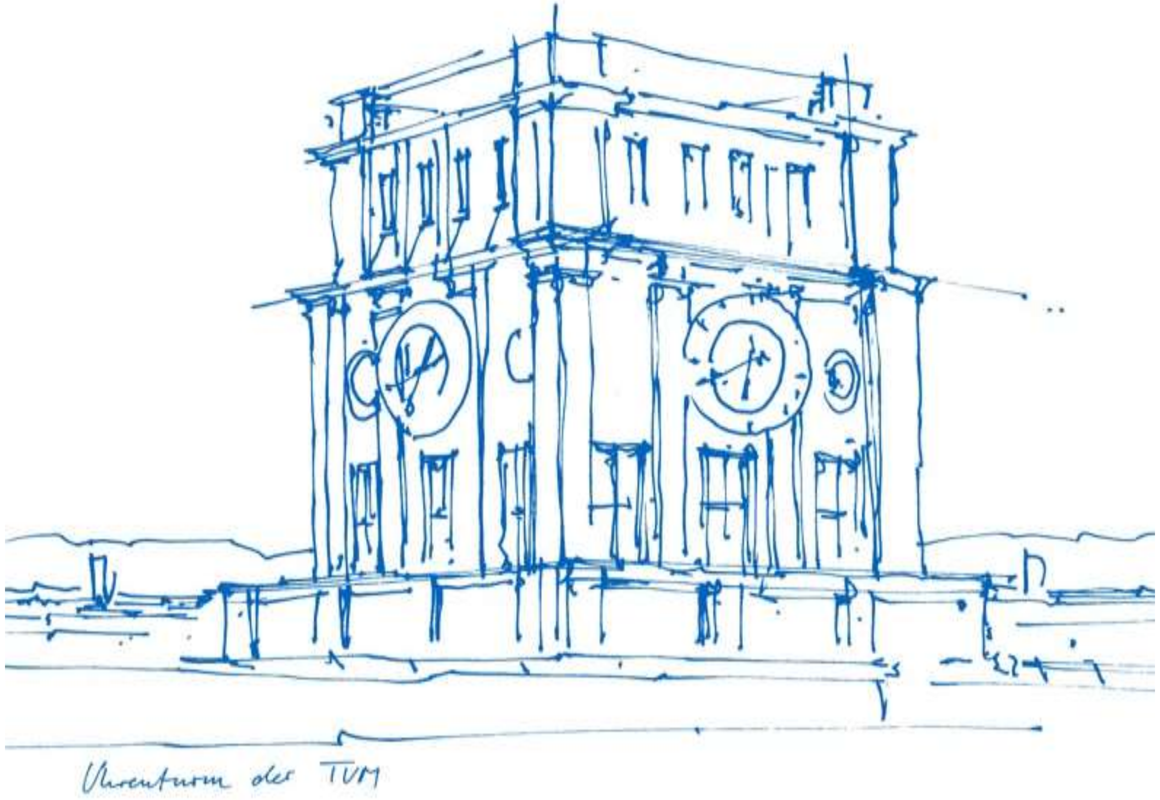
Chair of Communication Networks
TUM School of Computation, Information and Technology
Technical University of Munich

GEFÖRDERT VOM
Bundesministerium für Bildung und Forschung

Introduction to Molecular Communication
- basic concepts & experimental systems -



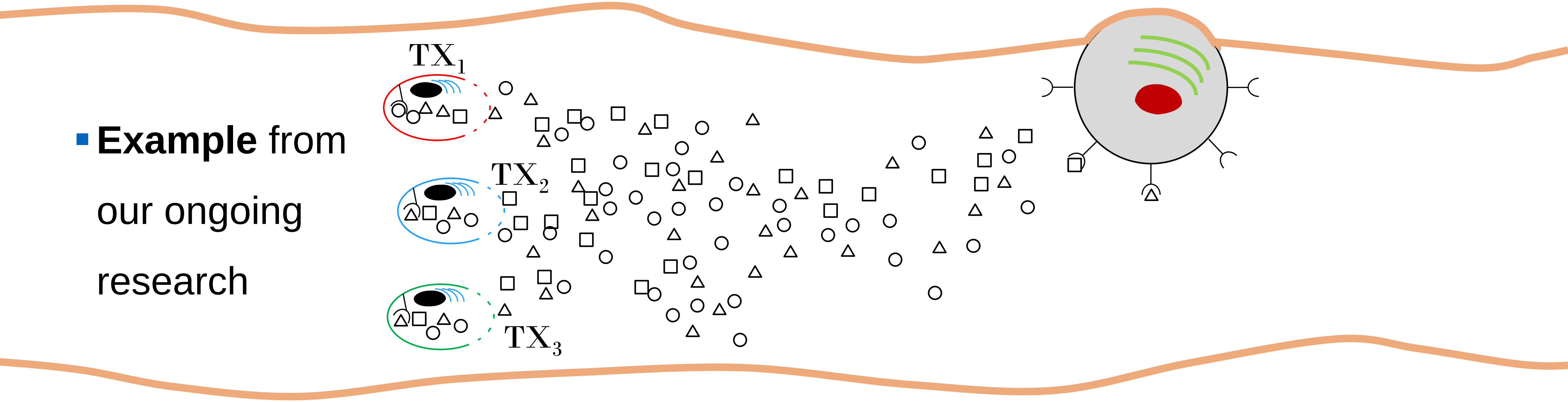
Wolfgang Kellerer
wolfgang.kellerer@tum.de

Alexander Wietfeld
alexander.wietfeld@tum.de

GI/ITG KuVS Summer School of Internet of BioNano Things
June 18-20, 2024, Hohwacht

Introduction to the Basics of **Molecular Communication**

- Possible **Applications**
- Propagation + Tx/Rx **Models**
- Molecular **Degrees of Freedom**
- Definitions and **Standardization**
- **Testbeds**
- **Simulations**
- **Example** from our ongoing research

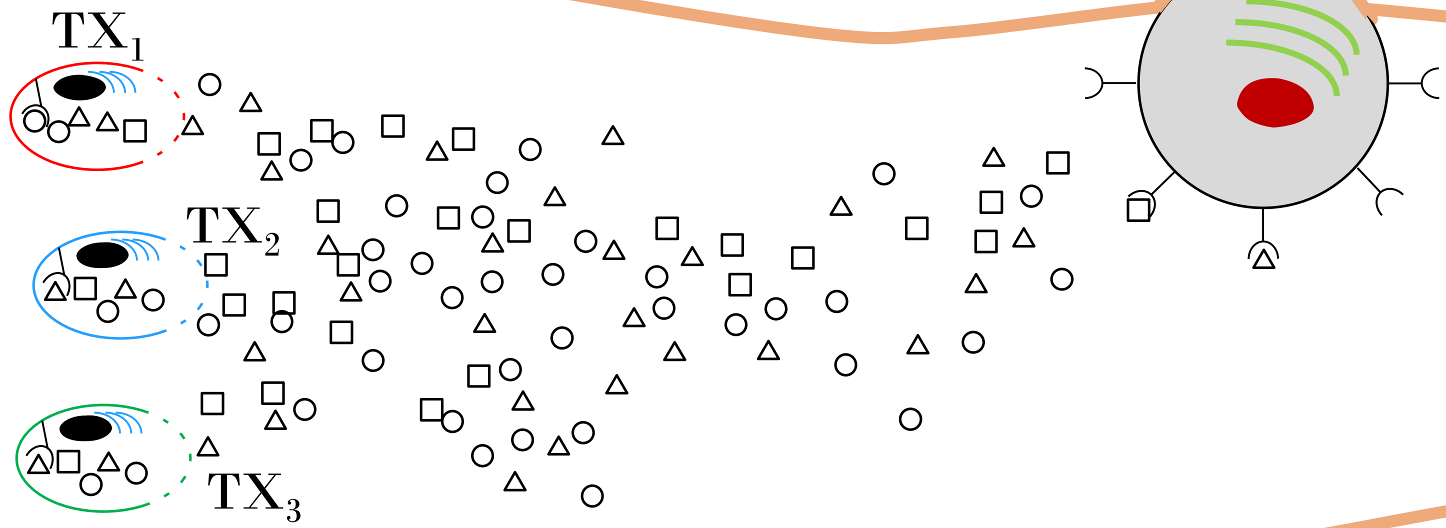


Introduction to the Basics of **Molecular Communication**

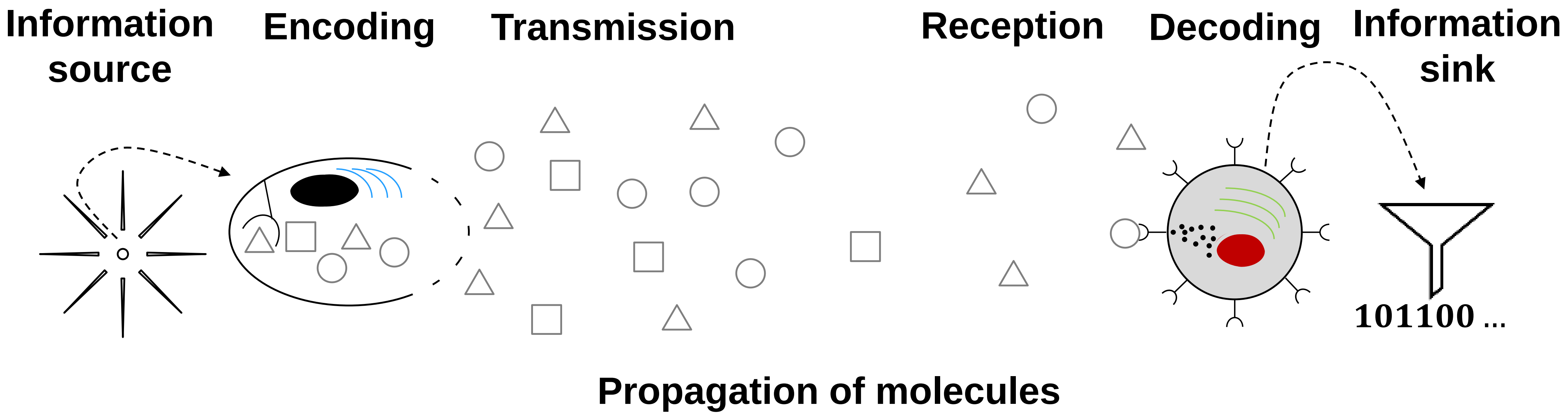
- Possible **Applications**
- Propagation + Tx/Rx **Models**
- Molecular **Degrees of Freedom**
- Definitions and **Standardization**
- **Testbeds**
- **Simulations**

