Continuous Process Intensification

L1: General Introduction to Process Intensification

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ज्ञानम् परमम् ध्येयम्

FCPI
Foundation for Continuous Process Intensification

GenZ Materials
Continuous Process Intensification

processintensification

Technical sessions		
10:00 – 11:15	Tutorial 1 (FCPI): Introduction to Continuous Process Intensification	75 min
11:15 – 11:45	High Tea	
11:45 – 13:30	Tutorial 2 (FCPI): Tools, industrial examples &tutorial on how to intensify processes via continuous flow from lab to production	105 min
13:30 – 14:30	Lunch	
14:30 – 15:30	Tutorial 3 (FCPI): Introduction to Electro Organic Chemistry: Synthesis, tools and Processes	90 min
15:30 – 16:00	Tea break	
16:00 – 17:30	Tutorial 4 (IICT): Process Engineering- Use cases with Engineering interventions	90 min
19:00 – 21:00	Social hour	
Workshop (Day 2): 3rd July 2026		
09:30 – 11:00	Tutorial 5 (FCPI): Introduction to Mechano Organic Chemistry: Synthesis, tools and Processes	90 min
11:00 – 11:30	Tea break	
11:30 – 13:10	Tutorial 6 (FCPI): How to Intensify Processes via Electro and Mechano Chemistry	100 min
13:10 – 13.30	Formal closing of theory session Vote of thanks	
13:30 – 14:30	Lunch	
14:30 – 17:30	Exhibits Demonstration Session	180 min
17:30 – 18:00	Certificate collection Feedback from participants	30 min

Agenda

- **Future of Chemical Manufacturing**

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- **What is Process Intensification**

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  (Flow, Electro, Photo, Mechano)

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- **How to think in this new paradigm (POC to Production)**

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- **Do’s and do not’s of continuous process intensification**

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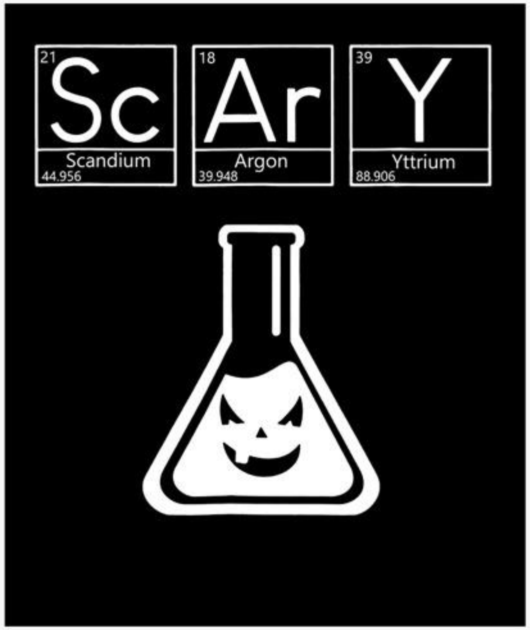
- Process Engineering

Chemistry: Catch 22



https://www.youtube.com/watch?v=rZQQAsphqBc&list=PLdesNkcRuf70shzcrbWS8dwixJdnSVYWD&index=3

Chemistry: Catch 22

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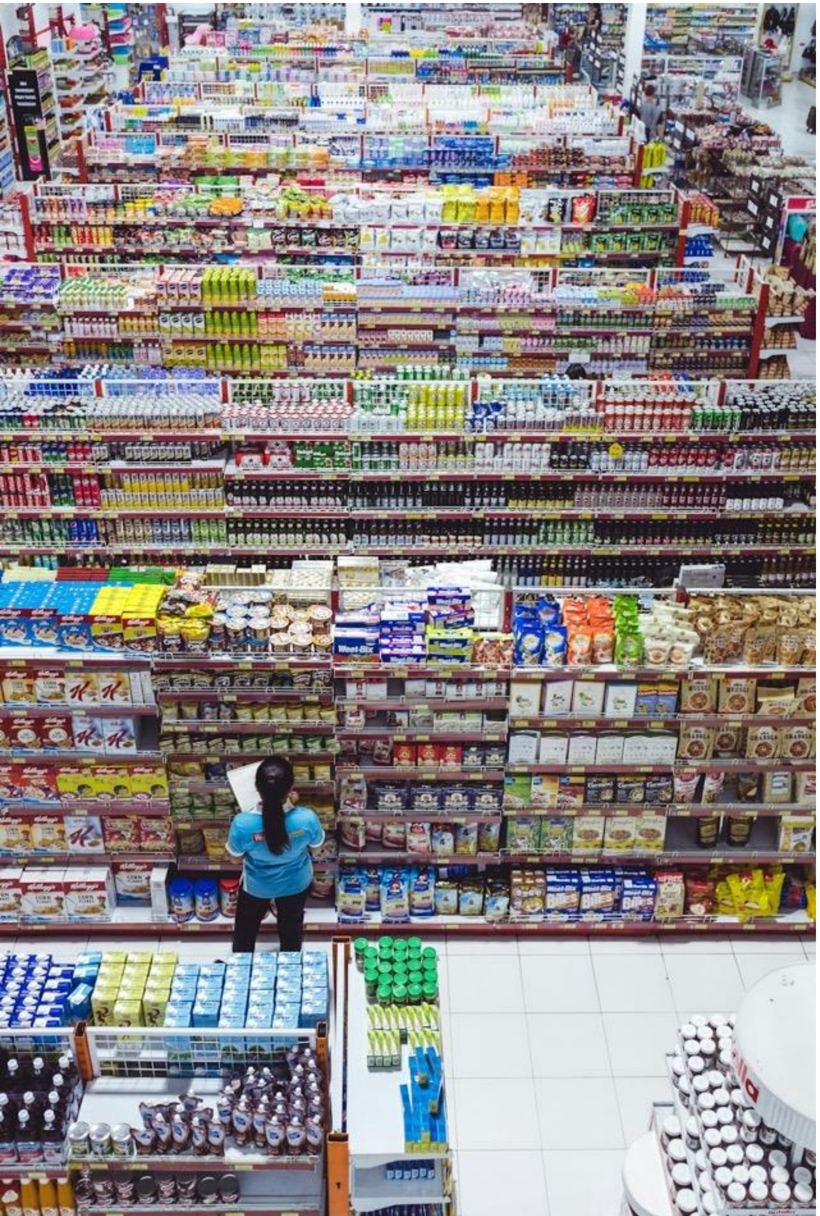
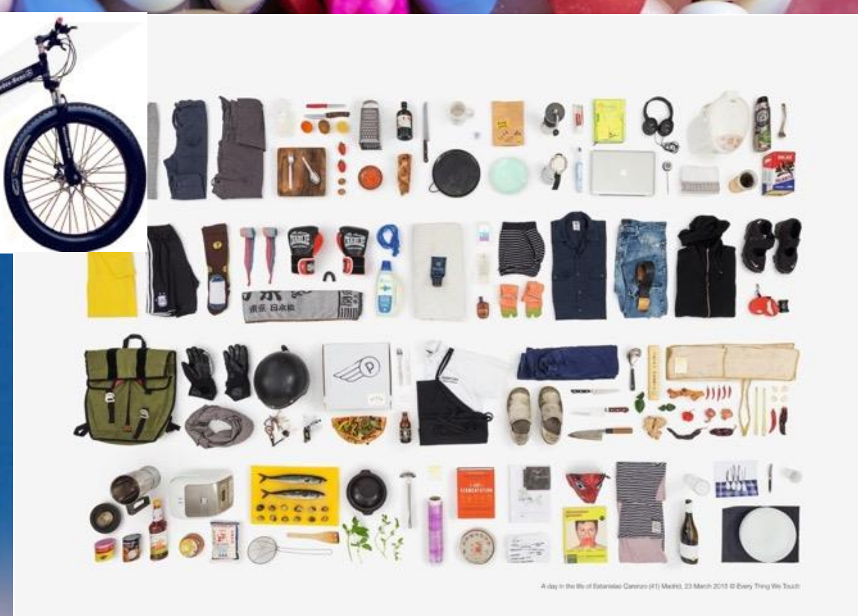
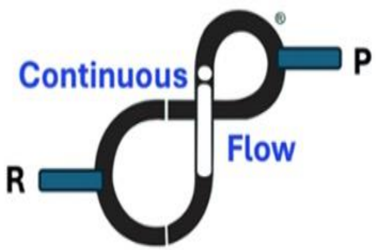
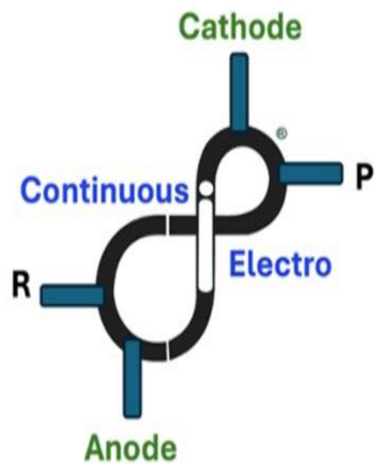
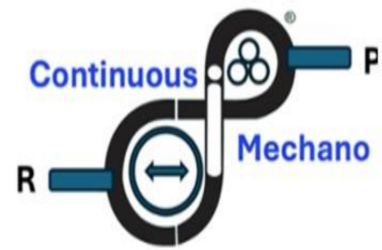


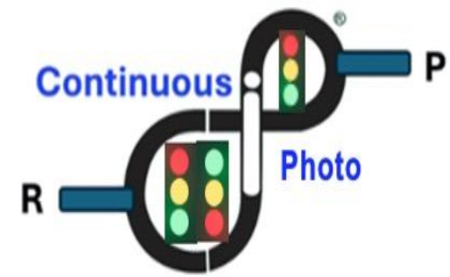


Continuous Process



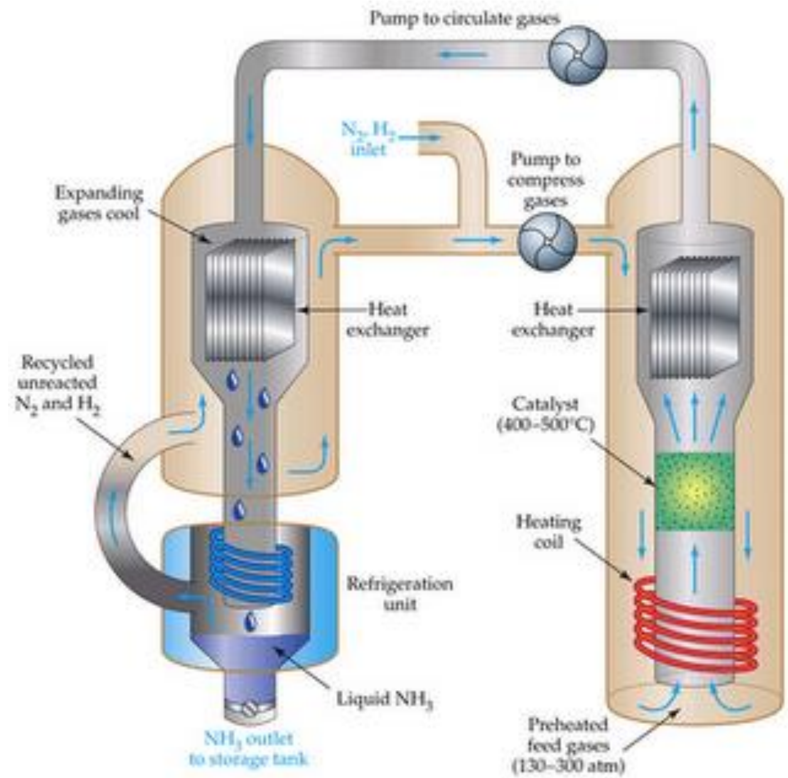






Flow **Electro** **Mechano** **Photo**

Continuous Process
What's the Big Deal?



