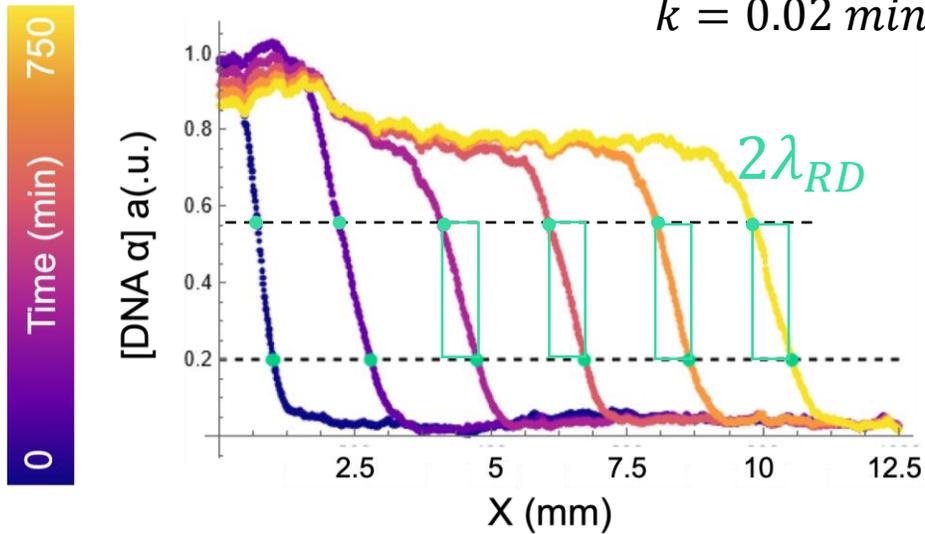
# FKPP theory captures well RD fronts

Front width:

$$\lambda_{FKPP} = \sqrt{\frac{D}{k}} = 0.3 \text{ mm}$$

*reaction rate*

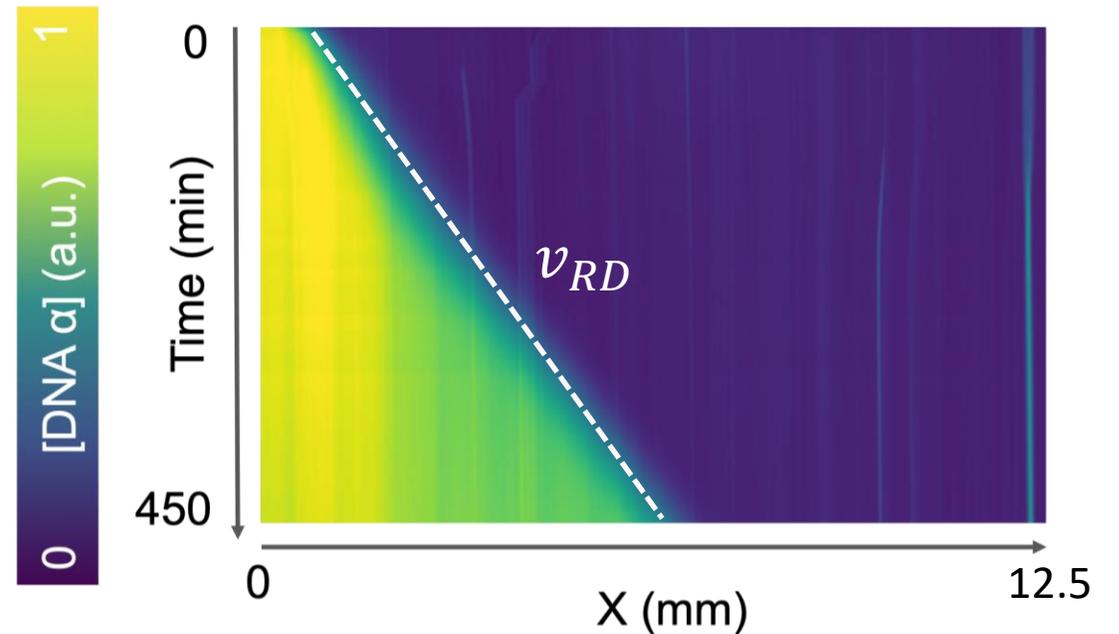
$k = 0.02 \text{ min}^{-1}$



$$\lambda_{RD} = 0.3 \text{ mm}$$

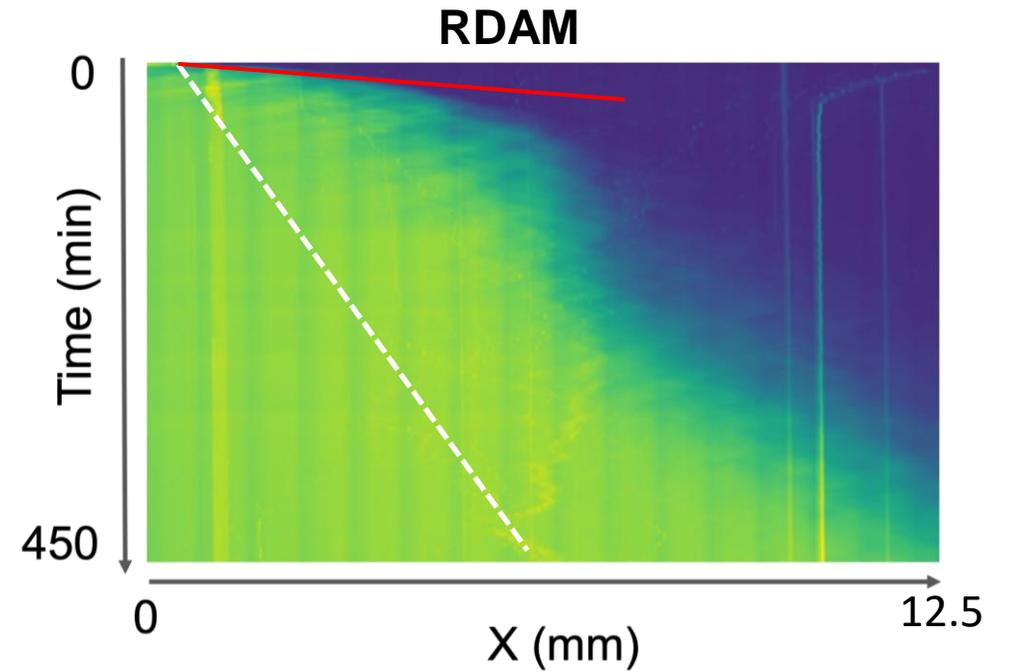
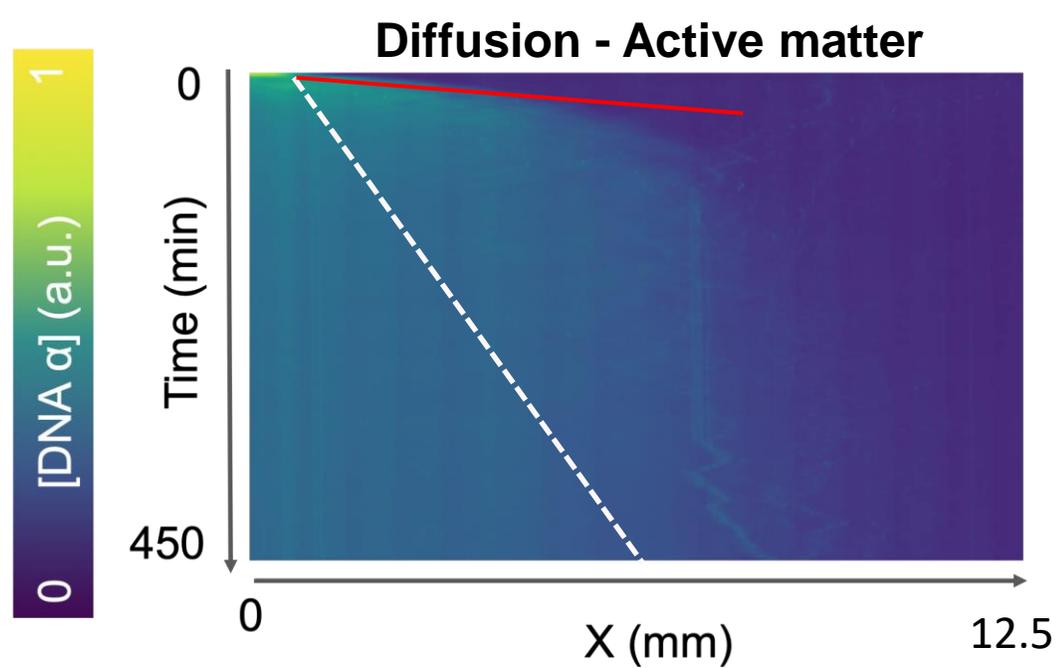
Front speed:

$$v_{FKPP} = 2\sqrt{kD} = 12.4 \text{ } \mu\text{m/min}$$

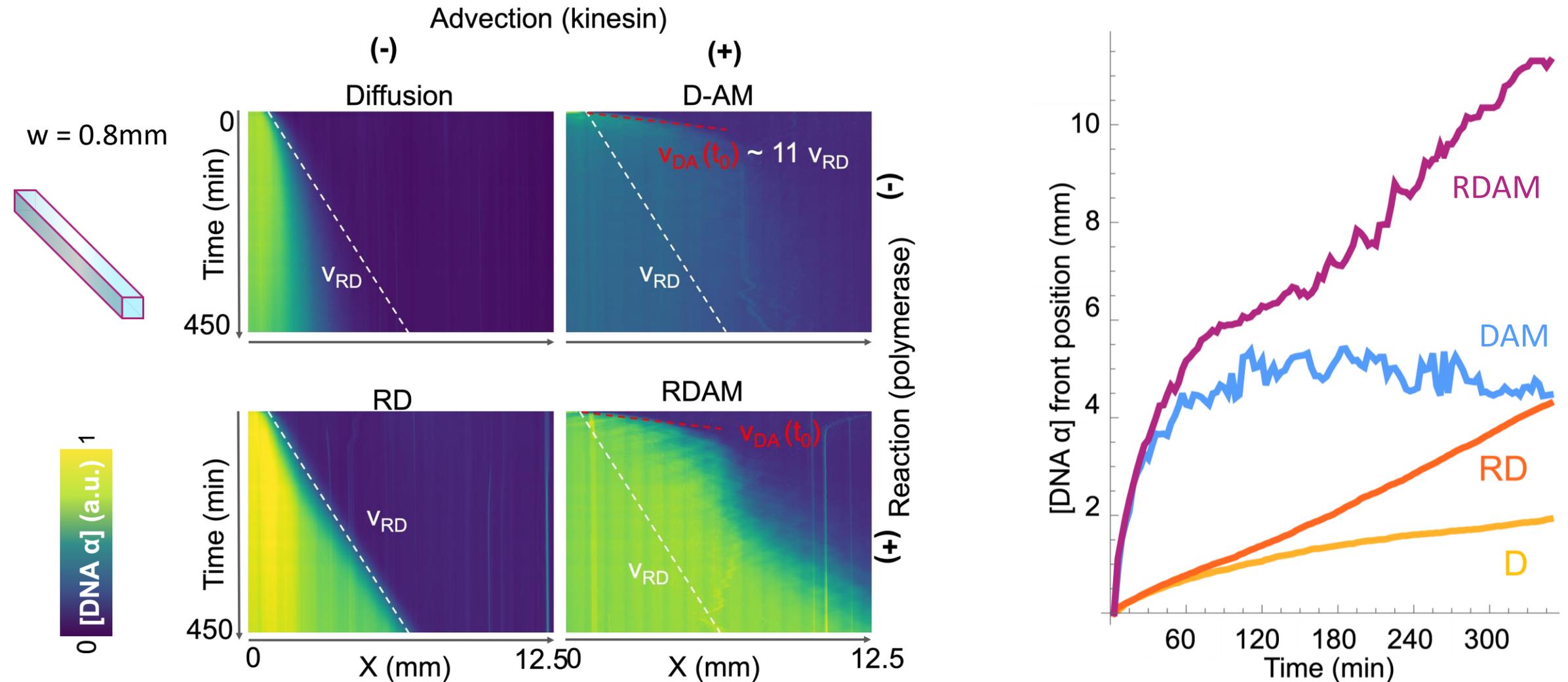


$$v_{RD} = 12.6 \text{ } \mu\text{m/min}$$

# +Activity : dramatic increase in front speed



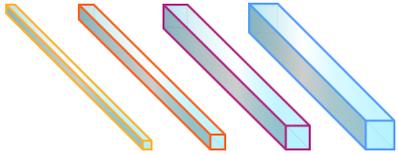
# Comparison of Reaction-Diffusion-Advection configurations



How does channel geometry affect RDAM fronts ?

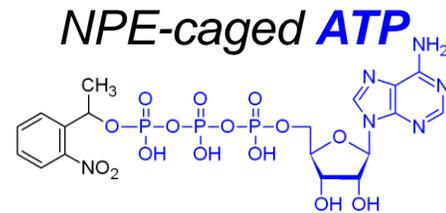
# Confinement determines transport of a RDAM front

Vary cross-section



+

1) 75 min of RD only

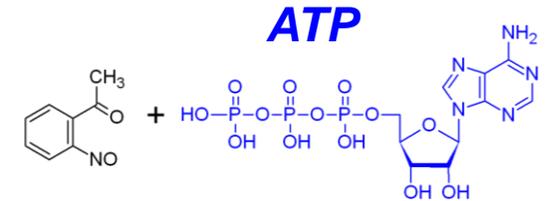


(no activity)