Tutorial

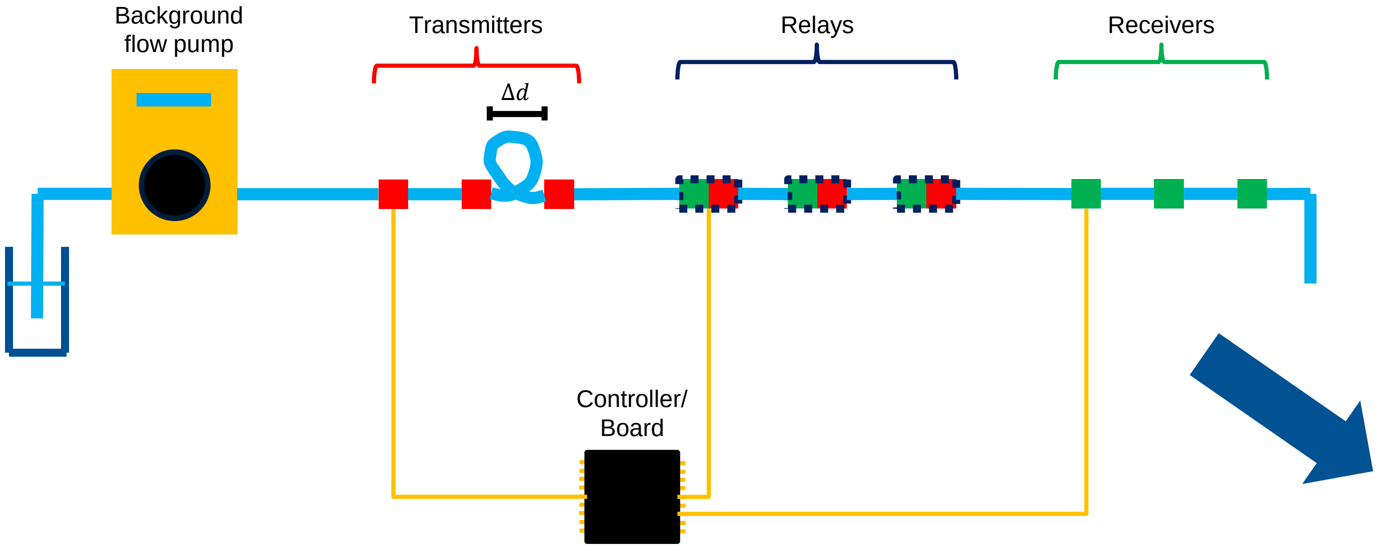
- **Example** from our ongoing research

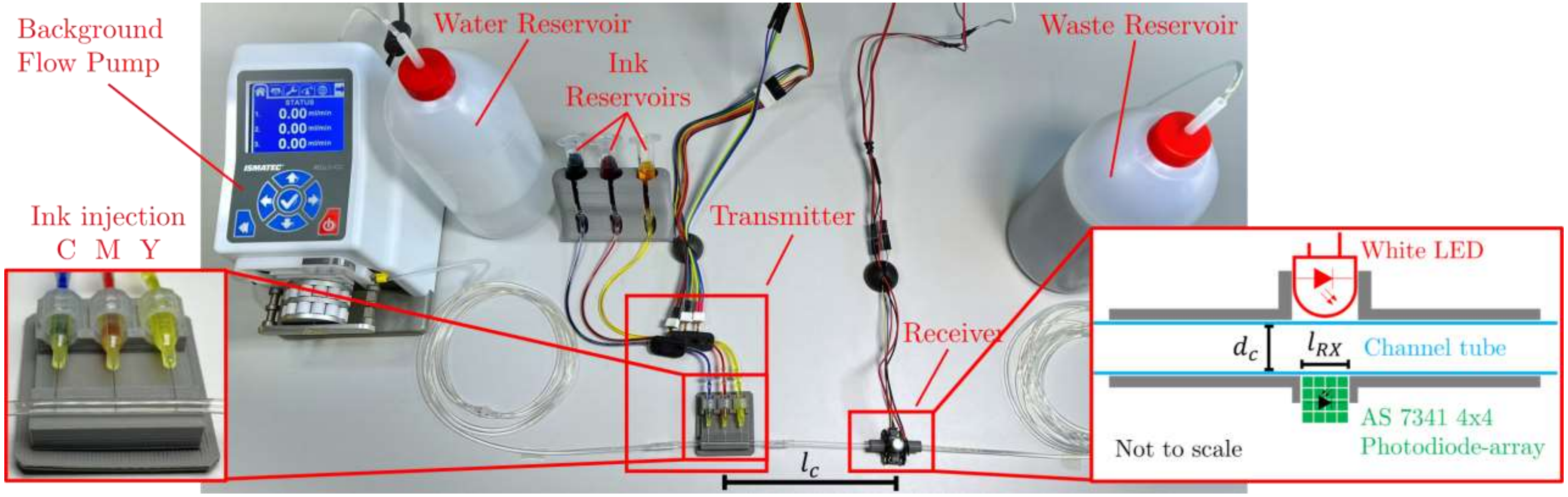


Basics of Molecular Communication (MC)



Possible abstraction (for experiments): liquid flow





Introduction to the Basics of **Molecular Communication**

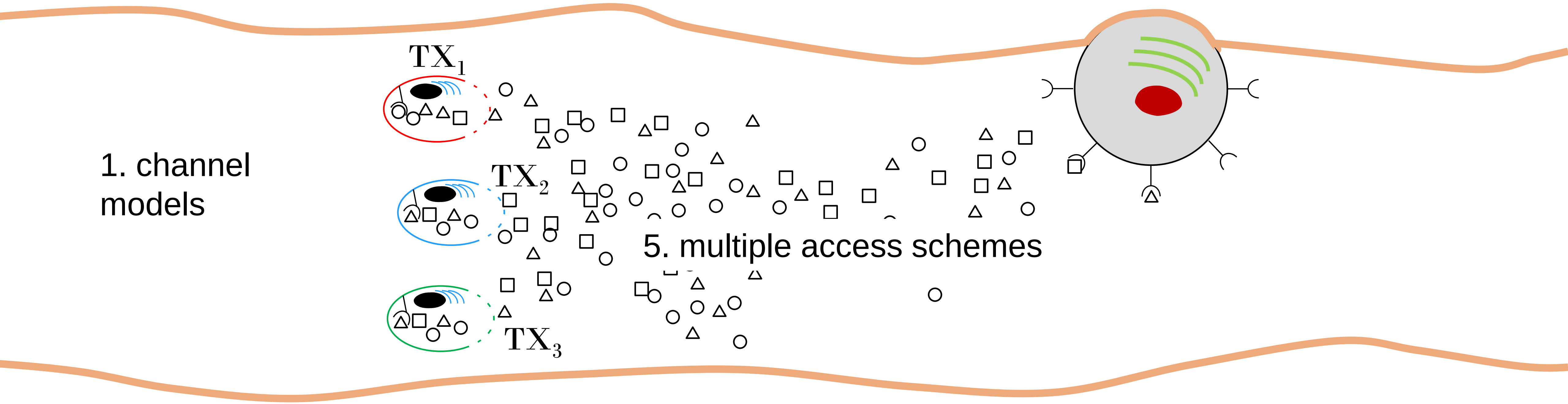
2. molecular propagation models

4. transmitter models

3. receiver models

1. channel models

5. multiple access schemes



Use Cases & Applications

Main Drivers for MC

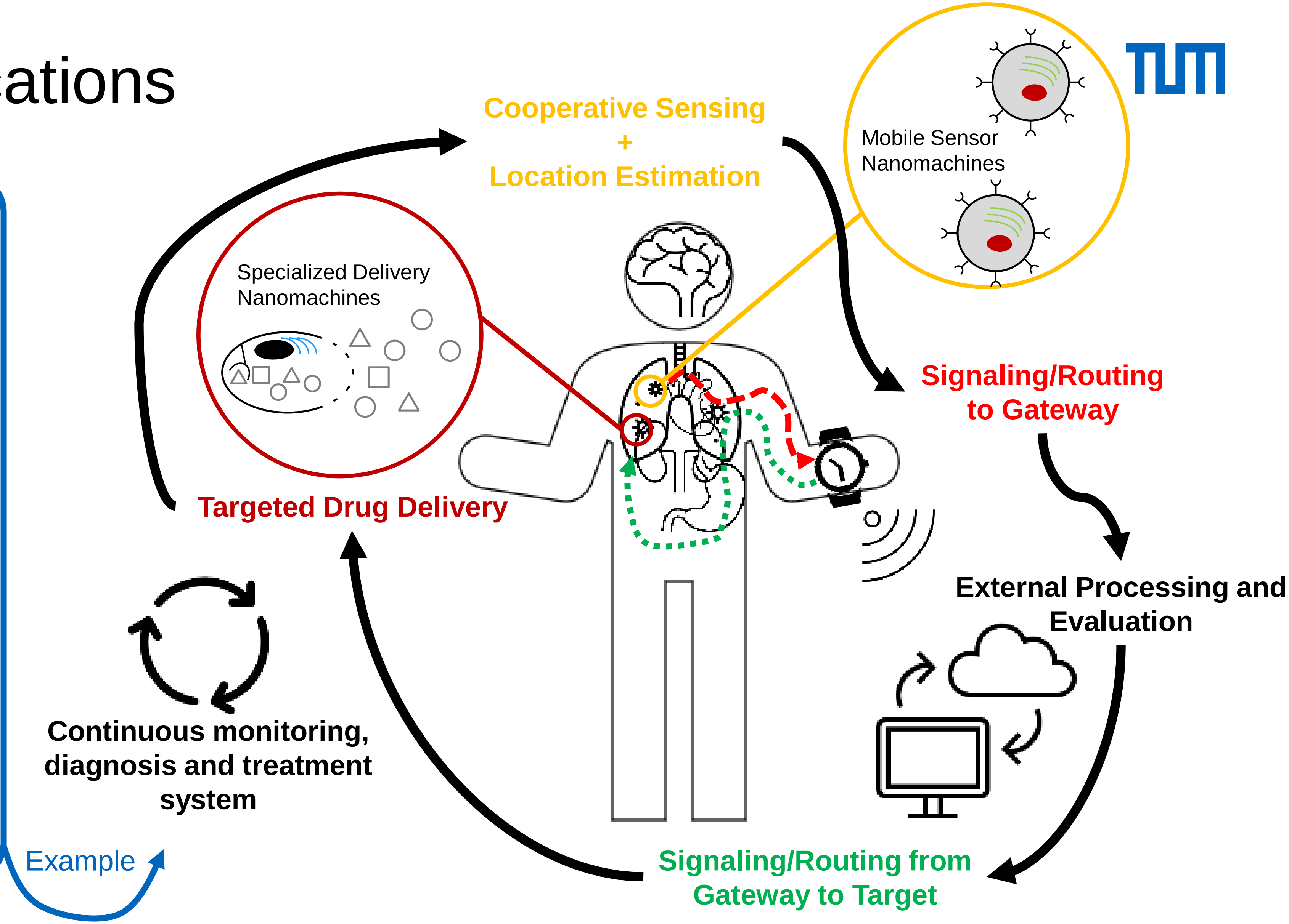
- EM-wave Deficiencies
- Bio-engineering advancements