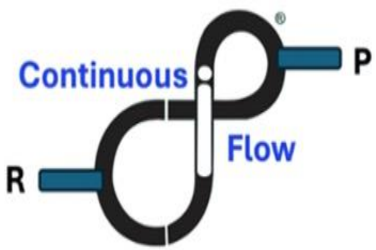
Haber–Bosch process: More than 100 Years Old

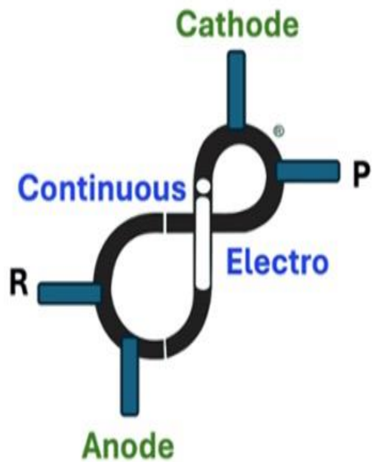
Continuous Process
What's the Big Deal?

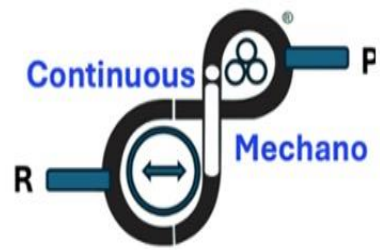
Continuous Process
What's the Big Deal?

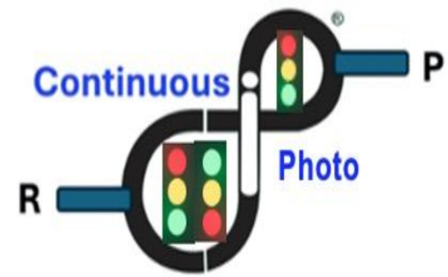
Continuous Process

What's the Big Deal?



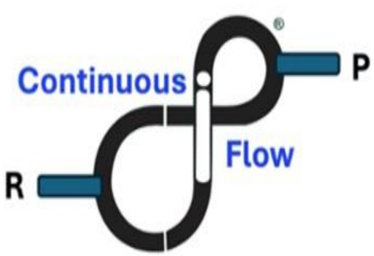


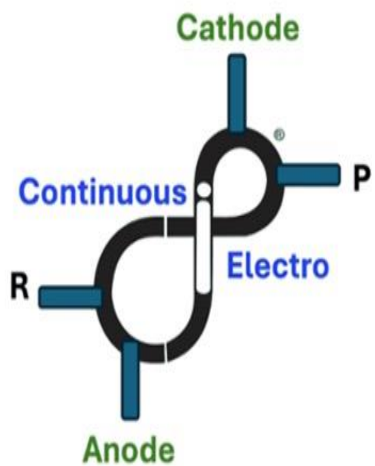


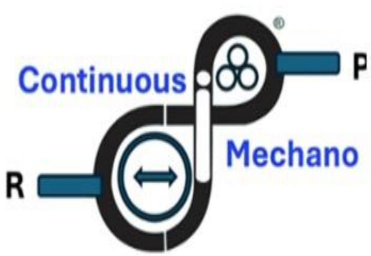


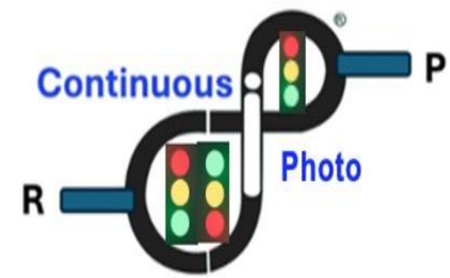
Flow **Electro** **Mechano** **Photo**

Continuous Process
Intensified









Flow **Electro** **Mechano** **Photo**

Continuous Process

Process Intensification Expert in Chemicals/Materials Domain

Develop Economical and Sustainable Processes

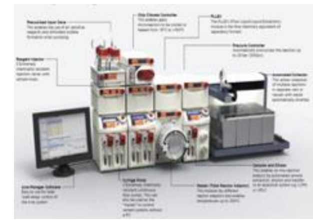
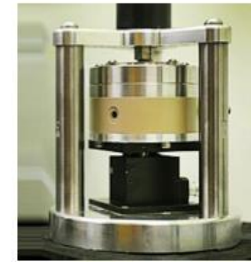
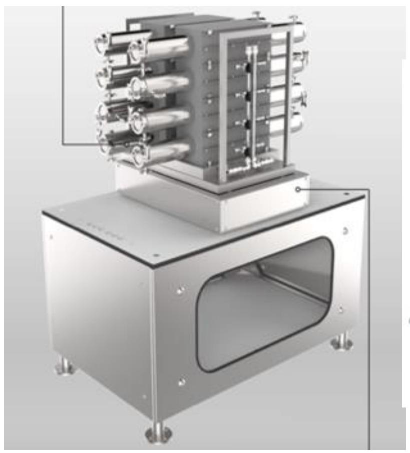
USP: Reduce Carbon Footprint without additional cost

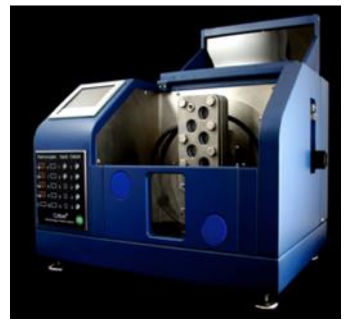
END to End Solution: from POC to COMMERCIAL

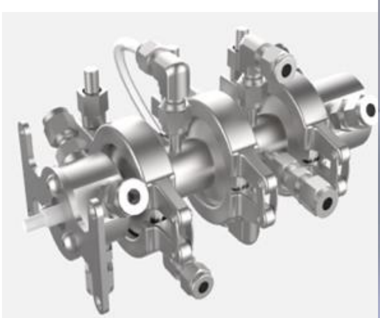
Facilities

Flow, Electro, Photo and Mechano





From mg to production scale

Industrial Collaboration

- ***UPL***
- ***Syngenta***
- ***Glandpharma***
- ***Jubilant Ingrevia***
- ***Rusan Pharma***
- ***Anthem***
- ***Kpatel Chemo***
- ***Transpek***
- ***Synergia***
- ***Dr. Reddy’s Lab***
- ***Virupaksha***
- ***Deepak Nitrite***
- ***Shri Sufurics***
- ***Syngene***
- ***Glochem***
- ***Sun Pharma***
- ***SABIC***
- ***Jay Chemicals***
- ***Rupak***
- ***Jubilant Ingrevia***
- ***Lupin***
- ***Arthi Industries***
- ***Metrochem***
- ***Alkem***
- ***Arch Pharma***
- ***Valiant***
- ***Mangalam***
- ***EISAI***
- ***Merck/Aldrich***
- ***SRF Chemicals***
- ***SAMI Labs***
- ***Sakar Healthcare***
- ***Delta Finochem***
- ***Medilux Labs***
- ***TBRL***
- ***DRILS***
- ***Samnan***
- ***MetaX***

Chemistry & Chem Eng

Language of Chemistry itself is changing very fast

- Solution phase chemistry above the bp of the solvent
- Inter over Intra molecular reactions
- Reactions above the decomposition temperature
- Homogeneous vs Heterogeneous Kinetic
- Time resolved synthesis (Retro Synthesis)
- Chemistry without chemicals (Electrochemical)
- Chemistry without solvents (Mechanochemical)