*UV light*

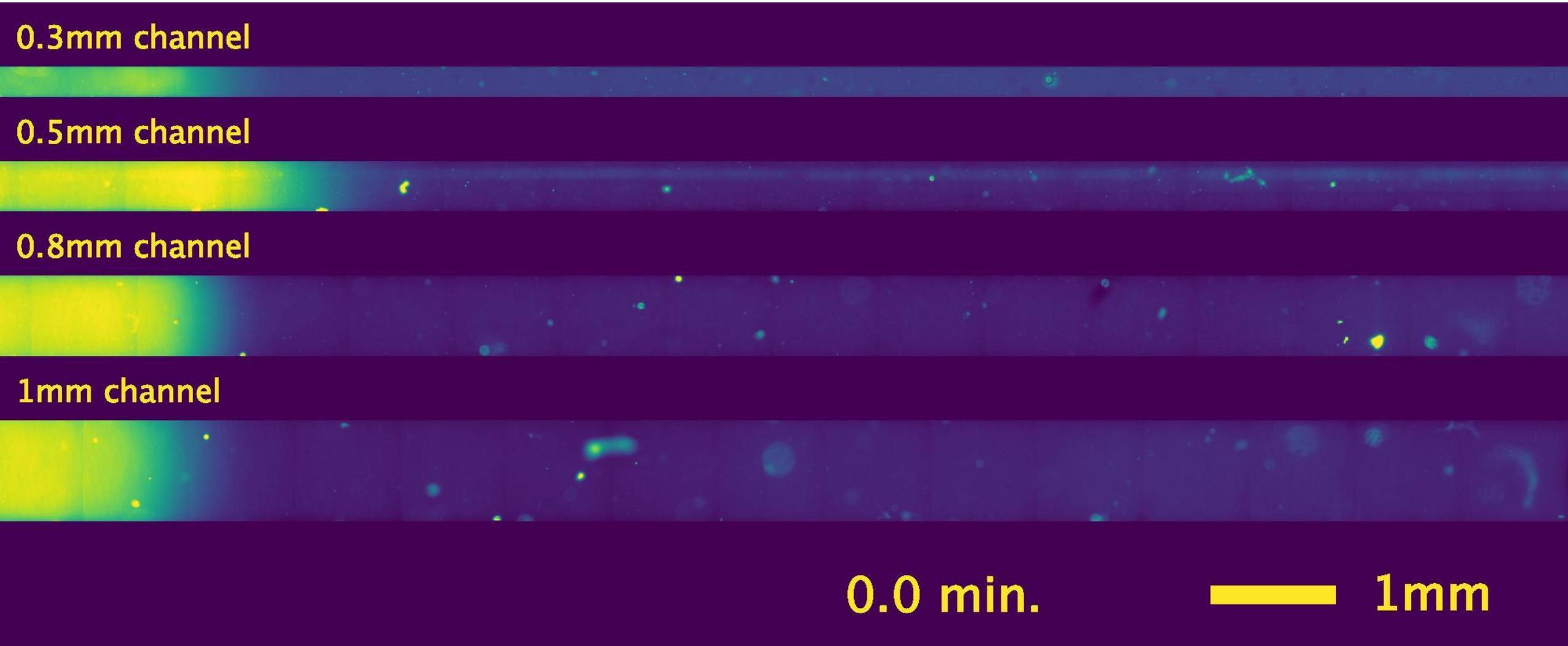


2) 7h RDAM



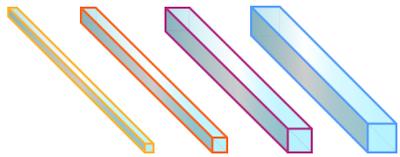
*Activity++*

# Confinement determines transport of a RDAM front



# Confinement determines transport of a RDAM front

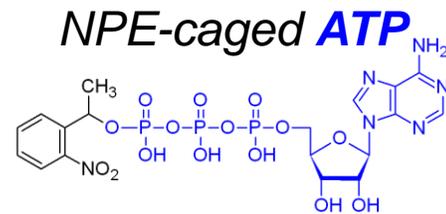
Vary cross-section



w = 0.3mm

1) 75 min of RD only

+

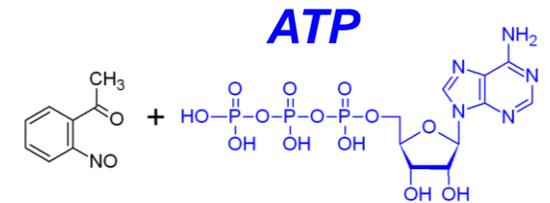


(no activity)