+

- Energy-efficiency
- Biocompatibility

Emerging application areas

- Biological
- Industrial
- Healthcare
- Environmental
- Information Communication Technology

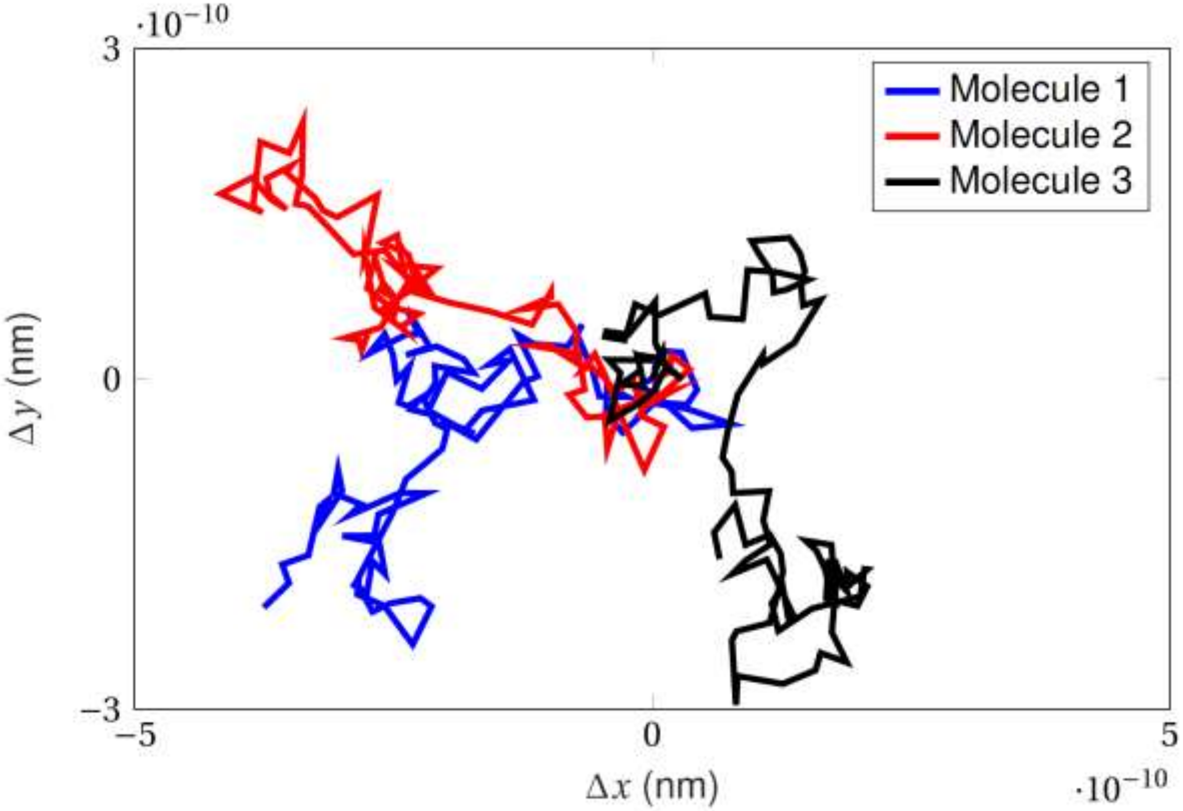


Nakano, Tadashi, Andrew W. Eckford, und Tokuko Haraguchi. *Molecular Communication*. 1. Aufl. Cambridge University Press, 2013. https://doi.org/10.1017/CBO9781139149693.

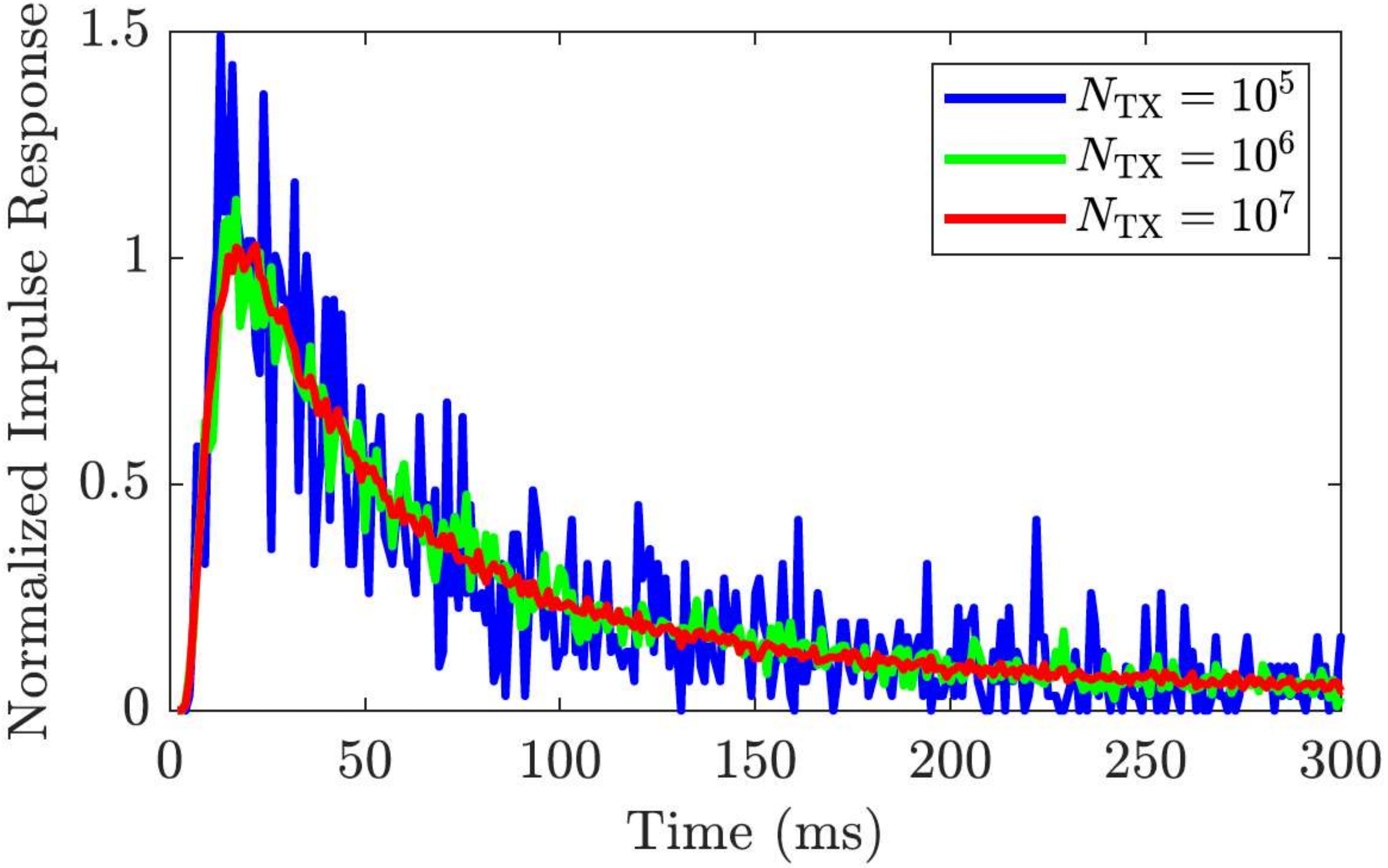
Felicetti, L., M. Femminella, G. Reali, und P. Liò. „Applications of Molecular Communications to Medicine: A Survey". *Nano Communication Networks* 7 (1. März 2016): 27–45. https://doi.org/10.1016/j.nancom.2015.08.004.

Diffusion-Based Molecular Communication (DBMC)