Future of Chemical Manufacturing

Human Intelligence

⬇

AI and ML

⬇

R & D and Manufacturing

⬇

Automation and Sustainability

⬇

Continuous Production

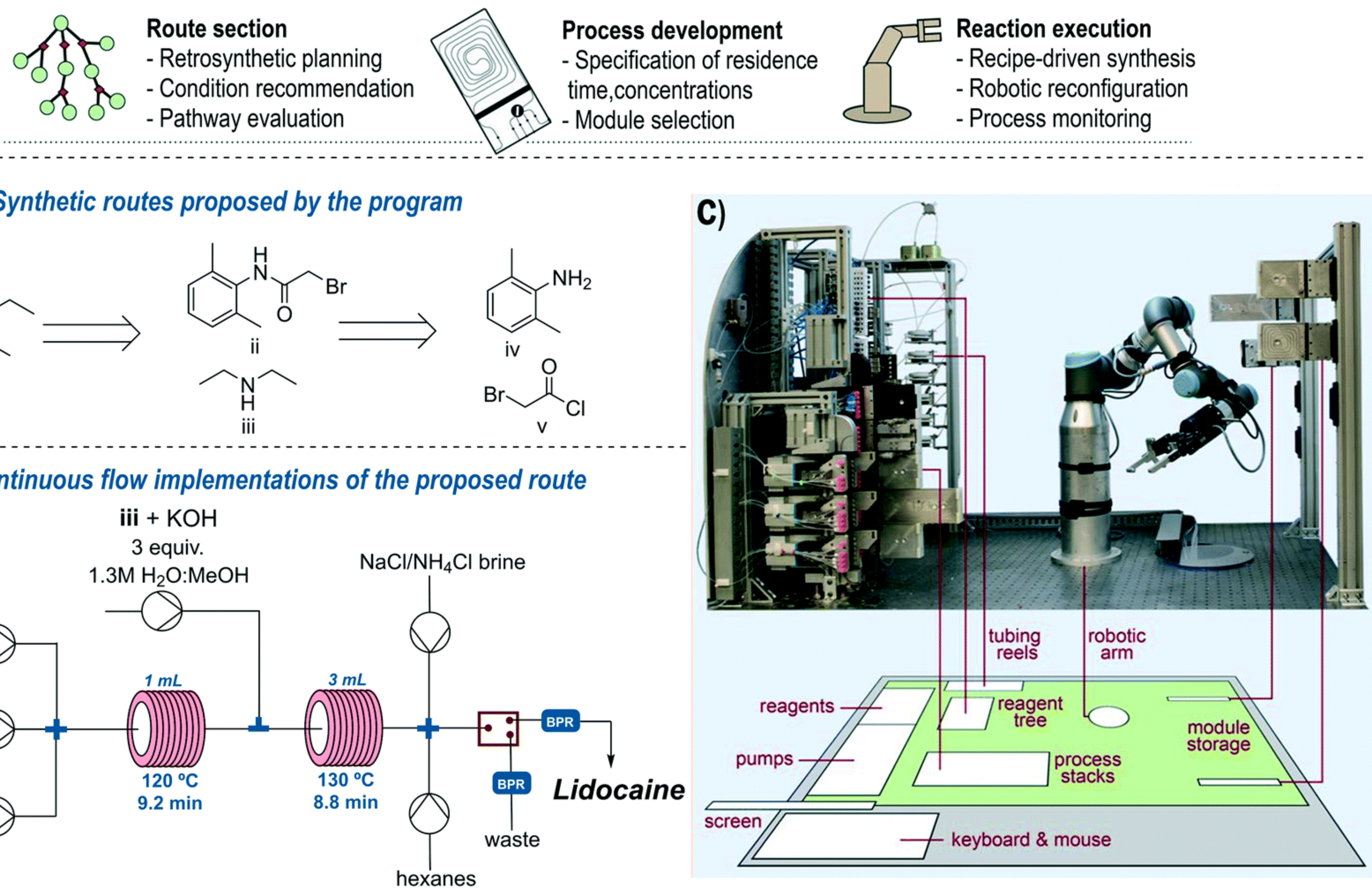
⬇

Electro_Photo_New Space

⬇

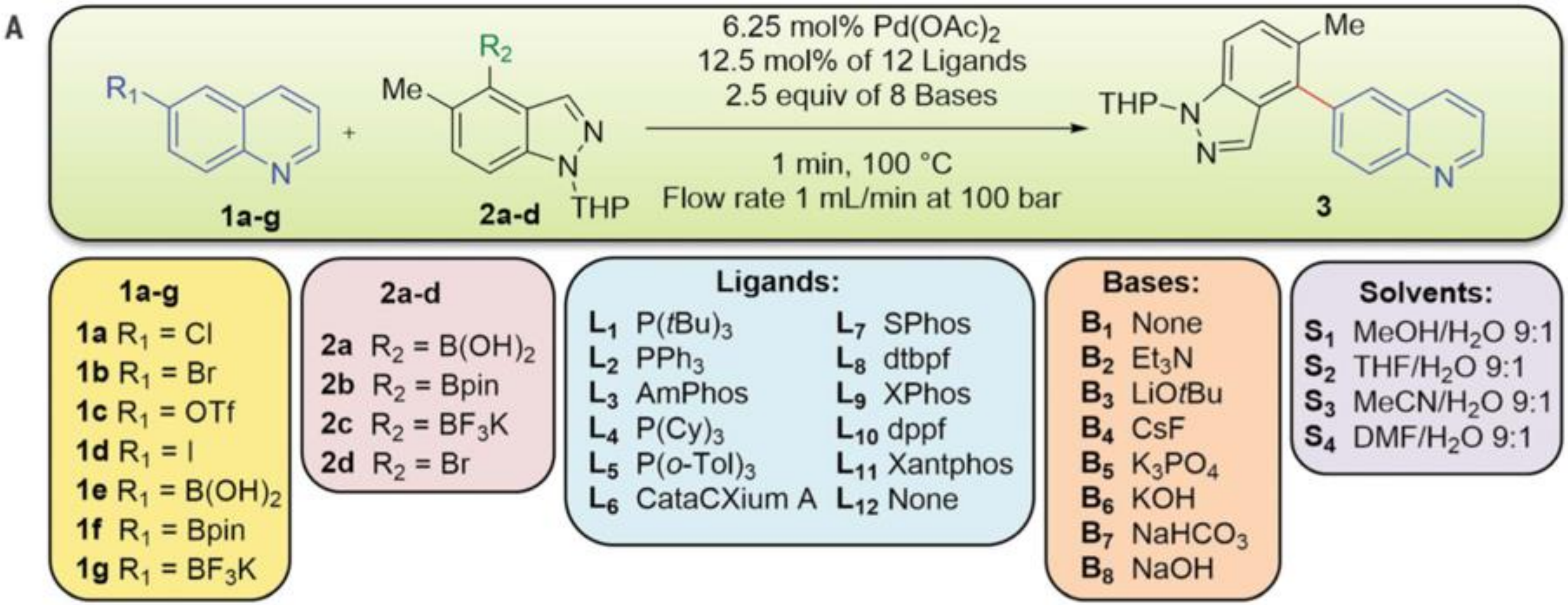
Flow and Mechano

AI & ML: Automation



React. Chem. Eng., 2021,6, 756-786

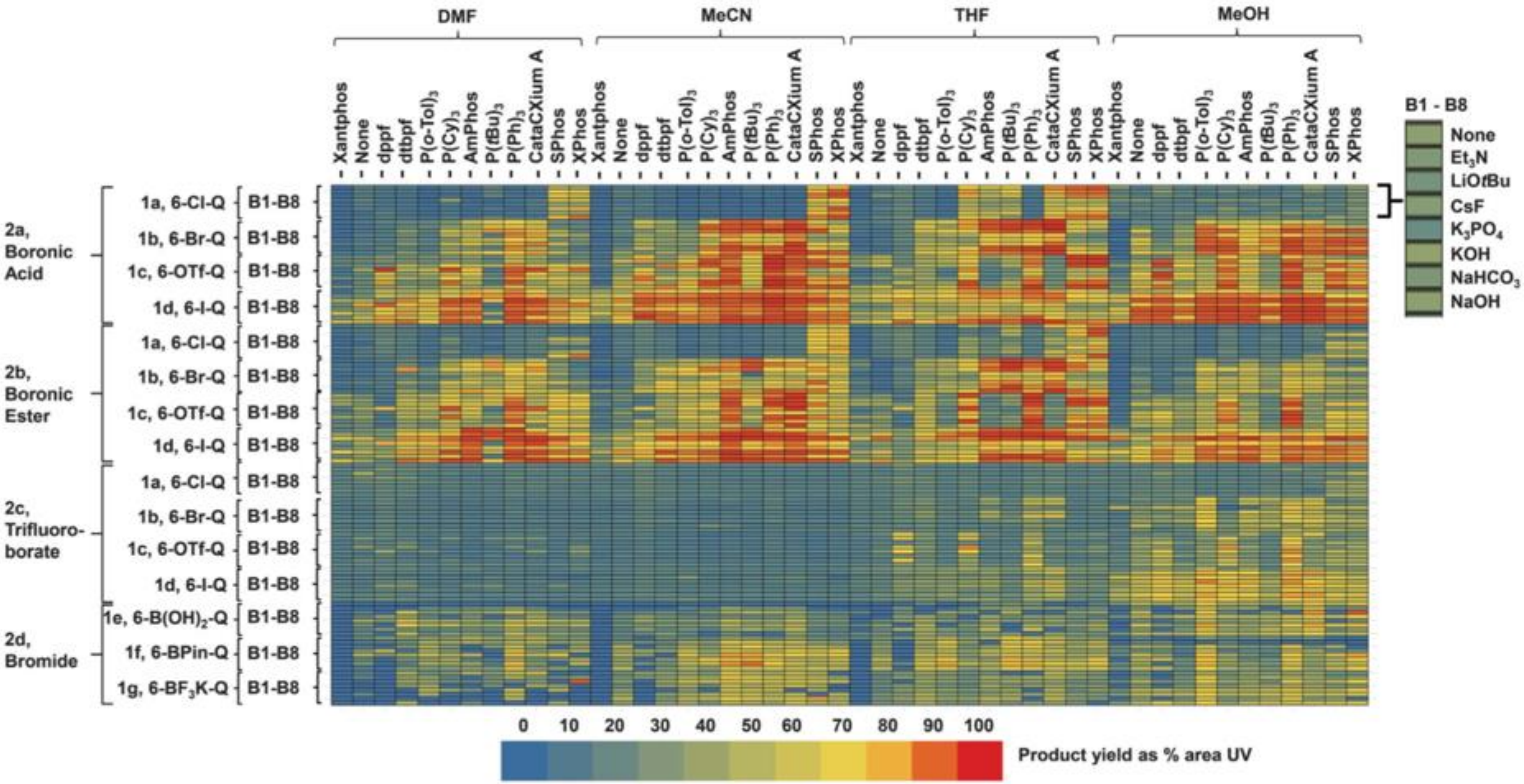
Autonomous Synthesis



A total of 5760 reactions evaluated in 3 days

Perera et al., Science 359, 429–434 (2018)

Ultrafast Optimization



Perera et al., Science 359, 429–434 (2018)

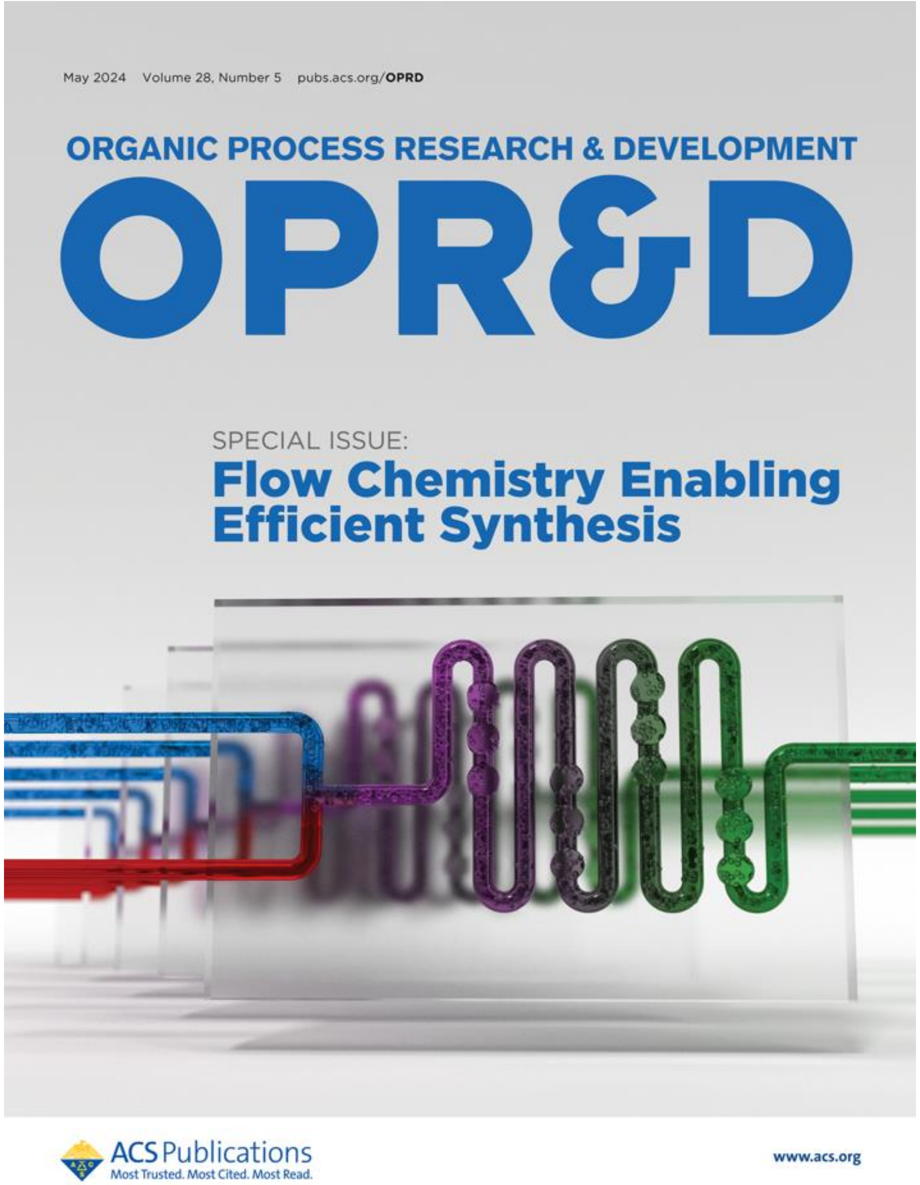
Common Observations

- **Flow is only when there is problem with batch**
- **Flow is too expensive**
- **Flow is not possible at large scale**
- **Flow is still at development stage (too many issues)**
- **Flow does not work**