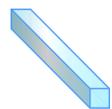
UV light



2) 7h RDAM



Activity++



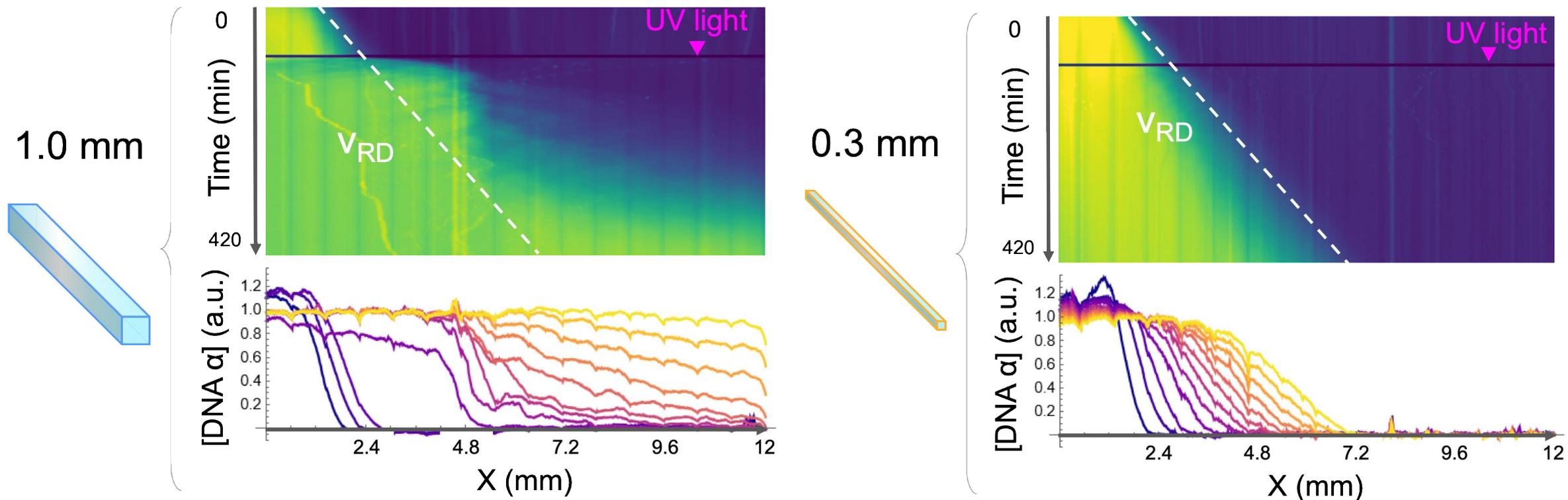
w = 1 mm

00:00:00 h:min:s

00:00:00 h:min:s

1 mm

# Confinement determines transport of a RDAM front

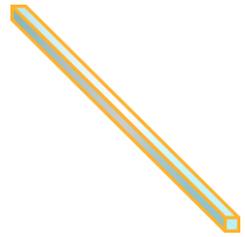


0 Time (min) 420

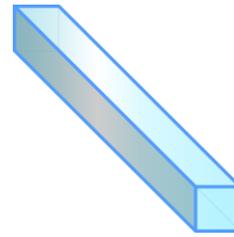
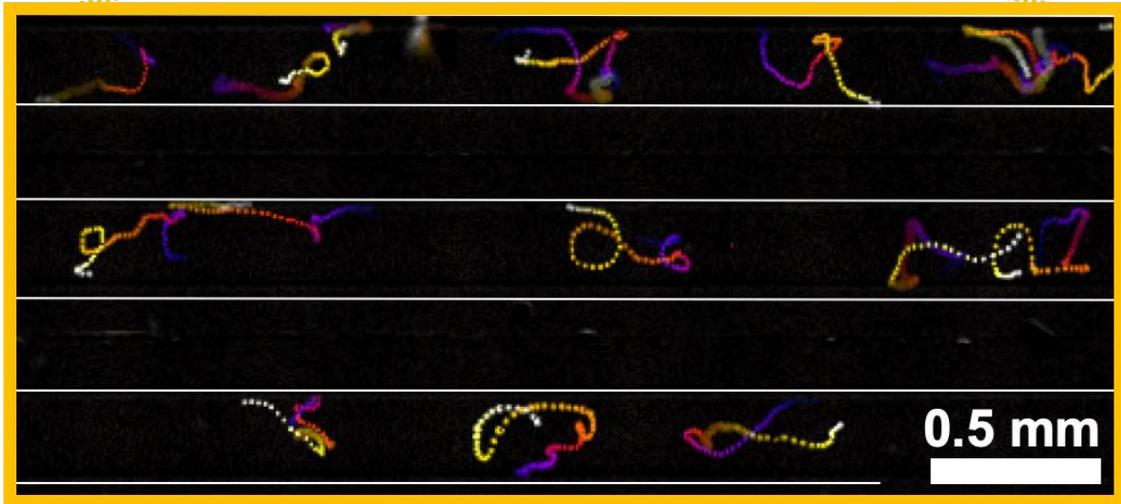
0 [DNA  $\alpha$ ] (a.u.) 1

**How is Active Matter affected by confinement ?**

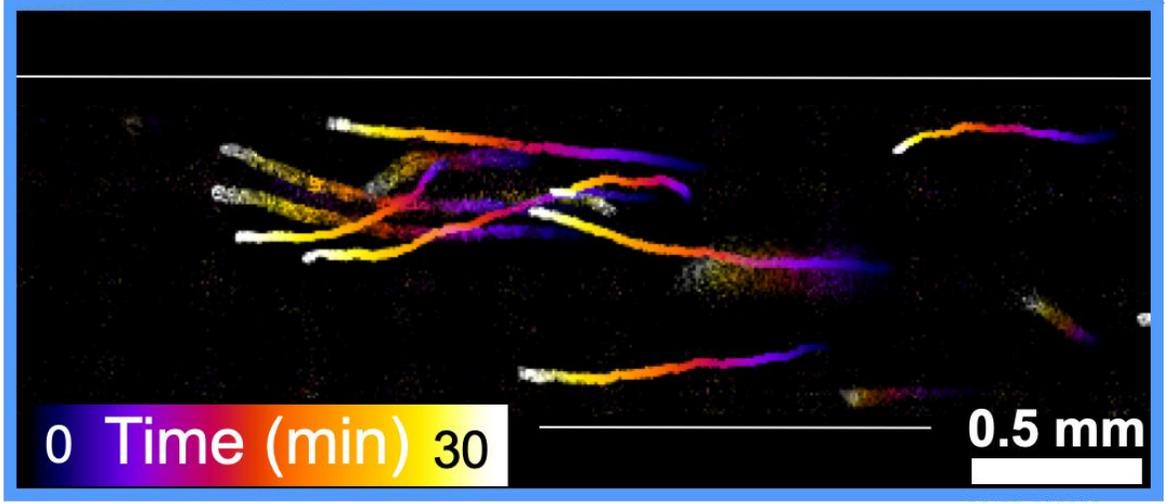
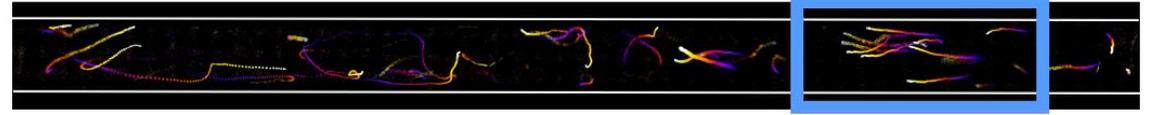
# Beads' trajectories differ greatly