- Brownian motion → diffusion

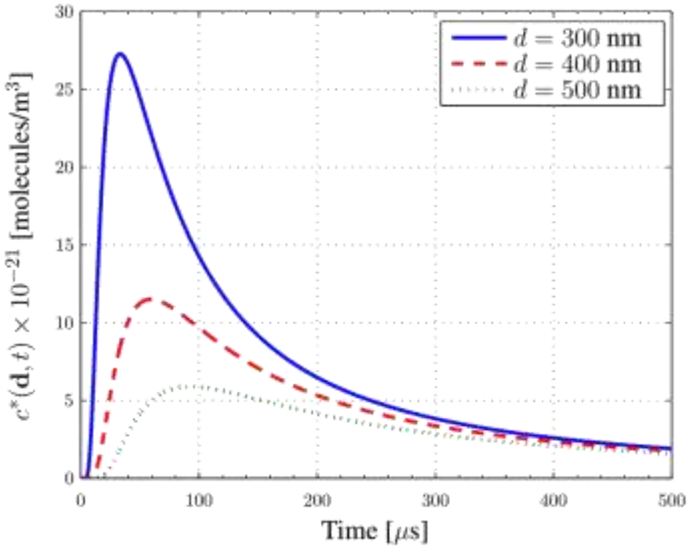


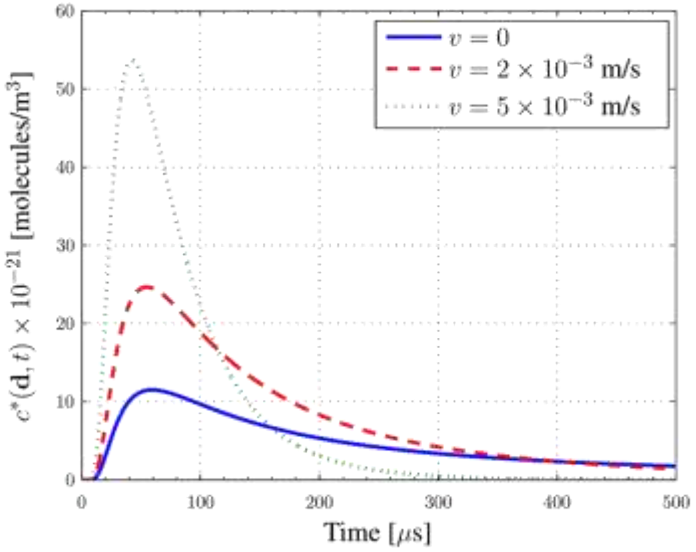
Diffusion Channel Impulse Response

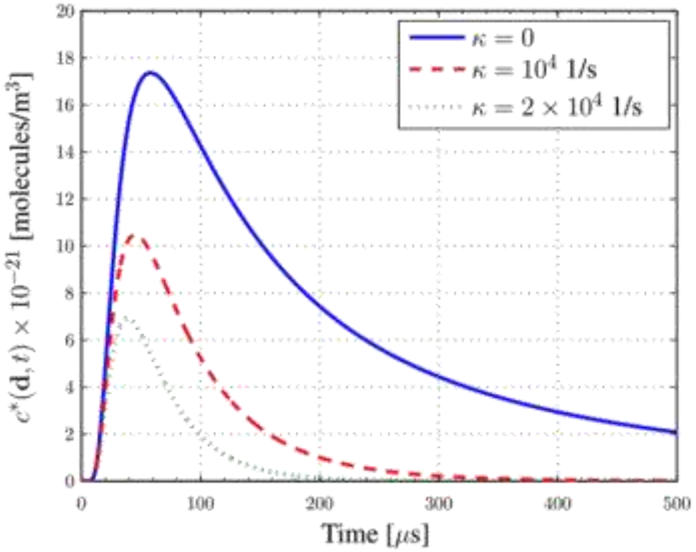


Molecular Propagation Modeling

molecule concentration c







Diffusion

Diffusion coefficient $\boldsymbol{D}$

Advection

Force-/flow-induced velocity $\boldsymbol{v}$

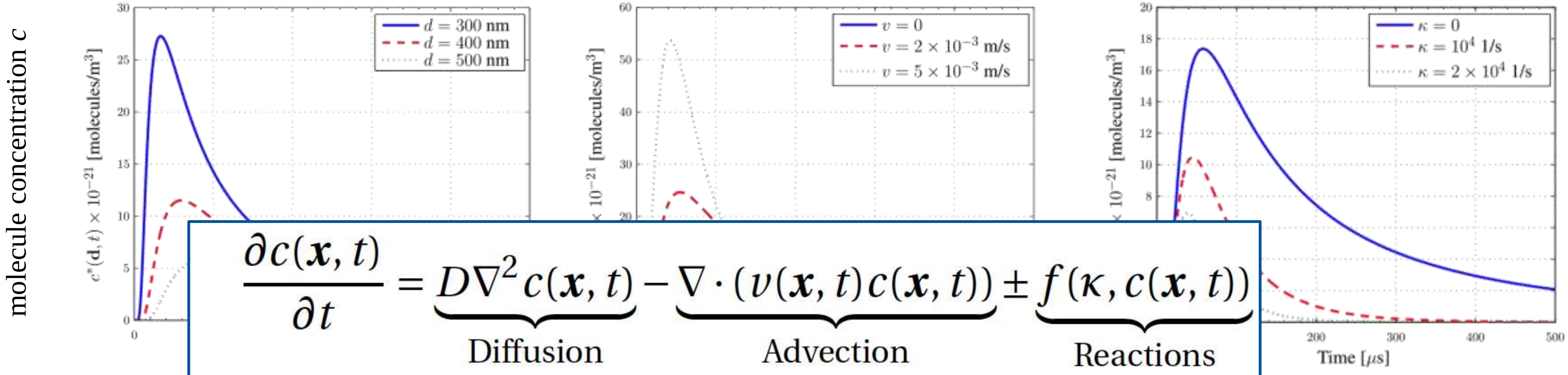
Reaction

Reaction rate constant $\boldsymbol{\kappa}$

Advection-reaction-diffusion equation

Jamali, Vahid, Arman Ahmadzadeh, Wayan Wicke, Adam Noel, und Robert Schober. „Channel Modeling for Diffusive Molecular Communication—A Tutorial Review". *Proceedings of the IEEE* 107, Nr. 7 (Juli 2019): 1256–1301. https://doi.org/10.1109/JPROC.2019.2919455.

Molecular Propagation Modeling



$$\frac{\partial c(\boldsymbol{x},t)}{\partial t} = \underbrace{D\nabla^2 c(\boldsymbol{x},t)}_{\text{Diffusion}} - \underbrace{\nabla\cdot(v(\boldsymbol{x},t)c(\boldsymbol{x},t))}_{\text{Advection}} \pm \underbrace{f(\kappa, c(\boldsymbol{x},t))}_{\text{Reactions}}$$

Diffusion	Advection	Reaction
Diffusion coefficient $\boldsymbol{D}$	Force-/flow-induced velocity $\boldsymbol{v}$	Reaction rate constant $\boldsymbol{\kappa}$

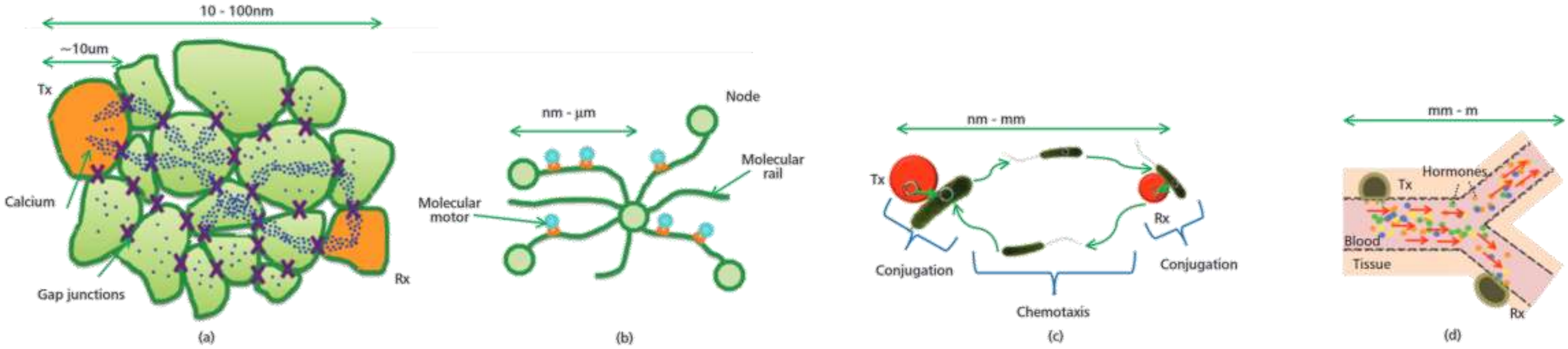
Advection-reaction-diffusion equation

Jamali, Vahid, Arman Ahmadzadeh, Wayan Wicke, Adam Noel, und Robert Schober. „Channel Modeling for Diffusive Molecular Communication—A Tutorial Review“. *Proceedings of the IEEE* 107, Nr. 7 (Juli 2019): 1256–1301. https://doi.org/10.1109/JPROC.2019.2919455.

Molecular Propagation

Biological Transport

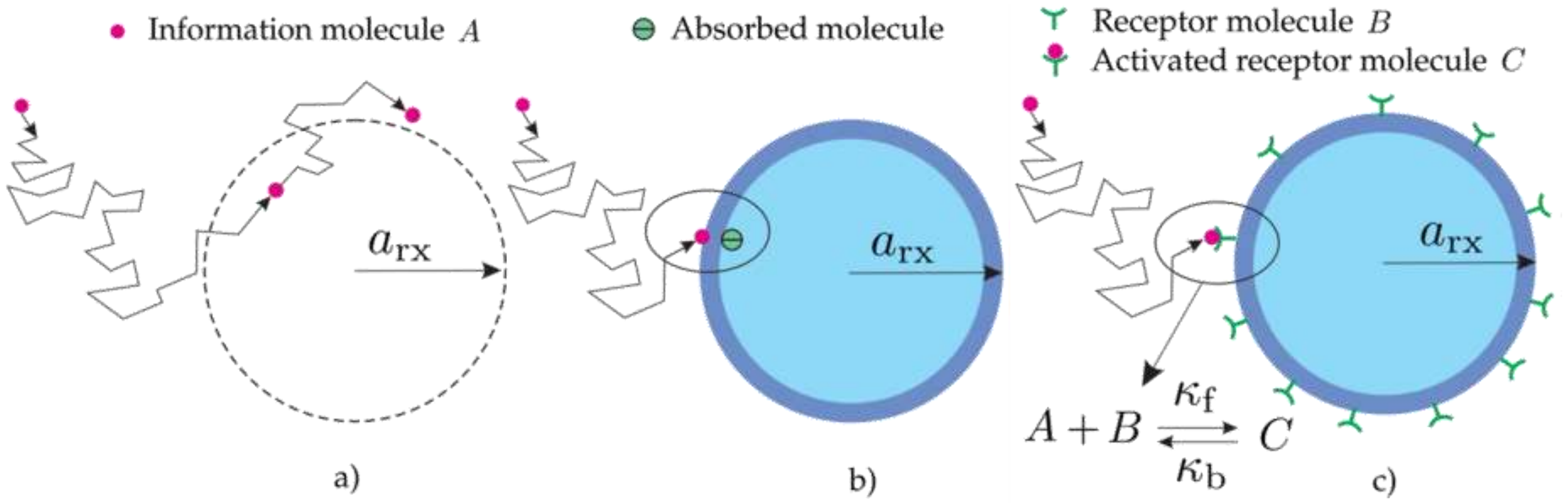
a)	**Very short range**	< 100 nm	between **adjacent** cells
b)	**Short range**	nm – µm	within the **same** cell
c)	**Medium range**	µm – mm	between **nearby** cells
d)	**Long range**	mm – m	between **distant** cells



Akyildiz, I. F., M. Pierobon, S. Balasubramaniam, und Y. Koucheryavy. „The internet of Bio-Nano things". *IEEE Communications Magazine* 53, Nr. 3 (März 2015): 32–40. https://doi.org/10.1109/MCOM.2015.7060516.