THINK IN FLOW AND NOT RUN BATCH IN FLOW

Flow is (will be) everywhere at every scale

Continuous Production

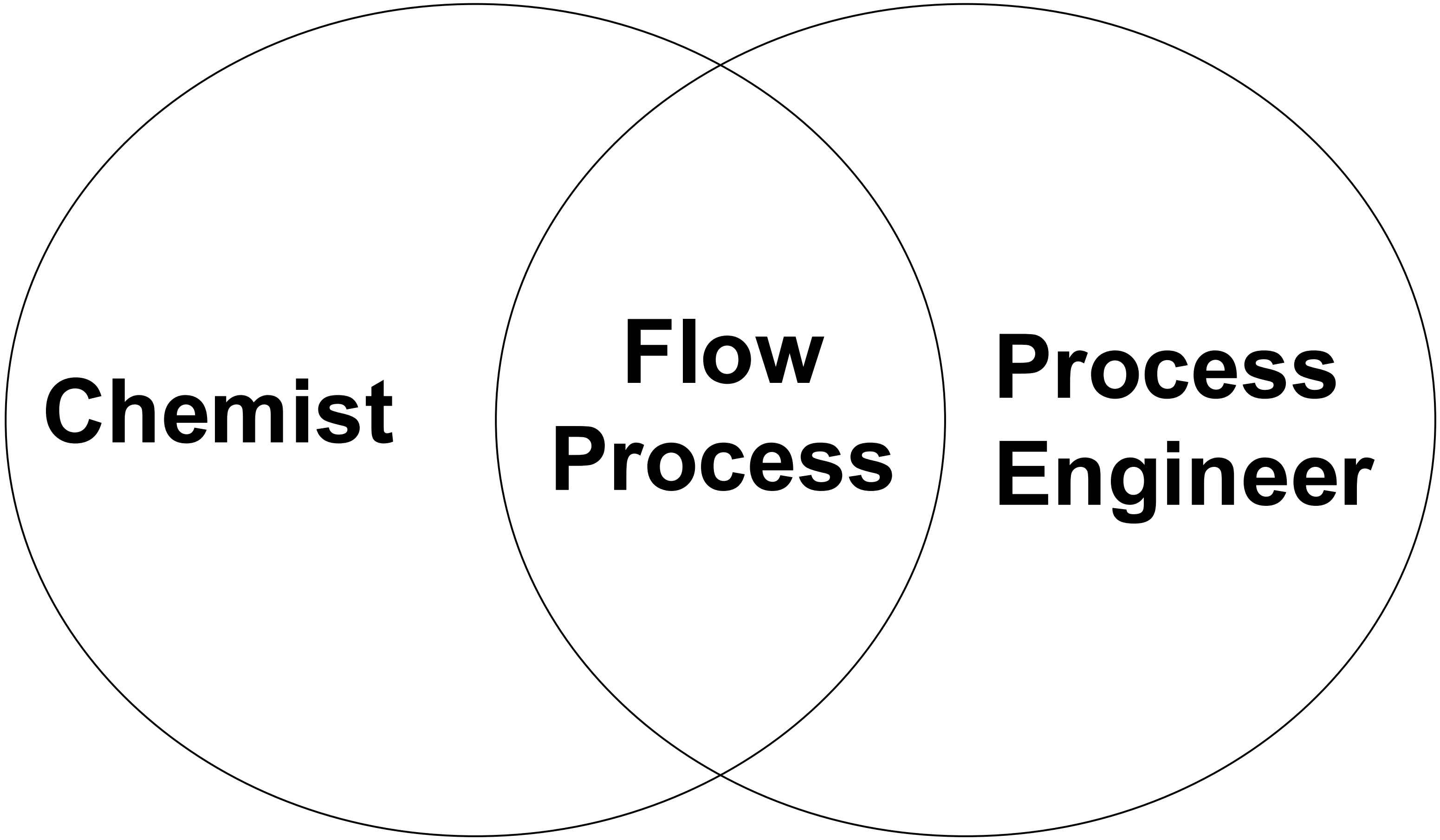


OPRD, May 2024

5th Special issue on Flow

Continuous manufacturing today is a mainstream technology that is widely implemented across fine chemicals, agrochemicals, and pharmaceuticals….

Continuous Production



There is no "ONE SOLUTION" for everything

There is "A SOLUTION" for almost everything

Continuous Production

Engineering Approach:

Design and fabricate continuous reactor for a process

No definite time-lines

Inherent risk in fabrication (Quality and Certification)

Science Approach:

Design chemistry to suit a given continuous flow reactor

Definite and shorter time-lines (Few Weeks)

No Fabrication Risk (Standardized Quality with Certification)

Process Intensification

What is a Chemical Reaction ?

Process Intensification

What is a Chemical Reaction ?

Breaking and Formation of Chemical Bonds

Process Intensification

What is a Chemical Reaction ?

Breaking and Formation of Chemical Bonds

Vibrational and Rotational Motions

Process Intensification

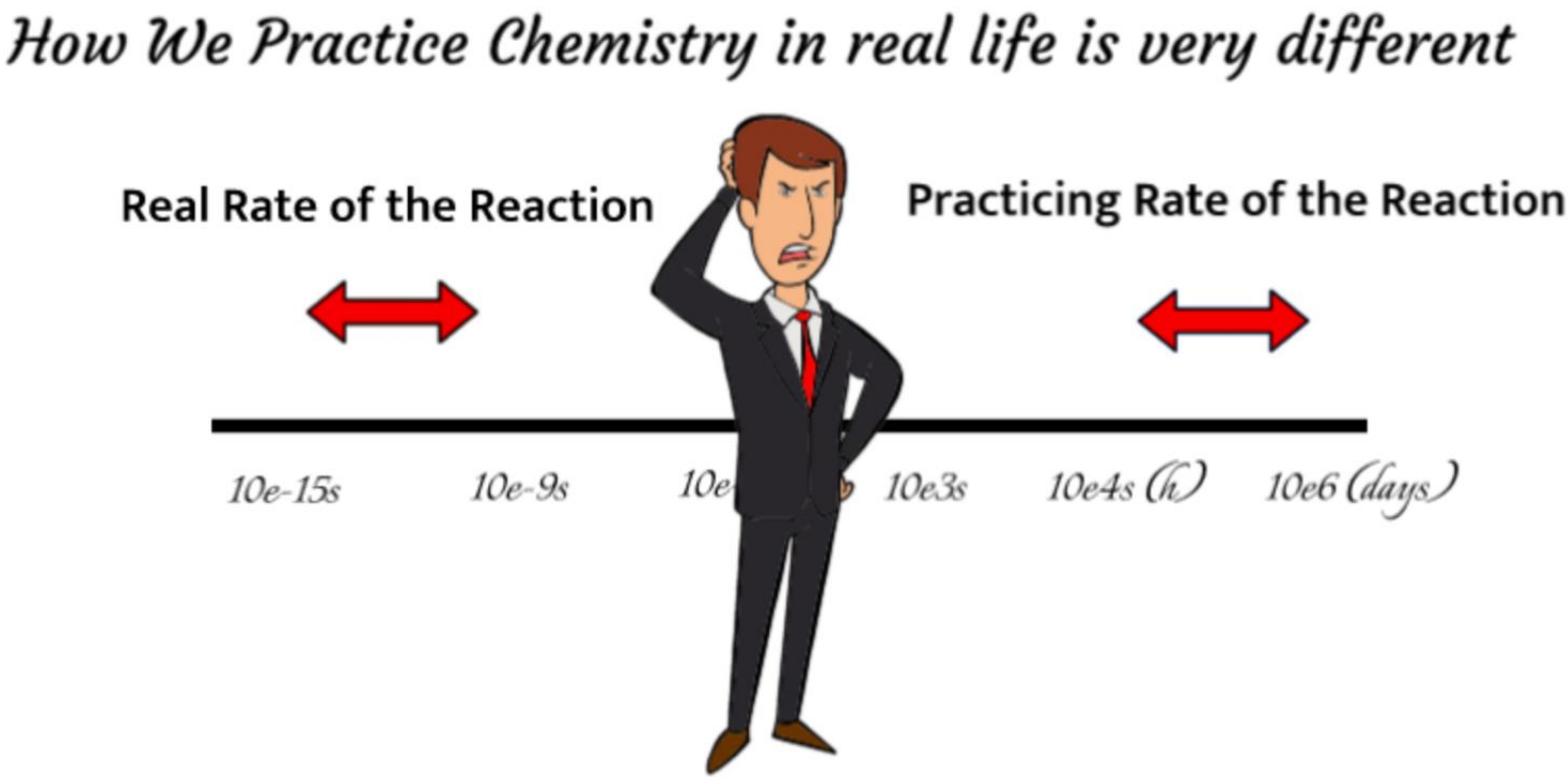
What is a Chemical Reaction ?

Breaking and Formation of Chemical Bonds

Vibrational and Rotational Motions

Time-Scale ~ Femtoseconds

Process Intensification



Process Intensification

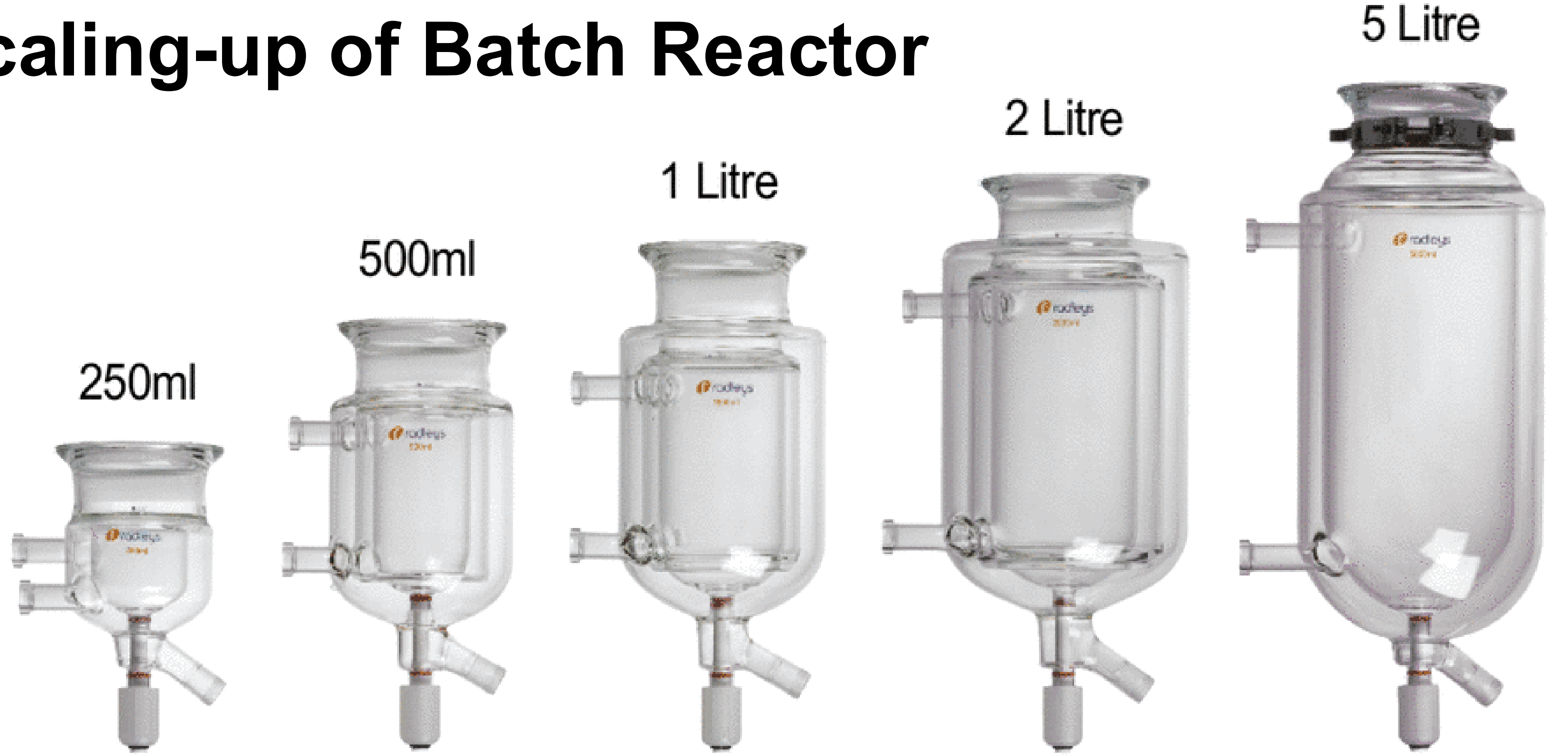
Reactions should happen in sub-nano second time scale