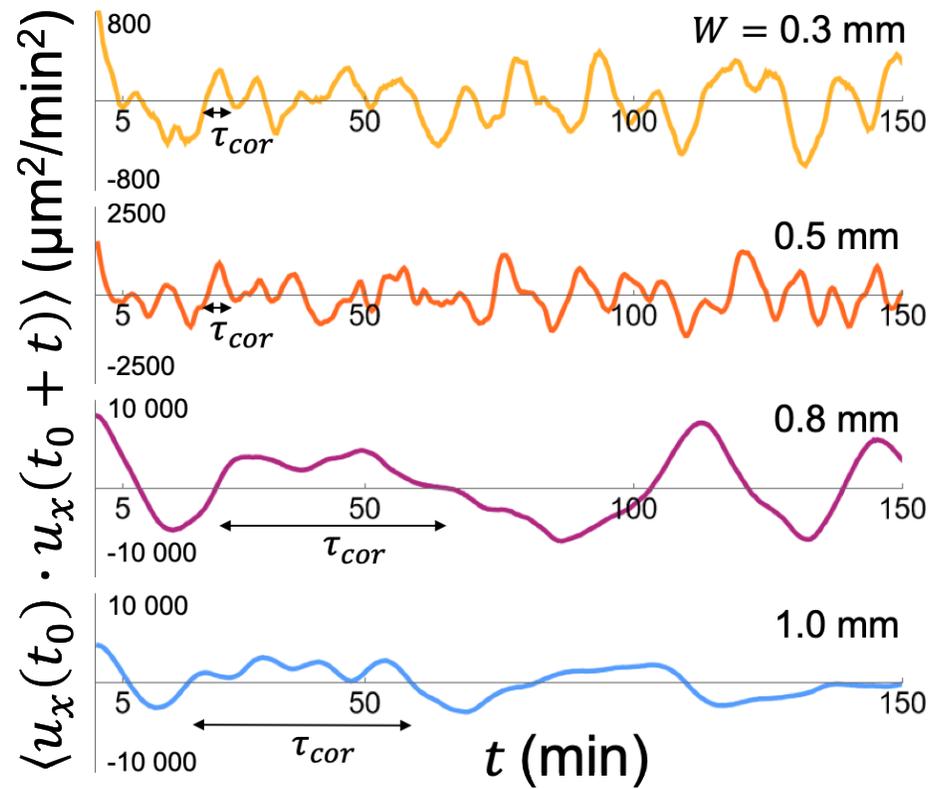
$W = 0.3$  mm



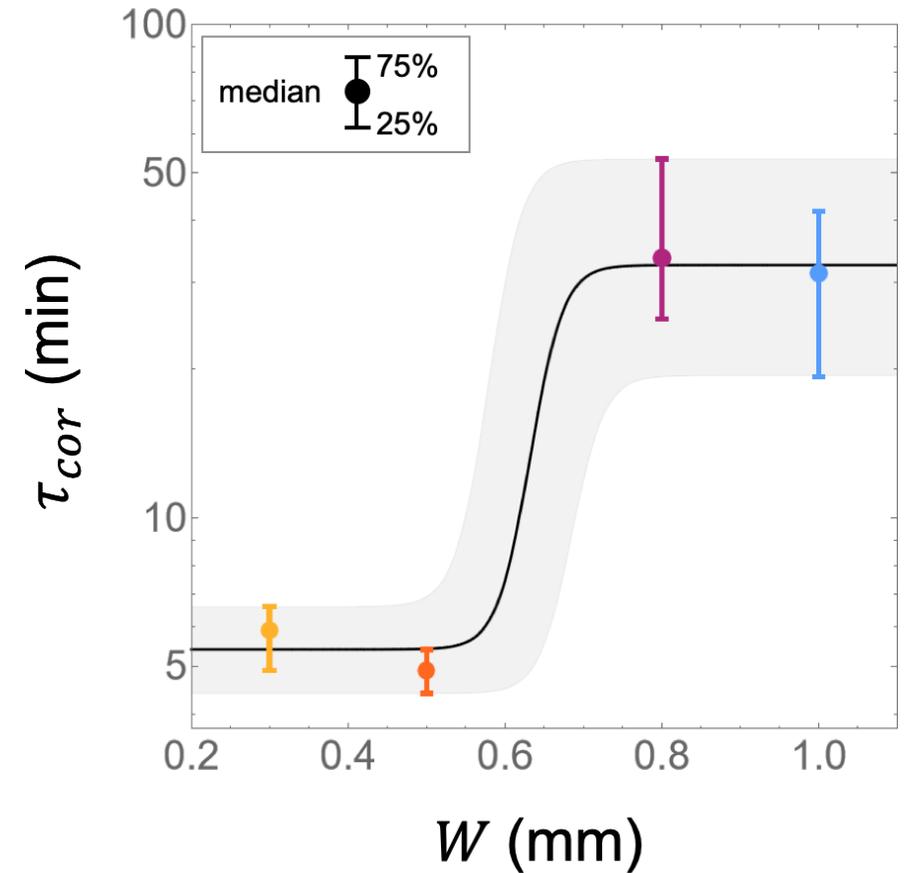
$W = 1$  mm



# Velocity correlation

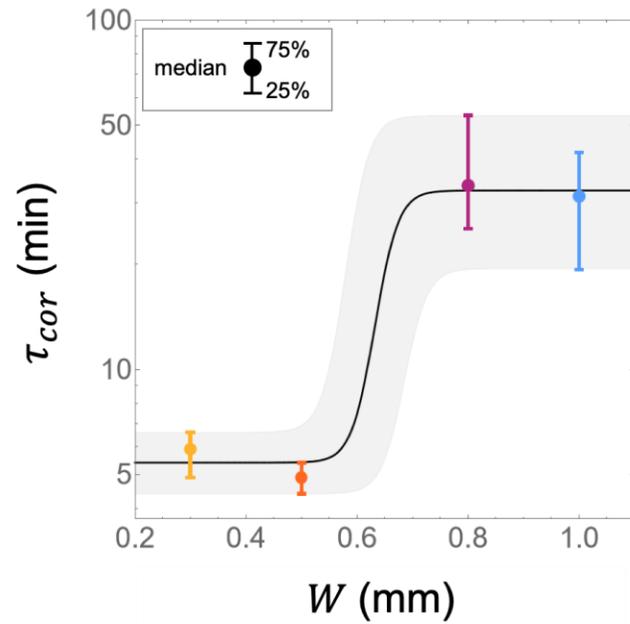


# Correlation time

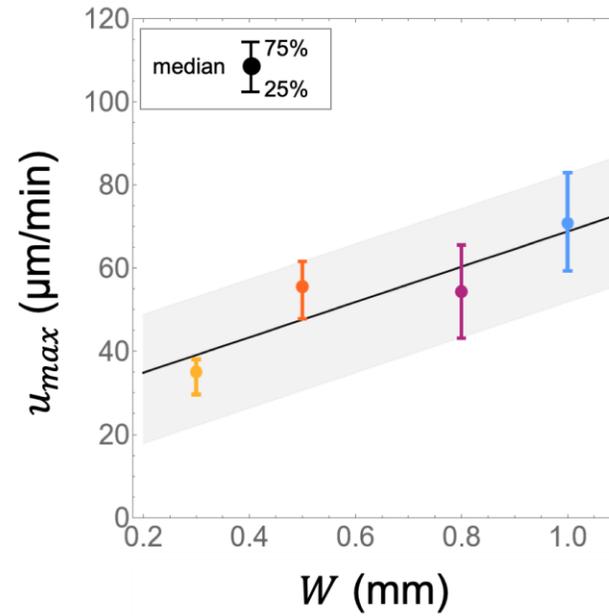


# Characterizing advection

## Correlation time

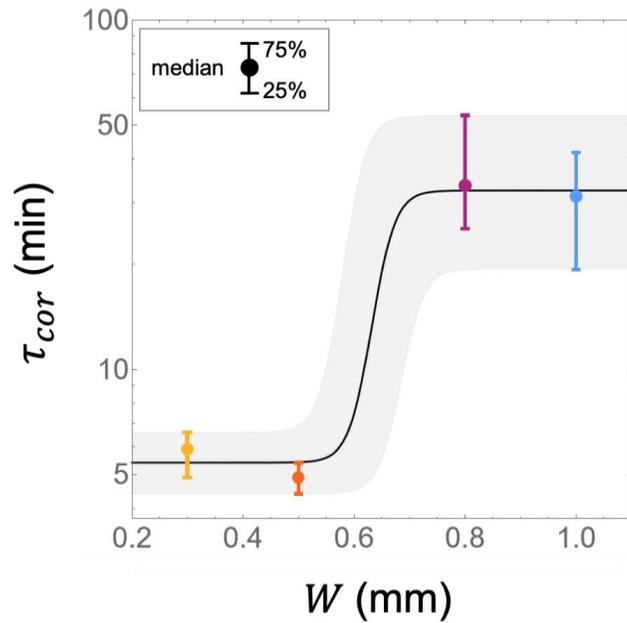