Receiver Models

a) **Passive**: information molecules (IMs) can **enter and leave** the cell across the receiver boundaries
b) **Absorbing: IMs** that reach the Rx are **absorbed** as soon as they hit the Rx surface (or parts of it)
c) **Reactive:** when IMs touch the “sensing area” of the Rx (e.g. receptors), a **chemical reaction** occurs



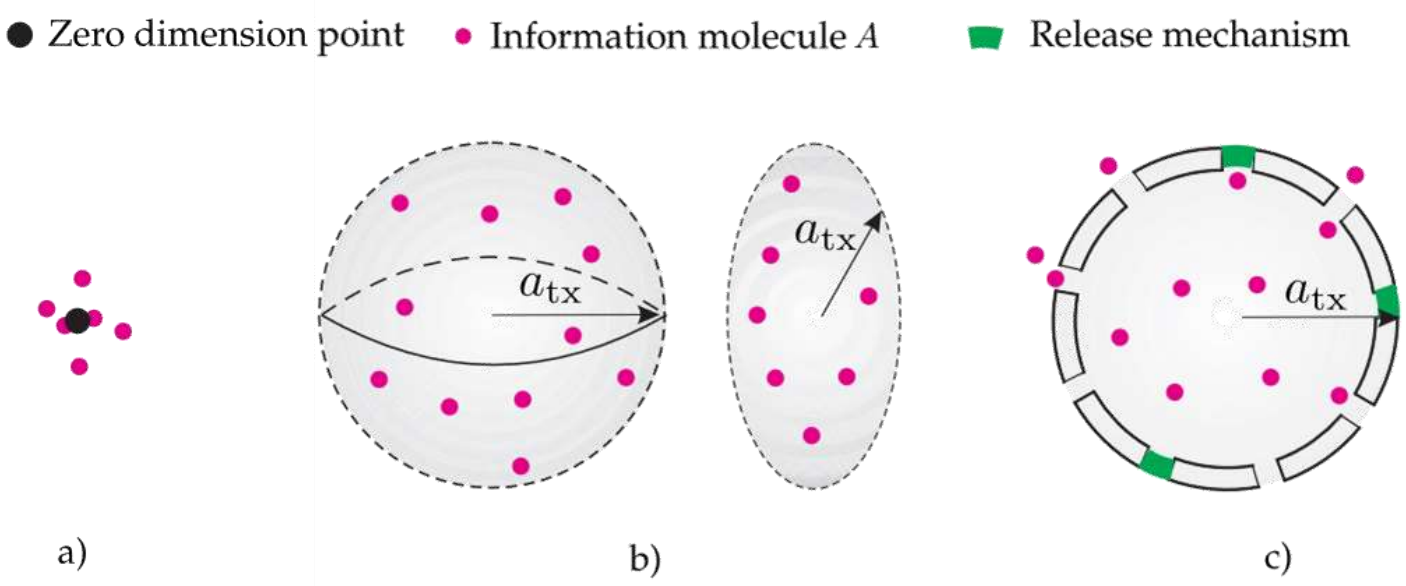
Jamali, Vahid, Arman Ahmadzadeh, Wayan Wicke, Adam Noel, und Robert Schober. „Channel Modeling for Diffusive Molecular Communication—A Tutorial Review“. *Proceedings of the IEEE* 107, Nr. 7 (Juli 2019): 1256–1301. https://doi.org/10.1109/JPROC.2019.2919455.

Transmitter Models

a) **Point**: **0D**-point, IMs produced **instantaneously** and released into the channel immediately

b) **Volume**: IMs are **distributed** over the transmitter volume, generated and released **instantaneously**

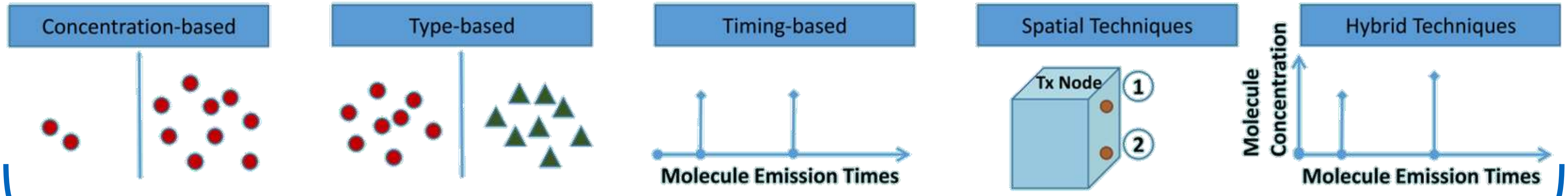
c) **Channel-based**: IMs within Tx **volume** are **released through channels** at the membrane, which open/close according to a model



Jamali, Vahid, Arman Ahmadzadeh, Wayan Wicke, Adam Noel, und Robert Schober. „Channel Modeling for Diffusive Molecular Communication—A Tutorial Review“. *Proceedings of the IEEE* 107, Nr. 7 (Juli 2019): 1256–1301. https://doi.org/10.1109/JPROC.2019.2919455.

Molecular Degrees of Freedom: Physical Resources

Dimensions for signal manipulation



Modulation/duplexing/multiple access schemes

Capability

- Interference mitigation
(between symbols, links, users, …)
- Throughput
- Multi-user/-channel
…

Trade-off

Complexity

- Processing requirements
- Synchronization requirements
- Tx/Rx structure
- Space constraints
…

Kuran, Mehmet Şükrü, H. Birkan Yilmaz, Ilker Demirkol, Nariman Farsad, und Andrea Goldsmith. „A Survey on Modulation Techniques in Molecular Communication via Diffusion“. *IEEE Communications Surveys & Tutorials* 23, Nr. 1 (2021): 7–28. https://doi.org/10.1109/COMST.2020.3048099.

Resources: Energy Perspective

Example: Molecule transmission for diffusion-based MC

$$E_T = nE_S + \frac{n}{c}(E_V + E_C + E_R)$$

Energy spent per pulse of n molecules [J]

1. **Synthesis** of a single molecule

2. Production of a **vesicle** carrying c molecules

3. **Carrying** the vesicle to the cell edge

4. **Releasing** molecules to the inter-cellular space

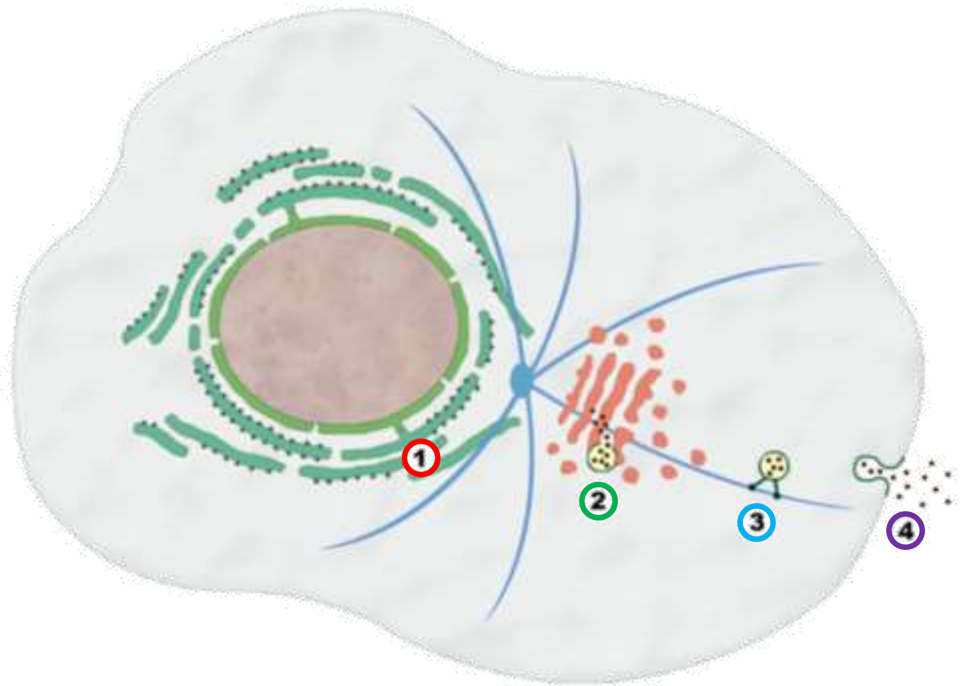


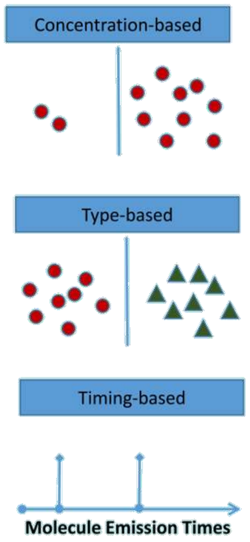
Fig. 3. Steps of exocytosis.

Given **energy production limit of the cell** (via mitochondria/ATP), the **number of IMs is limited**

Kuran, Mehmet Şükrü, H. Birkan Yilmaz, Tuna Tugcu, und Bilge Özerman. „Energy Model for Communication via Diffusion in Nanonetworks“. *Nano Communication Networks* 1, Nr. 2 (Juni 2010): 86–95. https://doi.org/10.1016/j.nancom.2010.07.002.

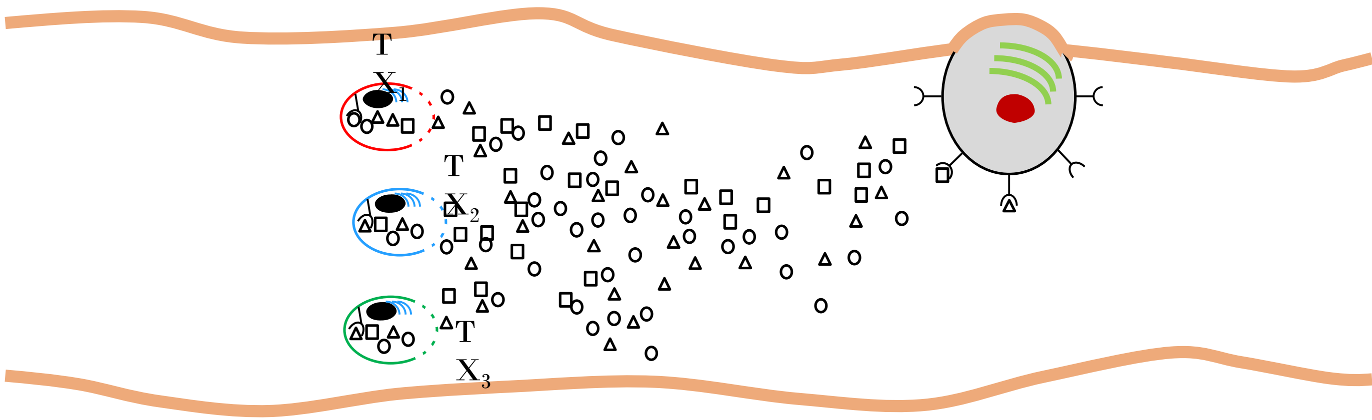
Physical Layer MC Techniques

- Modulation
  - Concentration shift keying
  - Type-based modulation
  - Timing-based modulation
  - Space-shift keying
  - Hybrid models