Dangerous due to technological limitations

Heat-Transfer dictates the rate in Batch Reactors

Process Intensification

Scaling-up of Batch Reactor



Heat Transfer Deteriorates →

$$\frac{A}{V} = \frac{1}{V^{1/3}}$$

Heat Management

Heat Generation

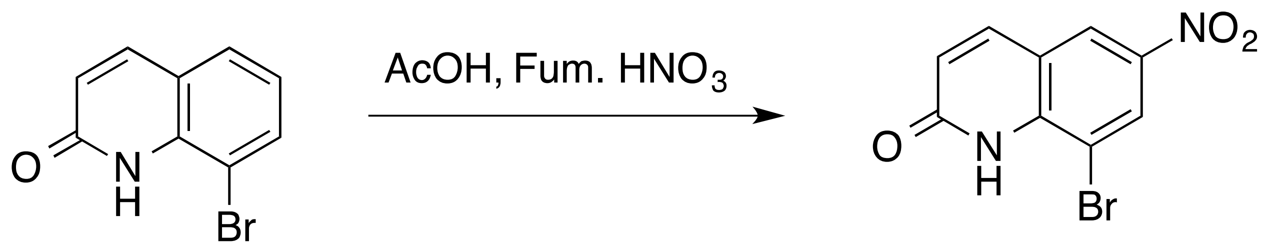
ΔH can be calculated or measured

DSC: Onset of Decomposition and heat generation

If the heat generation is alarming (>300 J/g), one has to make sure that system is always below this decomposition temperature

Heat Management

Novartis



Extremely Exothermic Reaction: Onset at 130 ºC (1373 J/g)

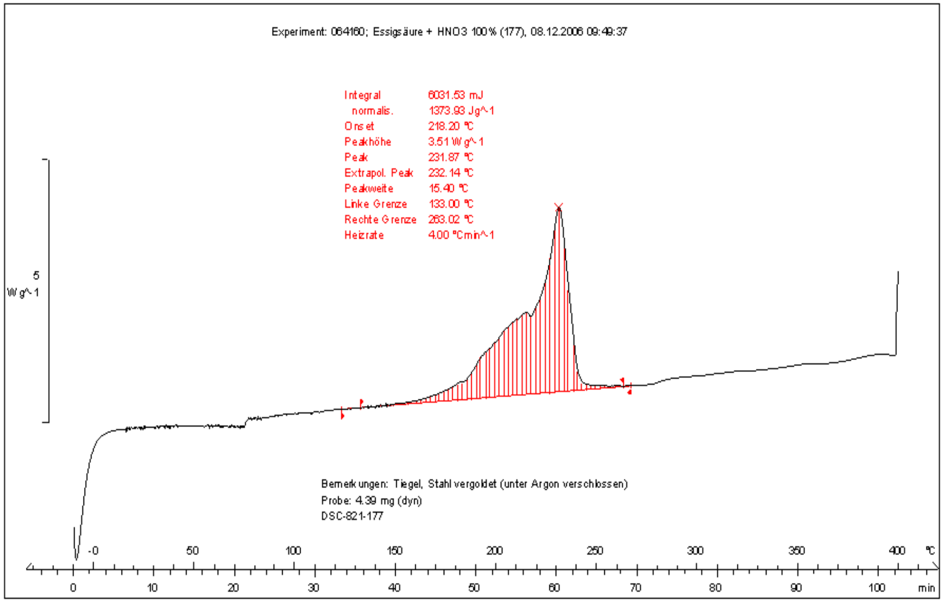


Abb. [6]: Dynamischer DSC-Thermostabilitätstest der Mischung Essigsäure/ Salpetersäure.

Batch process at 118 C for 15 min but at 0.1M scale

Process Intensification

Batch Reactor : SPEED vs CONTROL

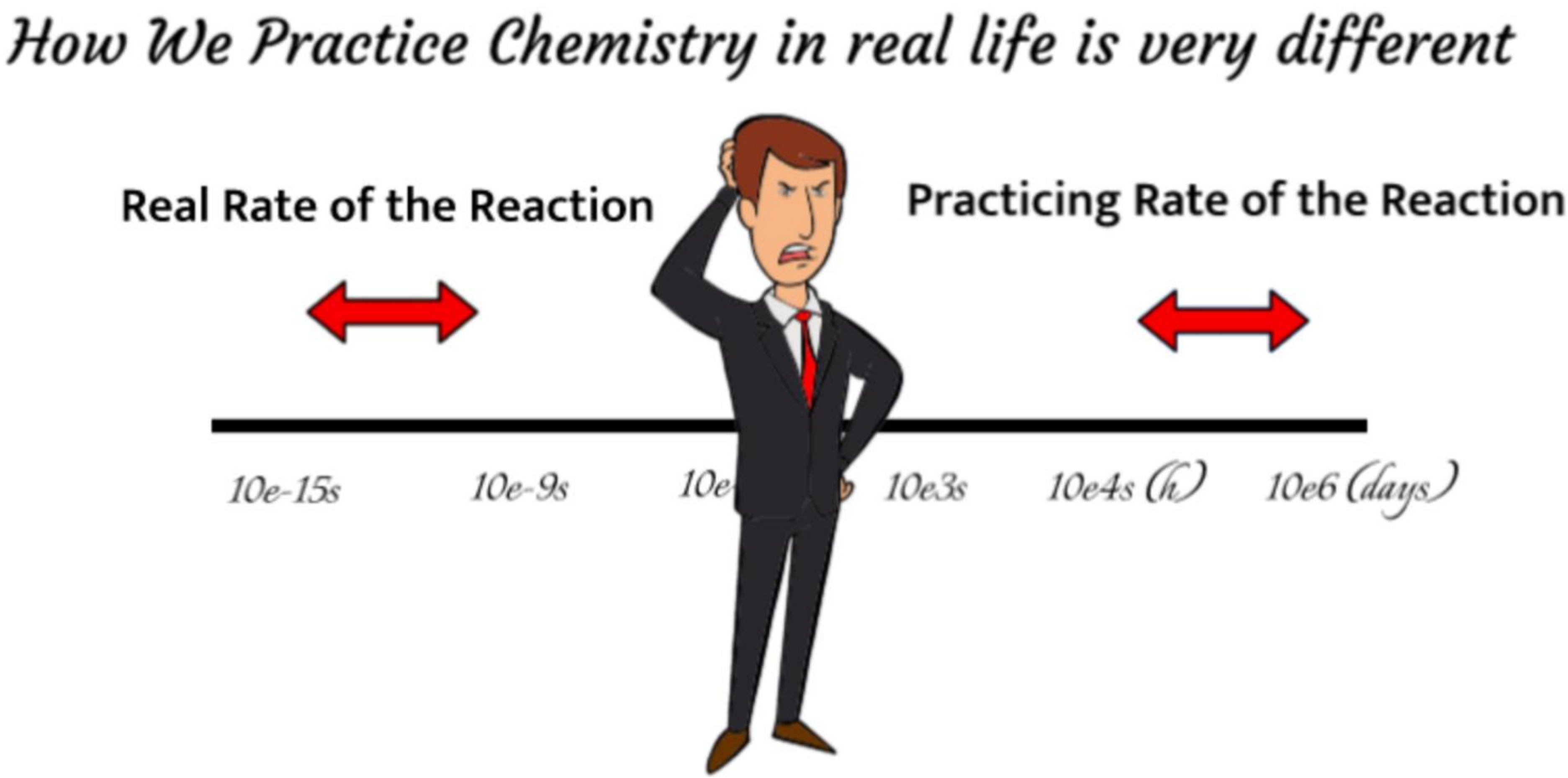
Sacrifice Speed : Slow Down the Reactions

Process Intensification

Batch Reactor : Technology is the Problem

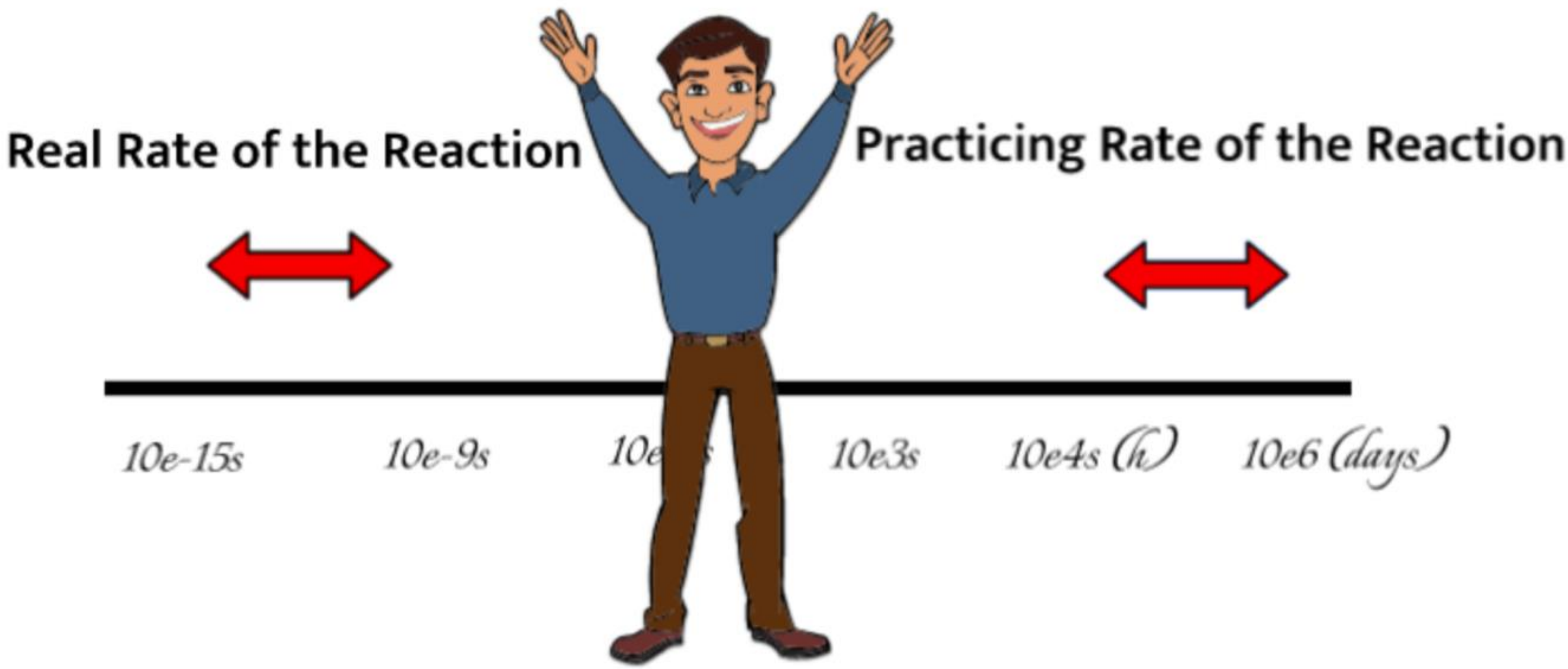
Sacrifice Speed to Gain Control

Process Intensification



Process Intensification

Conventional Batch Reactors have Poor Heat Trasnfer Rate



Process Intensification

Chemist

Process Intensification

Batch Reactor : SPEED vs CONTROL

Sacrifice Speed : Slow Down the Reactions

How does one control the rate of the reaction?