## Max velocity along x



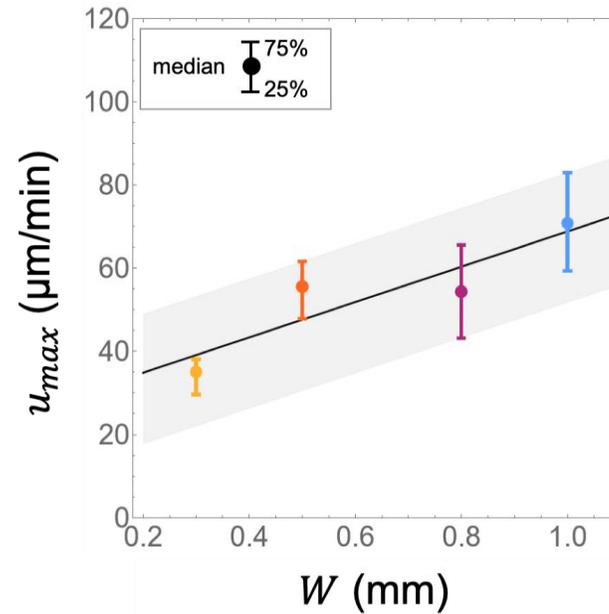
# Characterizing advection

## Correlation time



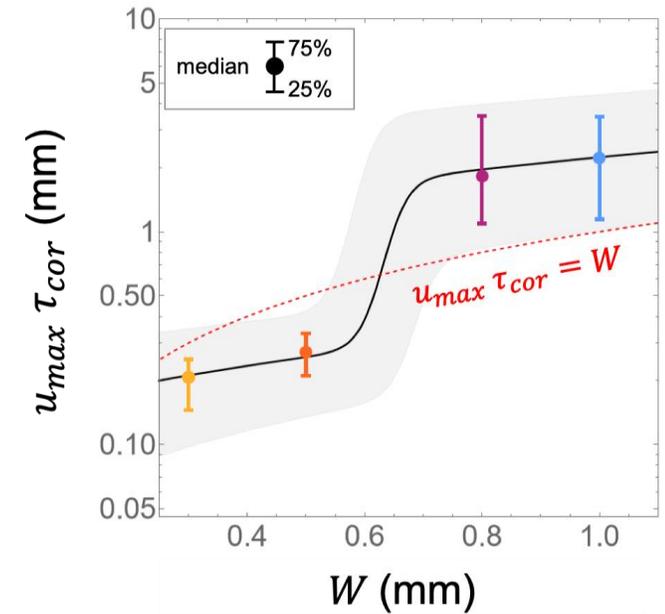
×

## Max velocity along x



=

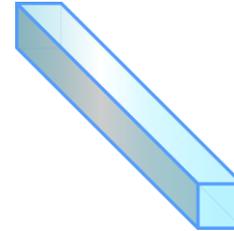
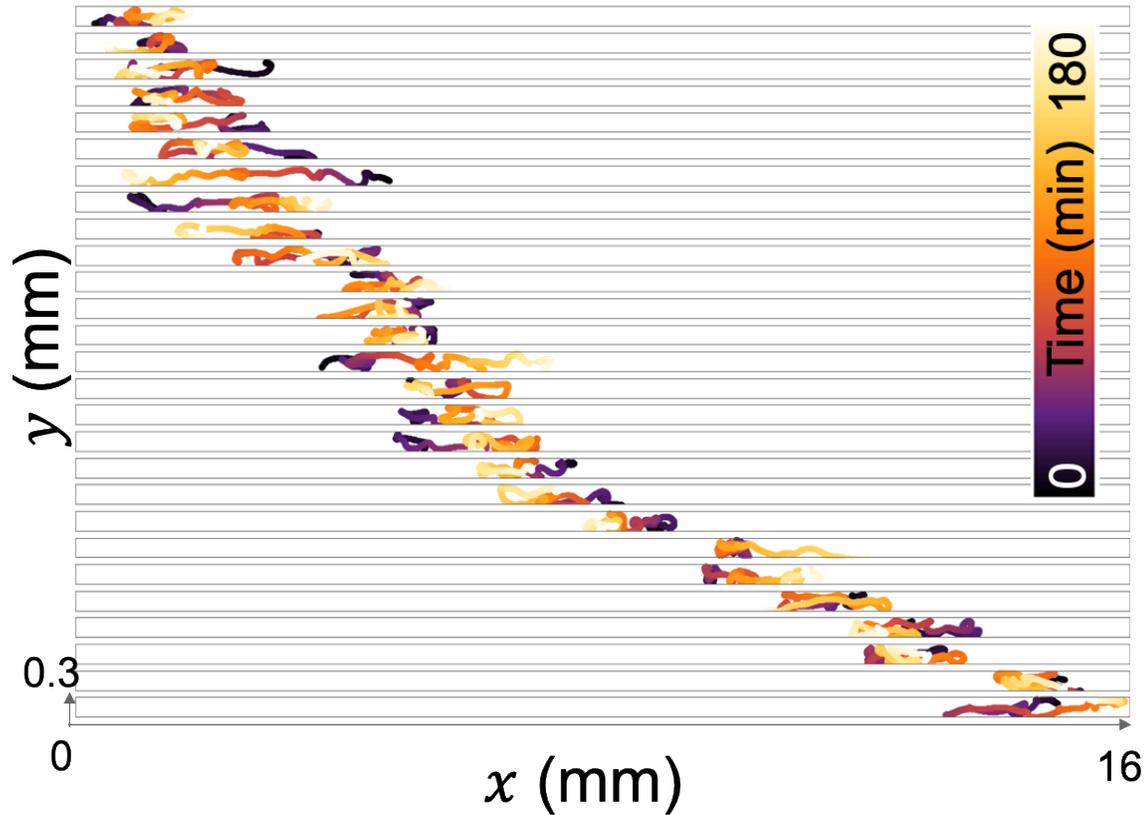
## Vortex Size