- Coding
  - Source, channel and network coding

- Multiple Access
  - TDMA (strict synchronization required)
  - MDMA (molecule-division multiple access)
  - NOMA (non-orthogonal multiple access)



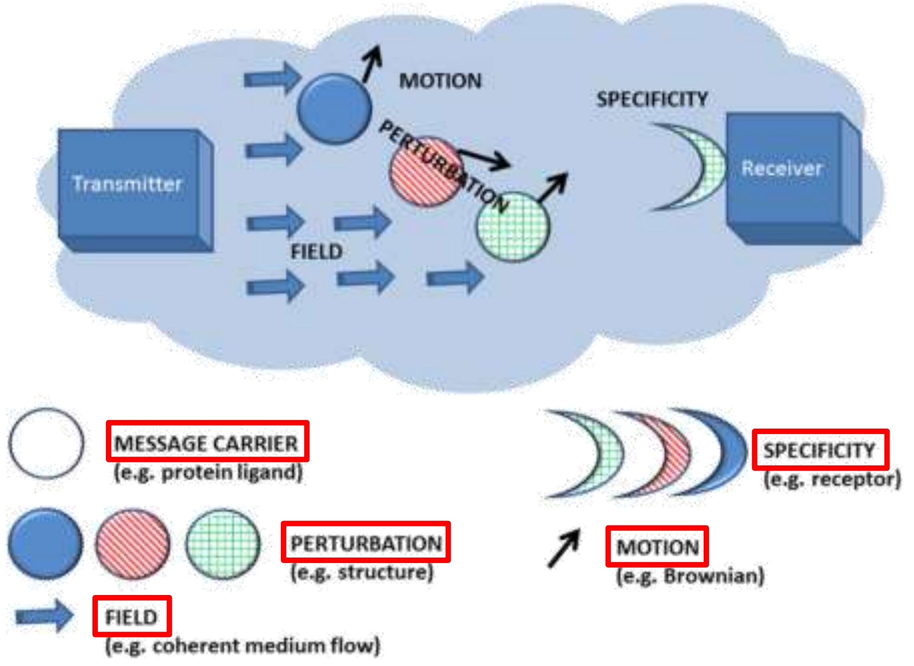
Standardization/Definition

IEEE P1906.1

Recommended Practice for Nanoscale and Molecular Communication Framework

Requirements	
Essential **components** at **nanoscale**	Leverage **unique properties** of **nanoscale**
Elements of **communication system**	**Not** purely a **phenomenon** of **nature**

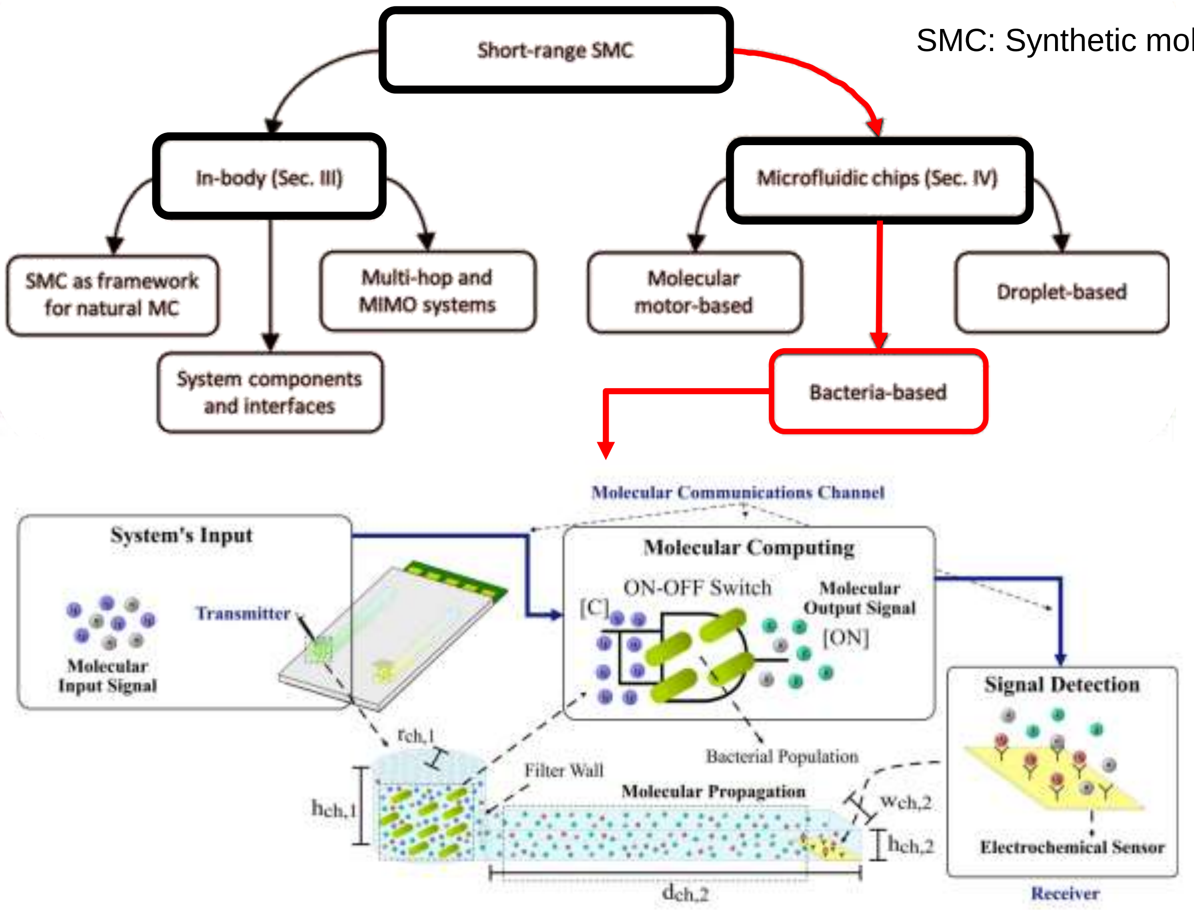
Framework

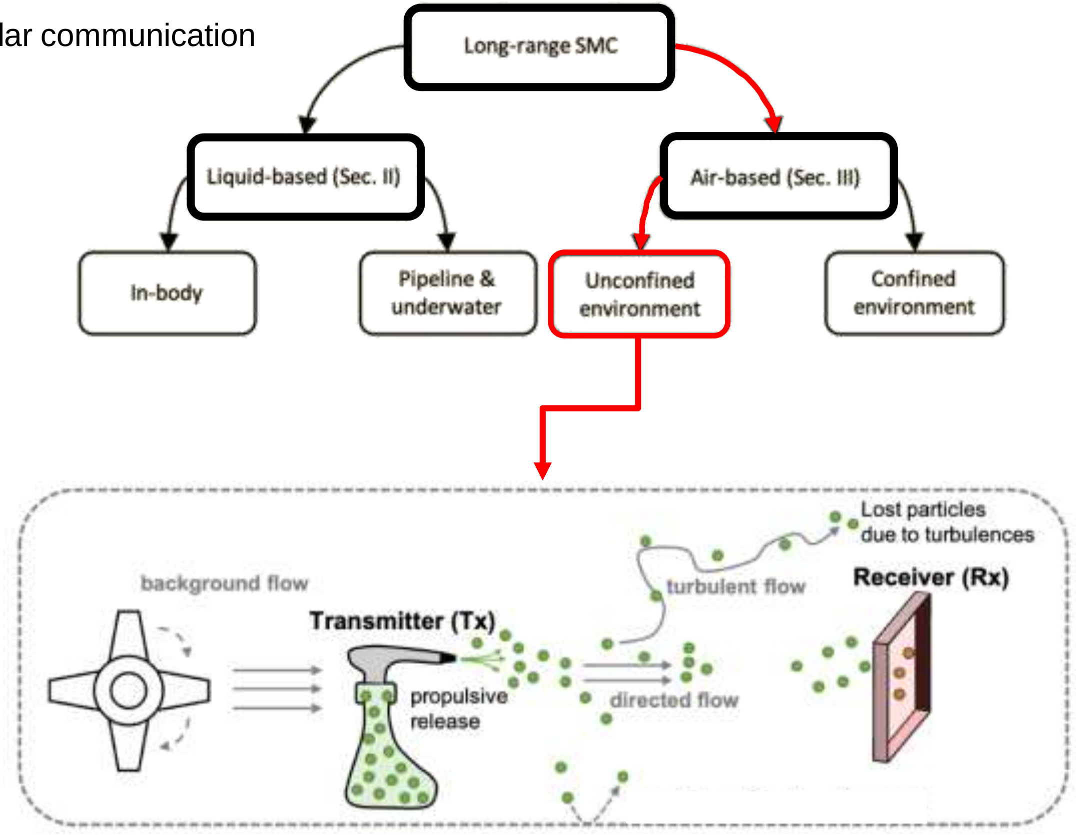


Bush, Stephen F., Janet L. Paluh, Giuseppe Piro, Vijay Rao, R Venkatesha Prasad, und Andrew Eckford. „Defining Communication at the Bottom". *IEEE Transactions on Molecular, Biological and Multi-Scale Communications* 1, Nr. 1 (März 2015): 90–96. https://doi.org/10.1109/TMBMC.2015.2465513.