Rate of Chemical Reactions

$$k = A\, e^{-Ea/RT}$$

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A = Fraction of Effective Collisions per unit time

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Molecules/time = (1/time) x molecules with Ea

Rate of Chemical Reactions

$$k = A\, e^{-Ea/RT}$$

A = Fraction of Effective Collisions per unit time

Ea/RT = Fraction of molecules with Activation Energy

Molecules/time = (1/time) x molecules with Ea

To Control Rate:

Control fraction of effective collisions
Control of mol with Ea

Rate of Chemical Reactions

$$k = A\,e^{-Ea/RT}$$

Transition State Theory:

Rate of Chemical Reactions

$$k = A\, e^{-Ea/RT}$$

Transition State Theory:

- **Number of Collision (Diffusion, Mixing, Conc.)**

Rate of Chemical Reactions

$$k = A\,e^{-Ea/RT}$$

Transition State Theory:

- Number of Collision (Diffusion, Mixing, Conc.)
- Orientation

Rate of Chemical Reactions

$$k = A\, e^{-Ea/RT}$$

Transition State Theory:

- Number of Collision (Diffusion, Mixing, Conc.)
- Orientation
- Activation Energy (Thermal or Mechanical)

Rate of Chemical Reactions

How does one control the rate of the reaction?

Rate of Chemical Reactions

How does one control the rate of the reaction?

Add Solvent

Rate of Chemical Reactions

How does one control the rate of the reaction?

Add Solvent **Low Throughput, more efluent**

Rate of Chemical Reactions

How does one control the rate of the reaction?

Add Solvent **Low Throughput, more efluent**

Decrease Temperature **Higher energy cost**

Rate of Chemical Reactions

How does one control the rate of the reaction?

Add Solvent **Low Throughput, more efluent**

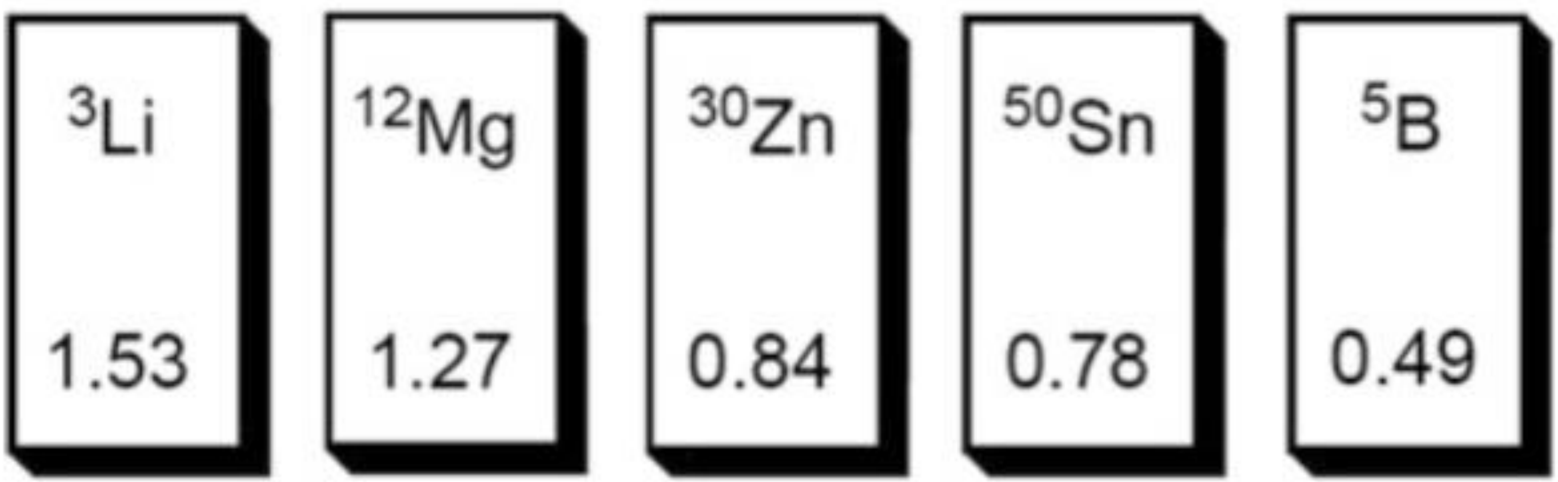
Decrease Temperature **Higher energy cost**

Change Chemistry

SPEED vs CONTROL

Reactivity of OMC

Decreasing Reactivity
(Increasing Functional Group Tolerance)



Decreasing Electronegativity difference
between Metal and Carbon

"Basics of Flow Microreactor Synthesis", J. Yoshida, Springer Briefs in Molecular Science, 2015

Process Intensification

How About SPEED & CONTROL ??

Process Intensification

How About SPEED & CONTROL ??

Continuous Flow Chemistry

Process Intensification

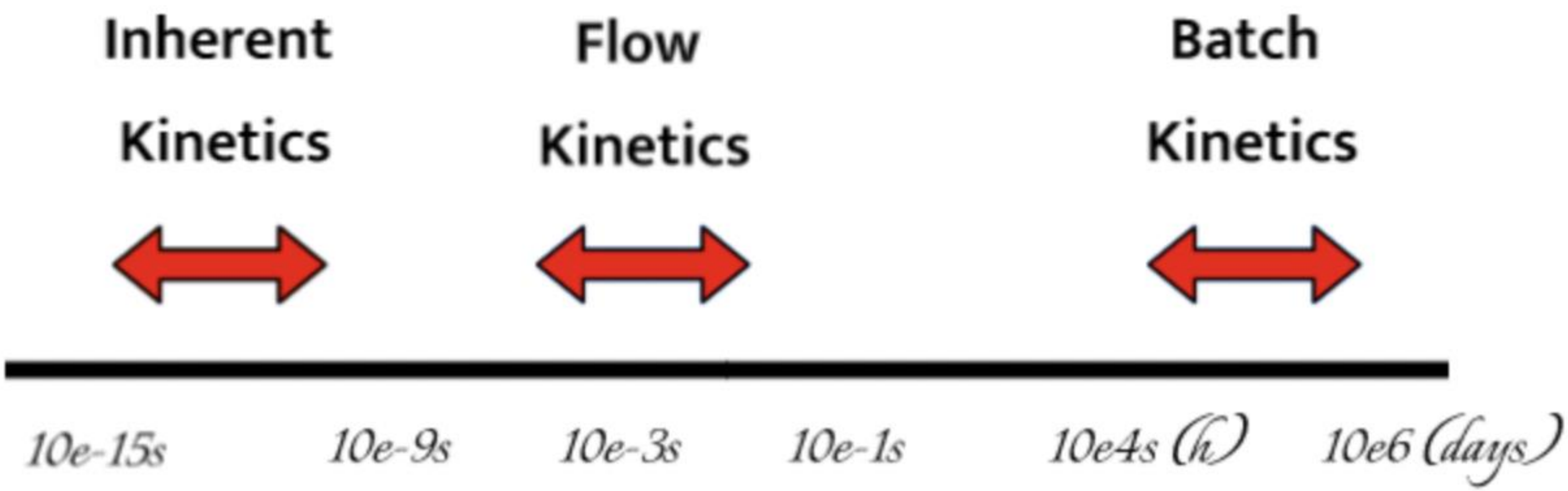
How About SPEED & CONTROL ??

Continuous Flow Chemistry

Fast Reactions or Ultrafast Reactions

Process Intensification

Current State of the Art in Process Intensification



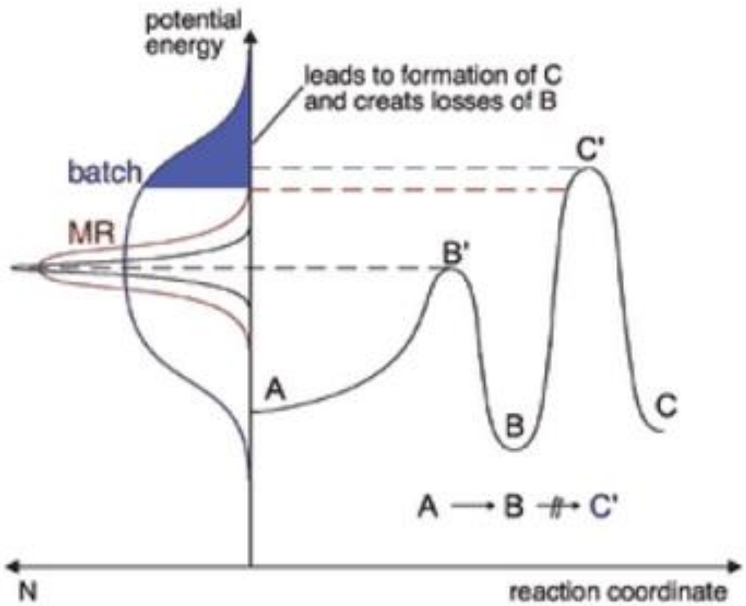
Why Conduct Fast Reactions

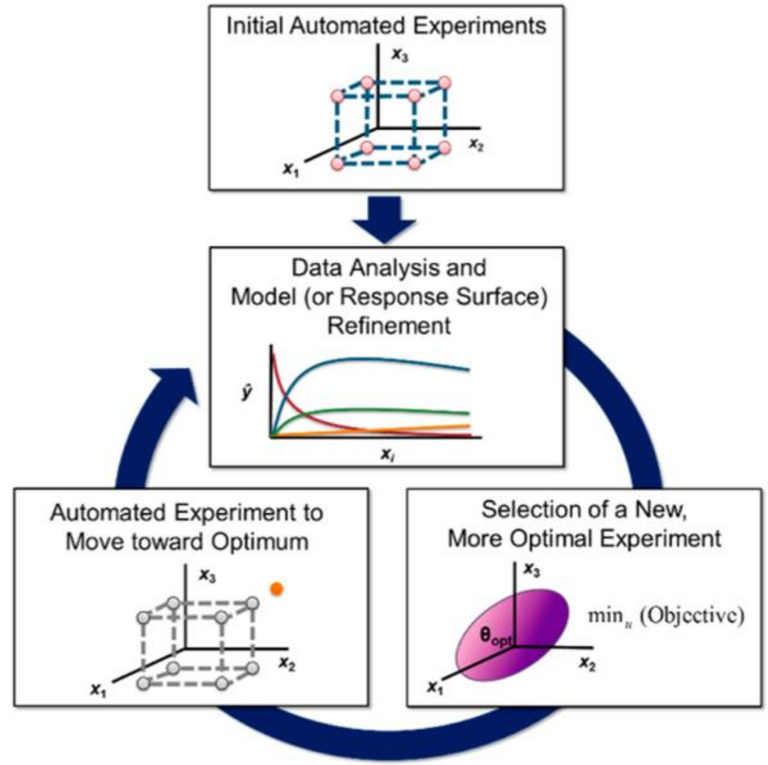
- Rapid Construction of Chemical Libraries
- Rapid Synthesis of Radioactive Probes
- On Demand Rapid Synthesis
- Cost of Production per Unit Volume Decreases
- Handling of Hazardous Chemical Intermediates
- TIME RESOLVED SYNTHESIS
- New chemistry Space
- New Process Window