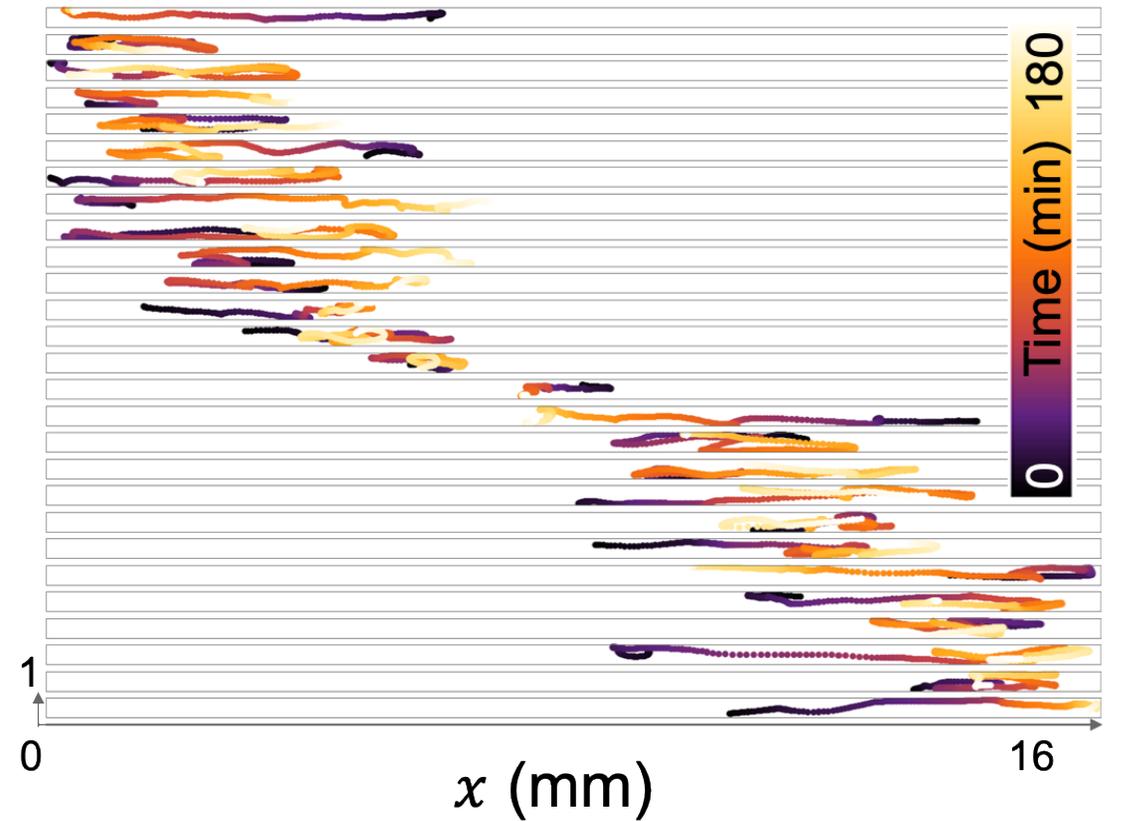
# Convection cells



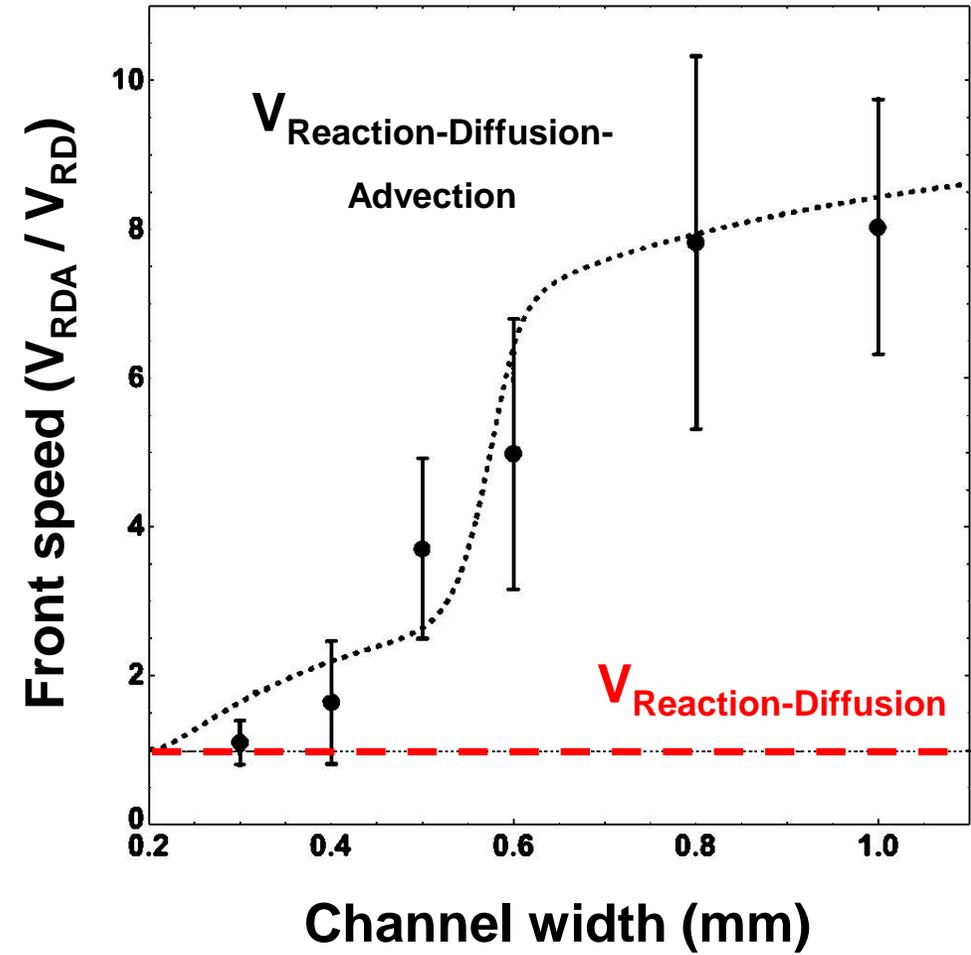
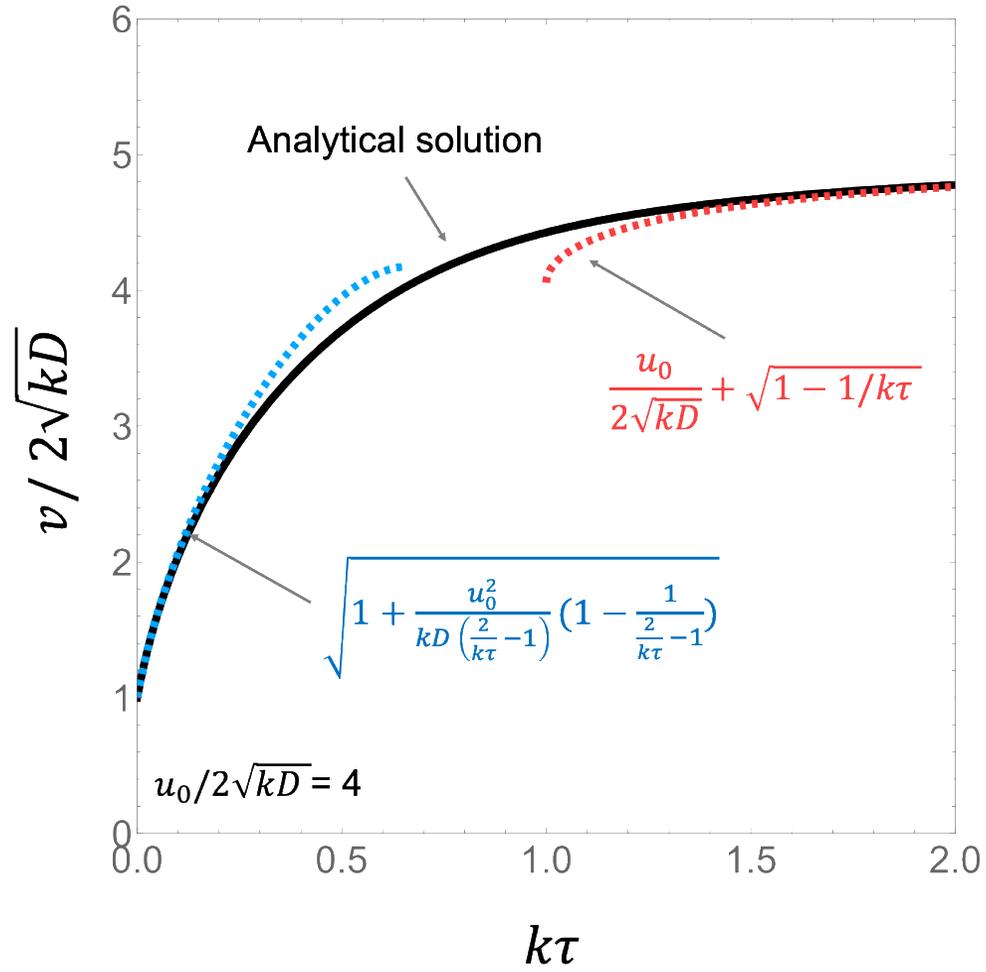
$W = 0.3$  mm