Testbeds

SMC: Synthetic molecular communication



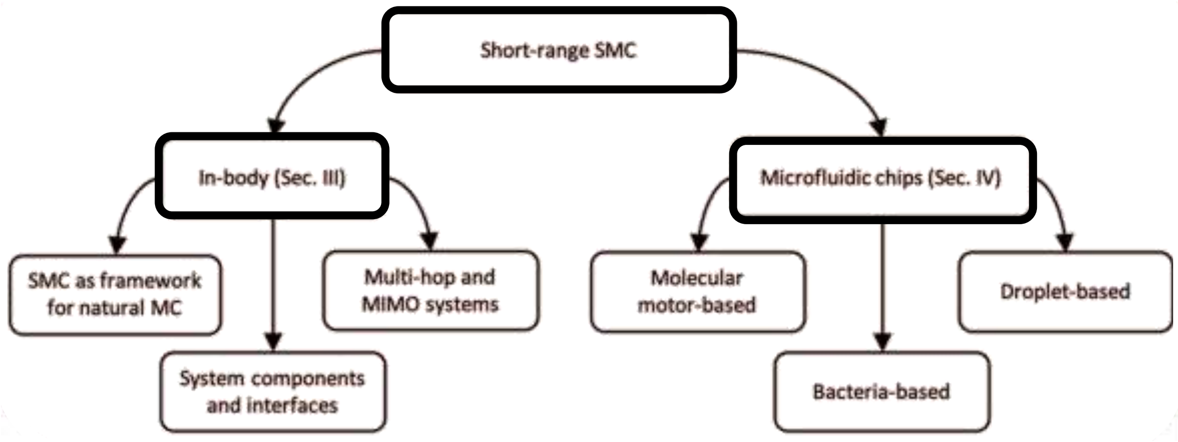


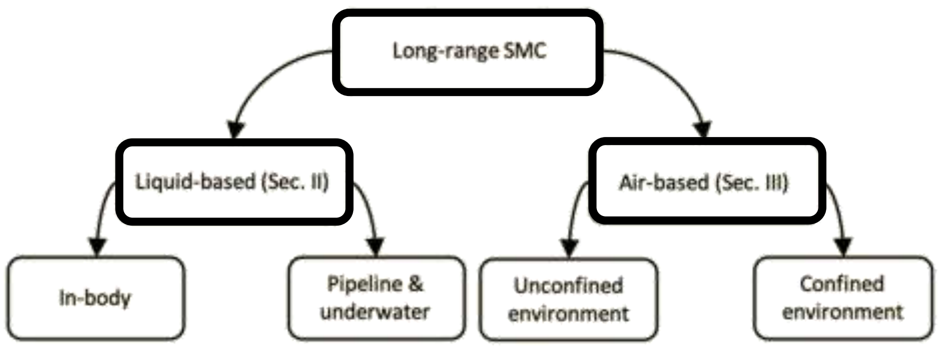
Martins, Daniel P., Michael Taynnan Barros, Benjamin J. O'Sullivan, Ian Seymour, Alan O'Riordan, Lee Coffey, Joseph B. Sweeney, and Sasitharan Balasubramaniam. "Microfluidic-Based Bacterial Molecular Computing on a Chip." *IEEE Sensors Journal* 22, no. 17 (September 2022): 16772–84. https://doi.org/10.1109/JSEN.2022.3192511.

Lotter, Sebastian, Lukas Brand, Vahid Jamali, Maximilian Schäfer, Helene M. Loos, Harald Unterweger, Sandra Greiner, u. a. „Experimental Research in Synthetic Molecular Communications – Part I: Overview and Short-Range Systems". arXiv, 16. Januar 2023. https://doi.org/10.48550/arXiv.2301.06417.

~. „Experimental Research in Synthetic Molecular Communications -- Part II: Long-Range Communication". arXiv, 16. Januar 2023. https://doi.org/10.48550/arXiv.2301.06424.

Testbeds





Consideration of:

Detailed ← **Nano-Bio Technology** → Limited

Limited ← **Communication Networks** → Detailed

Lotter, Sebastian, Lukas Brand, Vahid Jamali, Maximilian Schäfer, Helene M. Loos, Harald Unterweger, Sandra Greiner, u. a. „Experimental Research in Synthetic Molecular Communications – Part I: Overview and Short-Range Systems“. arXiv, 16. Januar 2023. https://doi.org/10.48550/arXiv.2301.06417.

~. „Experimental Research in Synthetic Molecular Communications -- Part II: Long-Range Communication“. arXiv, 16. Januar 2023. https://doi.org/10.48550/arXiv.2301.06424.

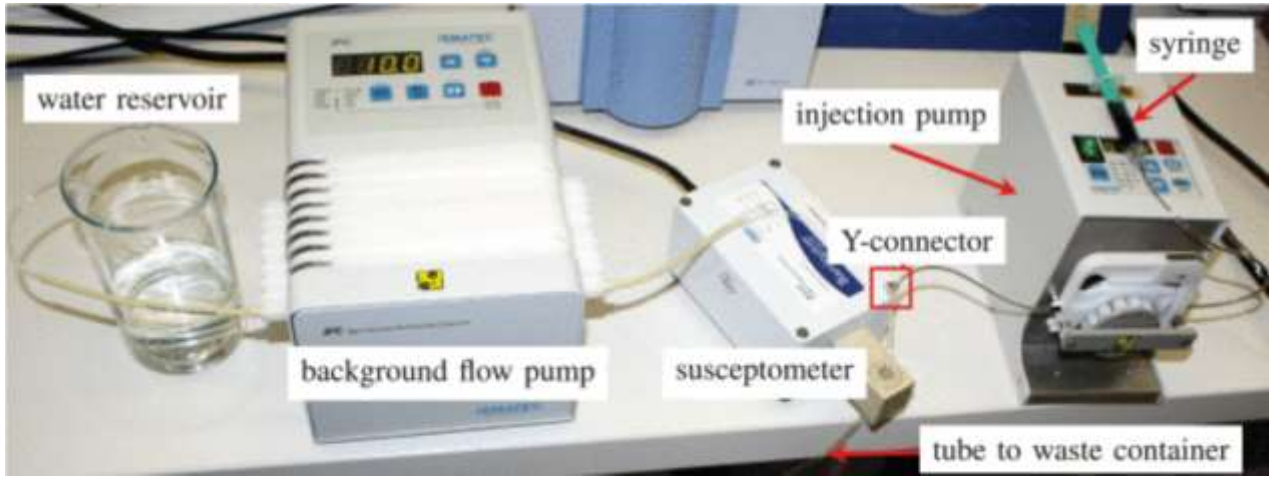
Testbeds

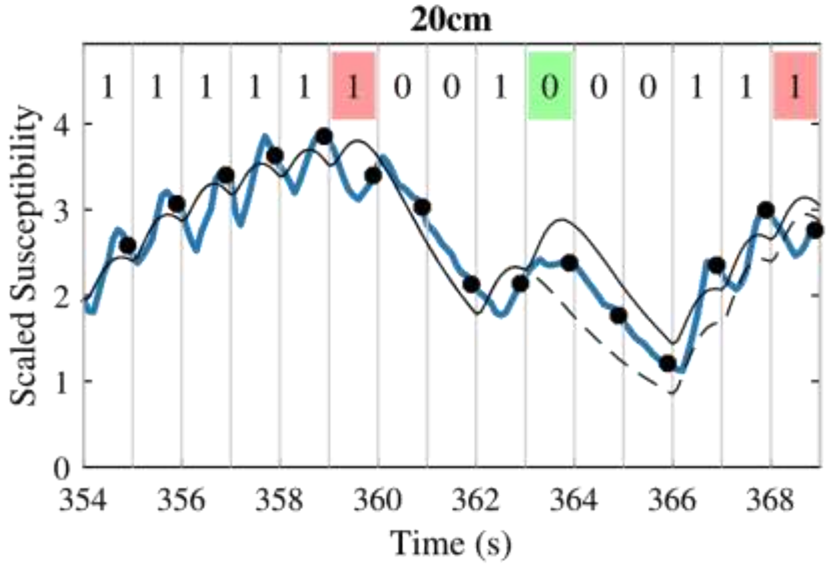
Long-range

Liquid-based

Example: Experimental System for Molecular Communication in Pipe Flow With Magnetic Nanoparticles

- **IMs:** Superparamagnetic iron oxide nanoparticles (**SPIONs**), **biocompatible**, established in medical field
- **Transmission**: Particles are **injected** into a **background flow of water** by the Tx „Volume“ transmitter
- **Propagation**: Transport via **flow** and undergoing dilution and elongation via **diffusion**
- **Reception**: Circular external **susceptometer** (Rx), which generates an **electrical signal** Passive receiver
- **System Parameters:** OOK modulation, 160 ms pulse, 4 s bit duration, [0 1 0] preamble for synchronization

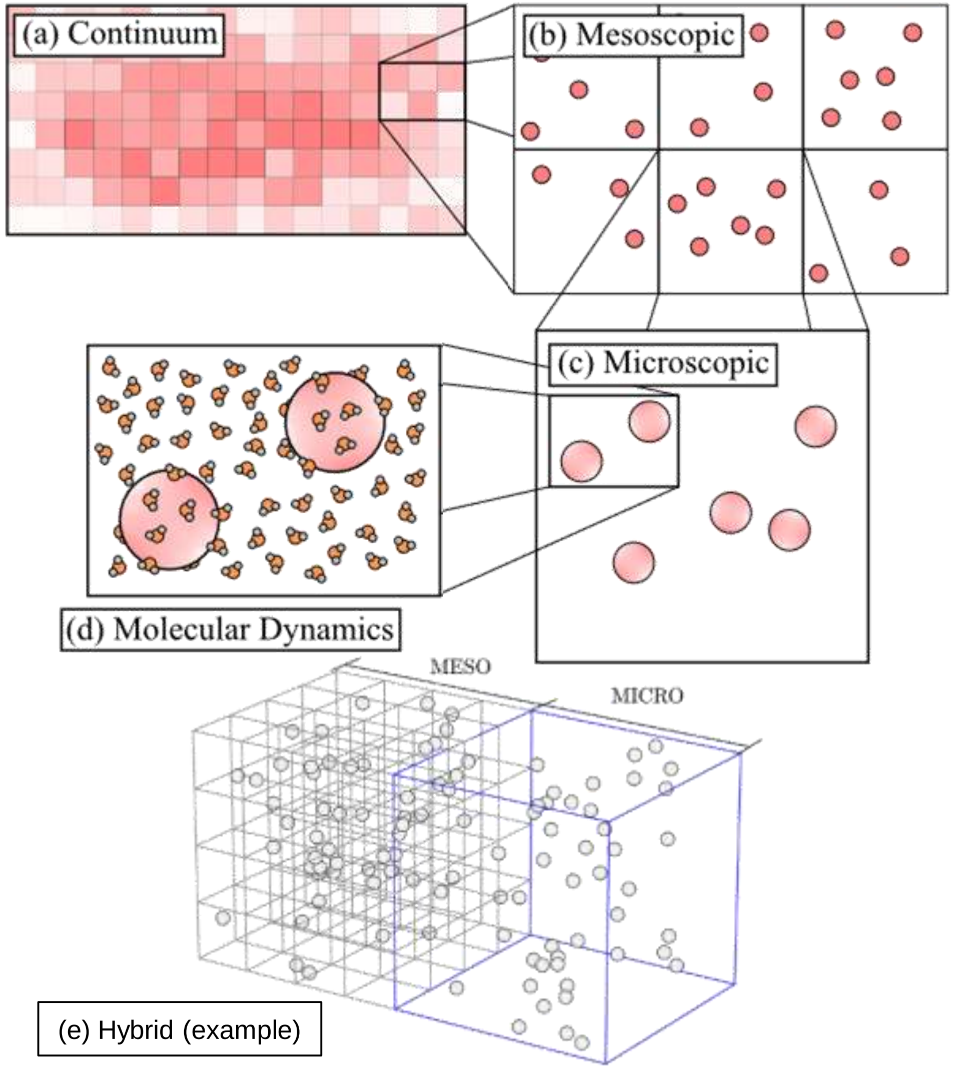




Wicke, Wayan, Harald Unterweger, Jens Kirchner, Lukas Brand, Arman Ahmadzadeh, Doaa Ahmed, Vahid Jamali, Christoph Alexiou, Georg Fischer, und Robert Schober. „Experimental System for Molecular Communication in Pipe Flow With Magnetic Nanoparticles“. IEEE Transactions on Molecular, Biological and Multi-Scale Communications 8, Nr. 2 (Juni 2022): 56–71. https://doi.org/10.1109/TMBMC.2021.3099399.