Flash Chemistry: Fast Organic Synthesis in Microsystems Jun-ichi Yoshida © 2008 John Wiley & Sons, Ltd. ISBN: 978-0-470-03586-3

Flow Process Benefits

Tighter Process Control & Automation

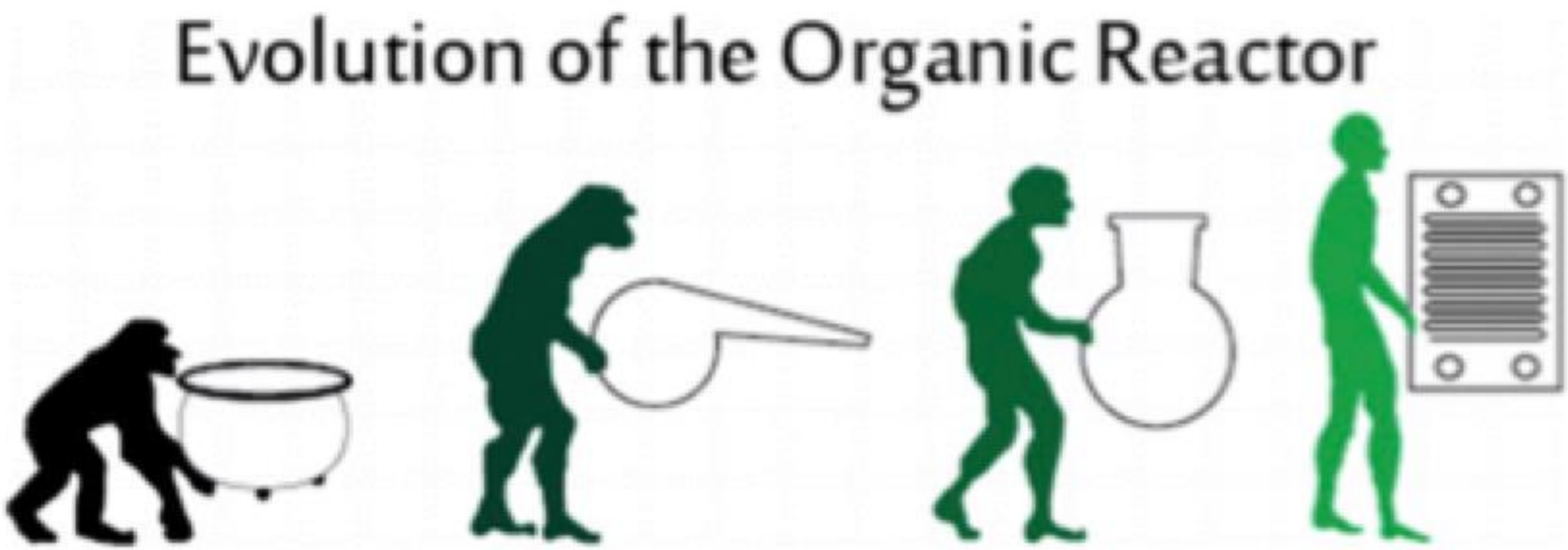


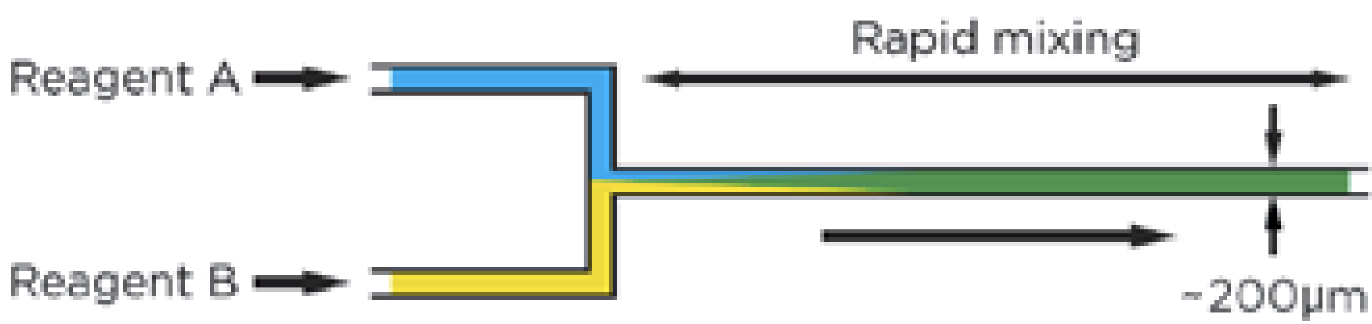


Reizmen and Jensen Acc. Chem. Res., 2016, DOI: 10.1021/acs.accounts.6b00261

http://www.sigmaaldrich.com/technical-documents/articles/chemfiles/microreactor-technology.html

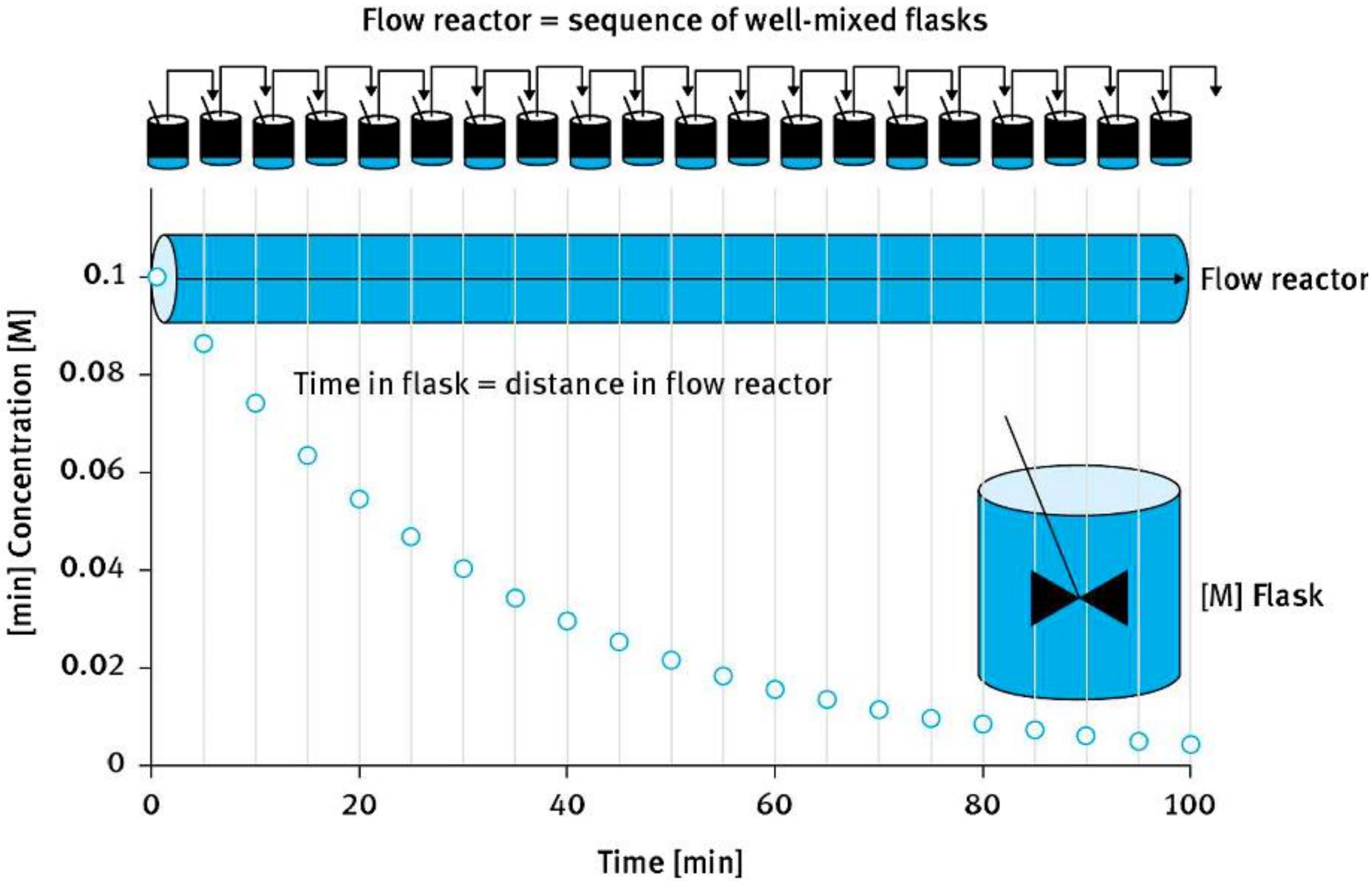
Continuous Flow Processes





Steven Ley et al

Flow Process



Heat Transfer and Mixing Improves

Flow Chemistry: F Darvas, G Dorman, V Hesse; De Gruyter; 2014

Process Intensification: The Goal

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

Slide: Charlotte Wiles

Flow Process Benefits

Exothermic Reactions
- Very good temperature control
- Accurate residence time control
- Efficient mixing
- Less chance for thermal run-away
- Higher productivity per volume
- High selectivity

Endothermic Reactions

- Control over T, p and residence time
- High selectivity
- Accessing new chemistry
- Higher productivity per volume
- High atom efficiency