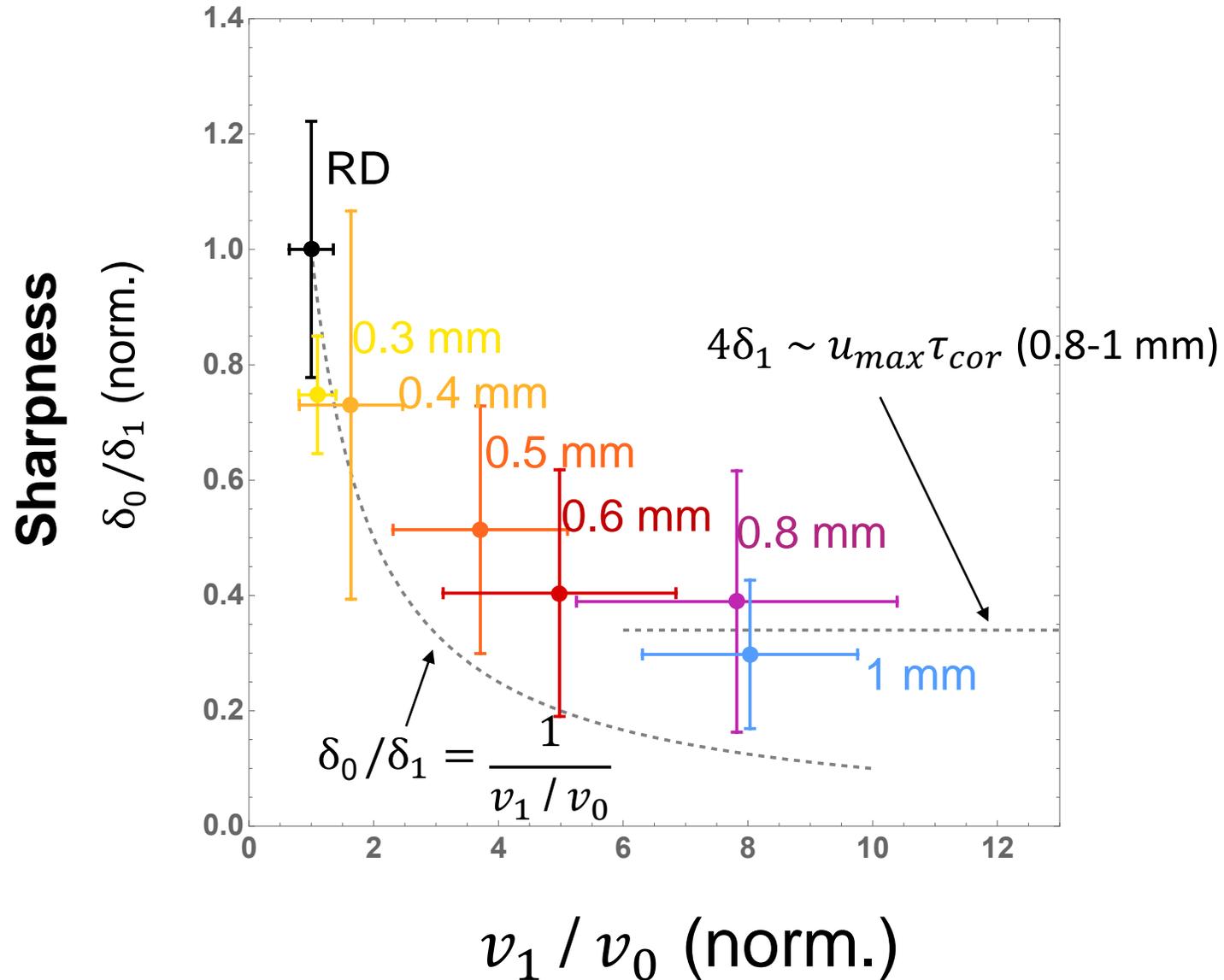
$W = 1$  mm



# Speed as function of geometry



# Effect of confinement on front speed & sharpness



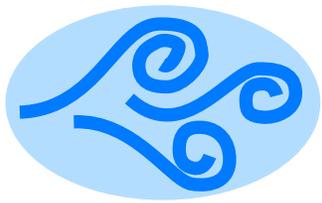
Speed: **x8**

Sharpness: **÷3**

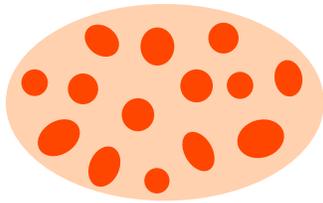
# MORPHOGENESIS VIA MECHANO-CHEMICAL COUPLINGS

## 1. State of the art

Mechanical & Chemical systems (separately)



Active gels

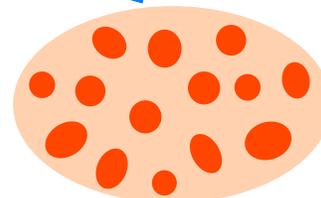


DNA Nanotech.

## 2. Latest work

Mechanics affect Chemistry

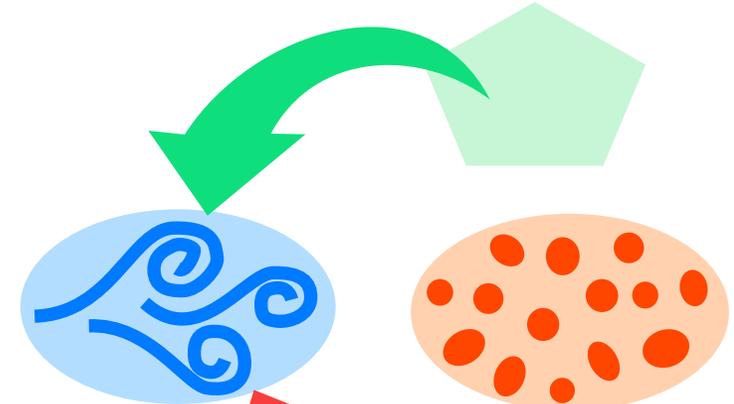
Advection



↳ Speed: x8  
depending on geometry

## 3. Ongoing work

Geometry & Chemistry control Mechanics



Program

Happy to discuss  
(Poster)

↳ Highly tunable &  
Complementary systems