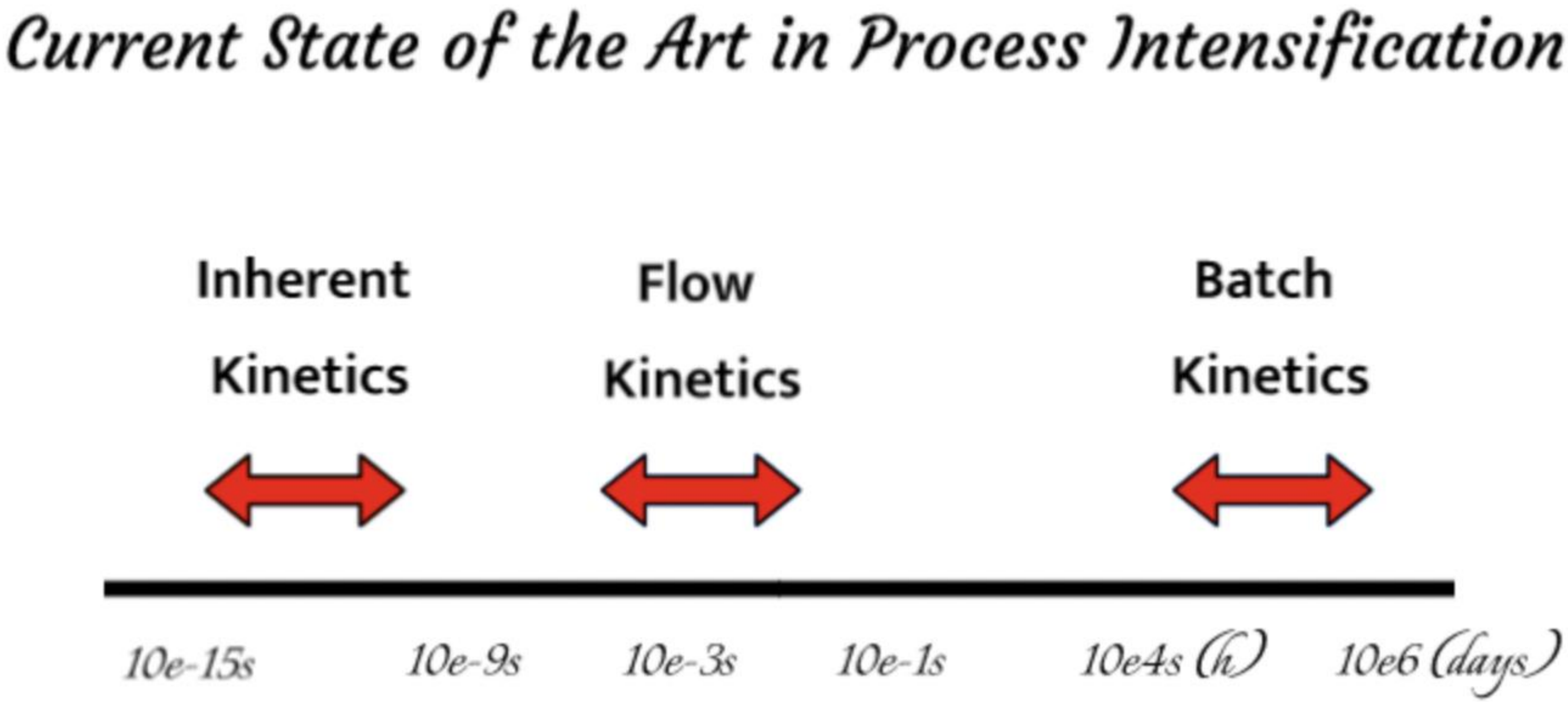
Reactions with gases

- Accurate gas flow regulation
- Increased safety
- Easy catalyst recycling
- High selectivity
- No Headspace

Scale up

- Increased safety
- Higher productivity per volume
- Selectivity
- Reproducibility

Process Intensification



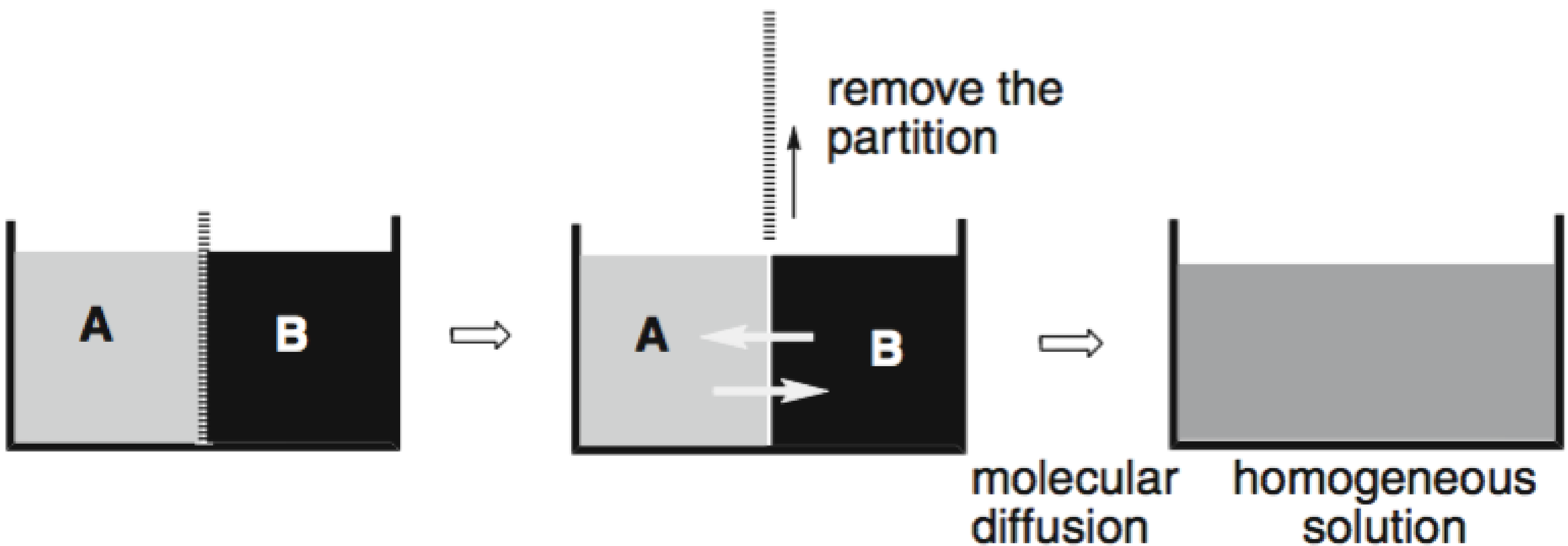
In theory: we can do reactions even in nano second

Rate of Chemical Reaction

Rate of mixing has to be faster than rate of reaction

SPEED vs CONTROL

Mixing



“Basics of Flow Microreactor Synthesis”, J. Yoshida, Springer Briefs in Molecular Science, 2015

SPEED vs CONTROL

$$t = d^2/2D$$

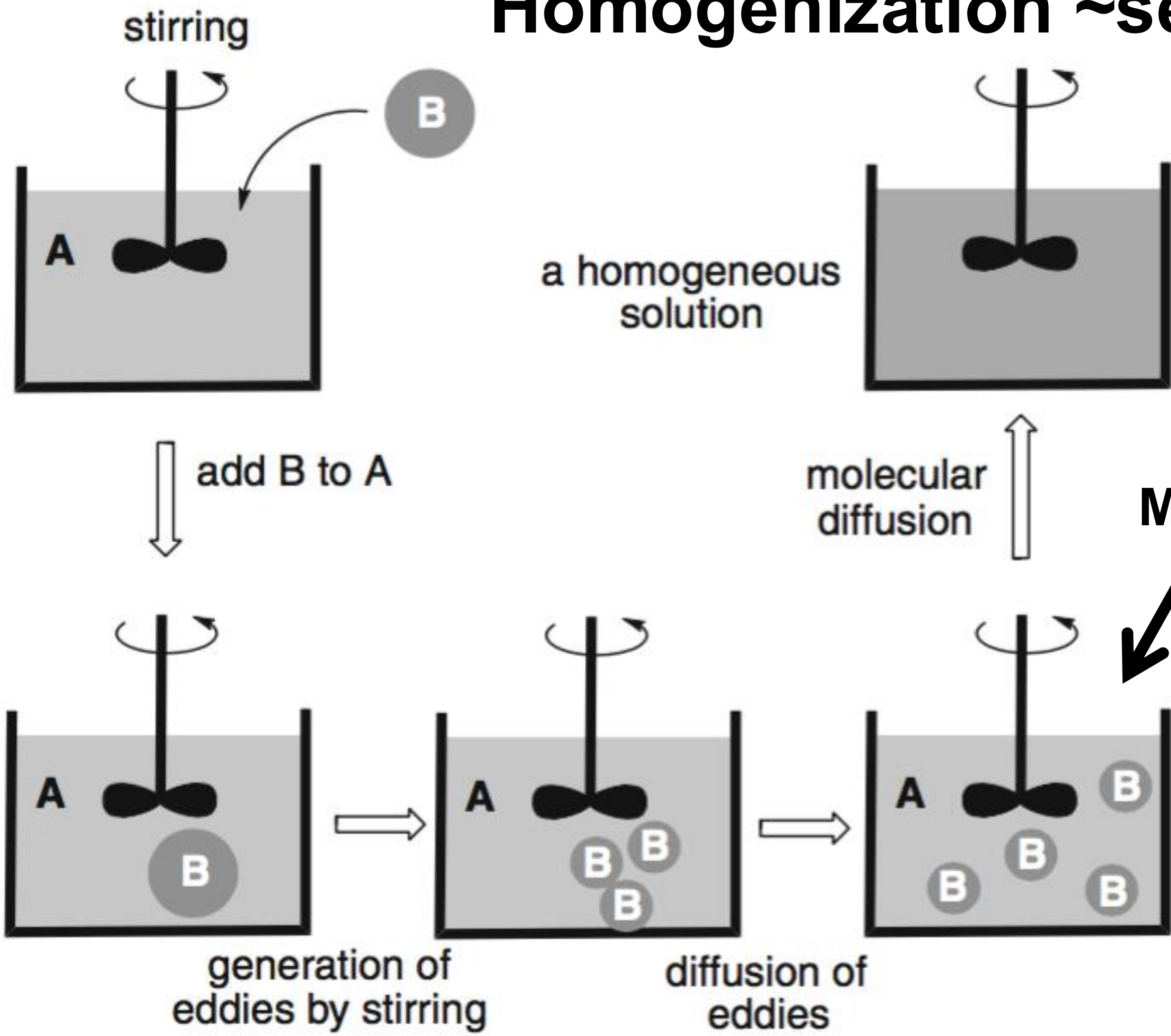
D for small molecules range from 1-3x10^{-5} cm^2/s

Diffusion distance (μm)	Diffusion time (s)	Note
1	0.0005	The size of a bacterium
10	0.05	The size of an animal cell
100	5	
1000 (1 mm)	500 (8.3 min)	
10,000 (1 cm)	50,000 (14 h)	

"Basics of Flow Microreactor Synthesis", J. Yoshida, Springer Briefs in Molecular Science, 2015

SPEED vs CONTROL

Homogenization ~seconds



Minimum size of these Eddies is 10-100 μ

"Basics of Flow Microreactor Synthesis", J. Yoshida, Springer Briefs in Molecular Science, 2015

SPEED vs CONTROL

Homogenization ~ seconds

Rate of the reaction ~ sub nanoseconds

Therefore, Mixing and Heat-Transfer limit the rate at which reactions can be carried out

“Basics of Flow Microreactor Synthesis”, J. Yoshida, Springer Briefs in Molecular Science, 2015

Summary

- PI is to improvement the rate of the reaction
- Reactions should happen in sub-nanosecond time domain
- Heat Transfer (Technology) dictates the rate of the reaction
- For ultrafast reactions, rate of mixing becomes limiting factor
- Mixing has to be faster that rate of the reaction
- Improvement in mixing and heat transfer lead to PI
- Continuous Flow Technology allows PI