Simulations

Type of Simulator	Scale	Space	Time	Output
Continuum (DiffEq-based)	Large	Discrete	Continuous	Molecule concentration
Mesoscopic (event-based)	Medium	Discrete	Continuous	Molecules per subvolume
Microscopic (particle-based)	Medium	Continuous	Discrete	Individual molecule paths
Molecular Dynamics (interaction-/ force-based)	Small	Implementation -specific	Implementation -specific	Individual molecule paths/inter-actions
Hybrid	Integrates different scales	Implementation -specific	Implementation -specific	Implementation -specific



Jamali, Vahid, Arman Ahmadzadeh, Wayan Wicke, Adam Noel, und Robert Schober. „Channel Modeling for Diffusive Molecular Communication—A Tutorial Review“. *Proceedings of the IEEE* 107, Nr. 7 (Juli 2019): 1256–1301. https://doi.org/10.1109/JPROC.2019.2919455.

Noel, Adam, Karen C. Cheung, Robert Schober, Dimitrios Makrakis, und Abdelhakim Hafid. „Simulating with AcCoRD: Actor-Based Communication via Reaction-Diffusion“. *Nano Communication Networks* 11 (März 2017): 44–75. https://doi.org/10.1016/j.nancom.2017.02.002.

Challenges

Inherent Challenges

- **Propagation** mechanisms
  - High-latency
  - High ISI
  - Highly stochastic
  - Low-throughput
  - Degradation & reaction noise
- **Low capability** of individual nodes

Concrete Research Challenges

- **Towards MC Networks**: Consideration of Layer 2 and upwards
- **Protocols** for bidirectional links
- Low-complexity **resource management**
- **Network simulation** frameworks

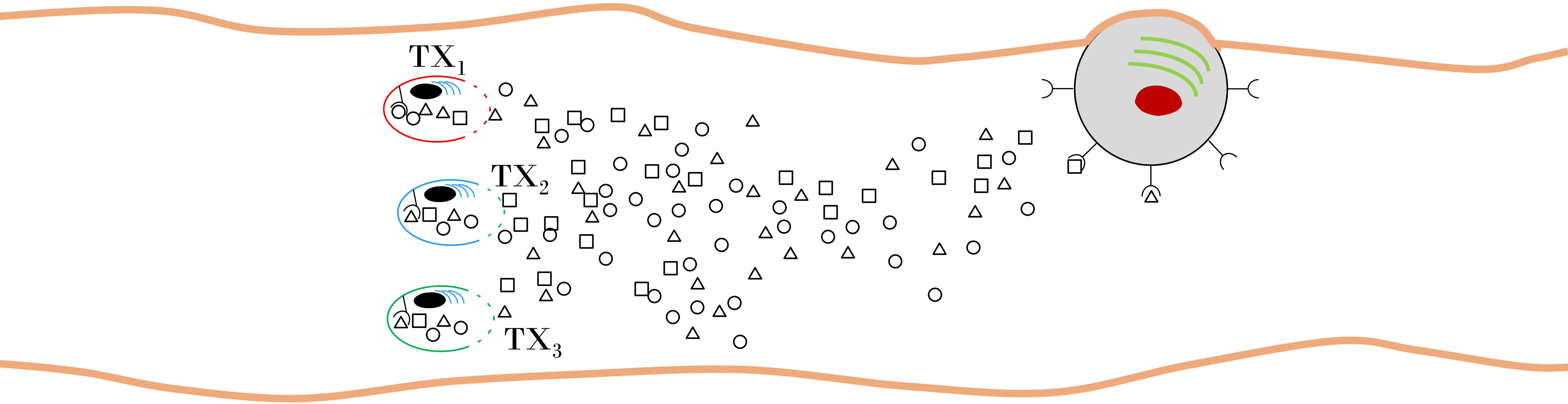
Overarching Goals

- **Interdisciplinary** cooperation
- **Implementation** of **biologically AND network-wise complex** testbeds
- Push **standardization**
- Develop consistent **metrics and benchmarks**

Introduction to the Basics of **Molecular Communication**

- **Example** from our ongoing research:

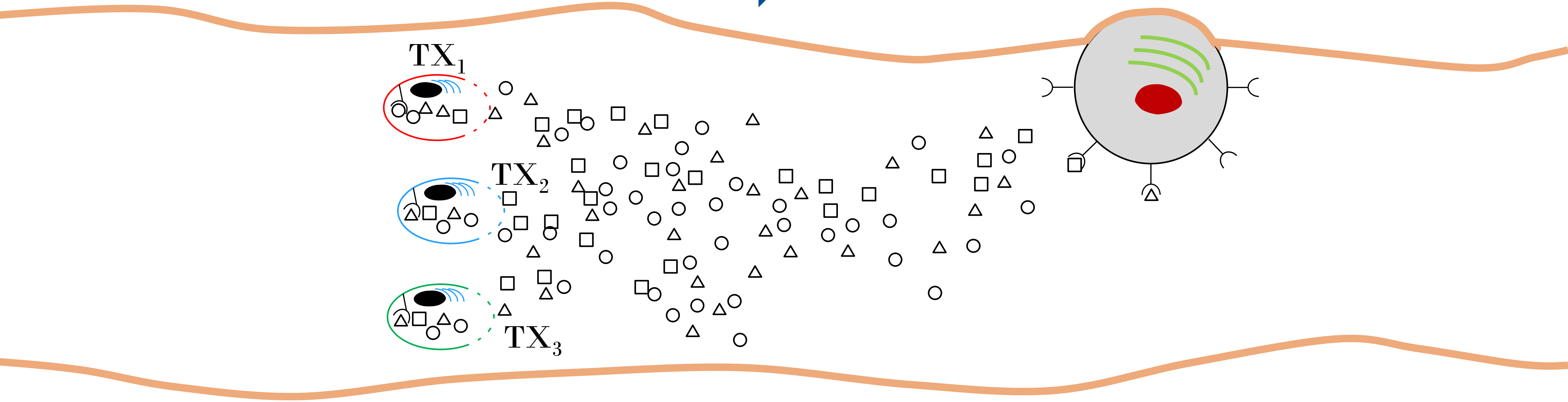
  molecular communication multiple access - theory and experiment



Internet of Bio-Nano-Things for future medical use cases

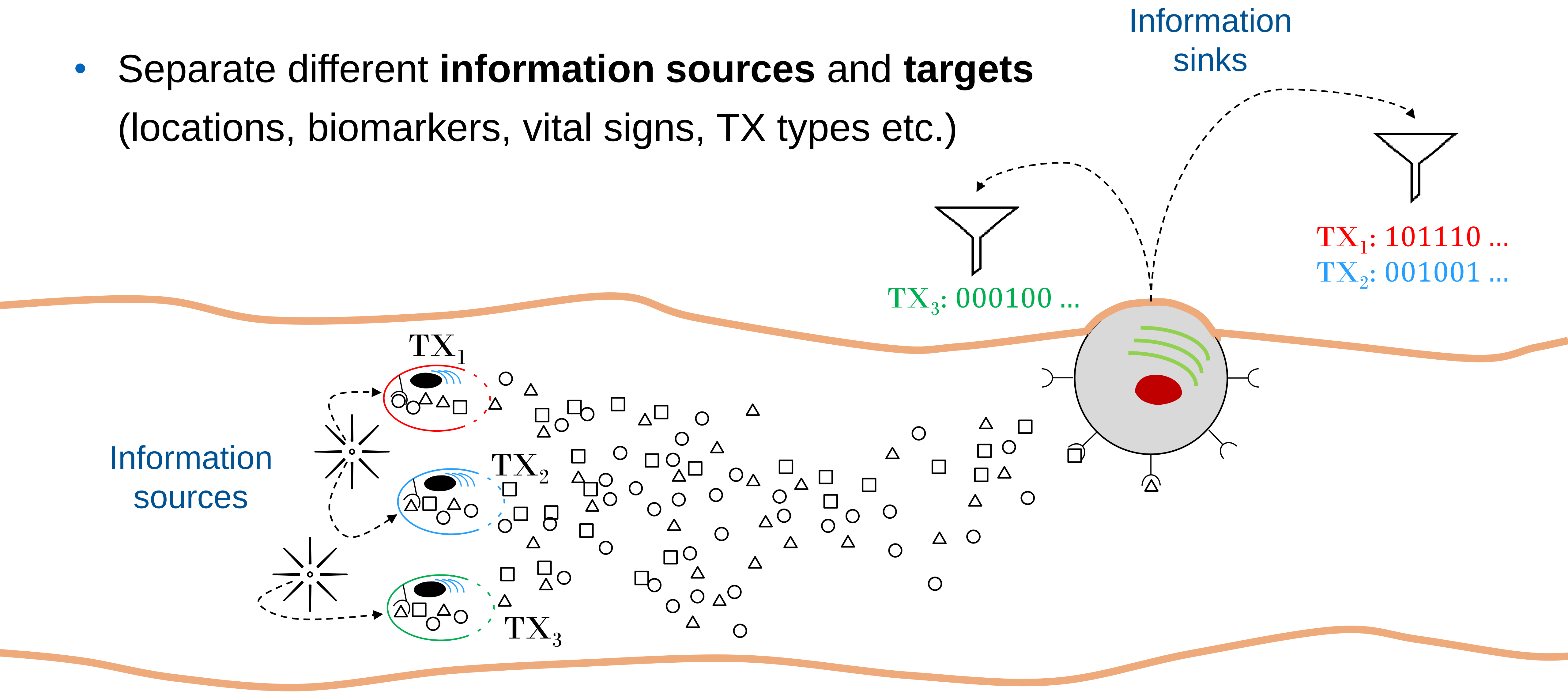
- **Bio-nano-machines** (BNMs) need to **communicate** to achieve **complex tasks**
- **Controlled** and **efficient** information exchange
- Large number of **different types** of BNMs

➡ **MC Networks**



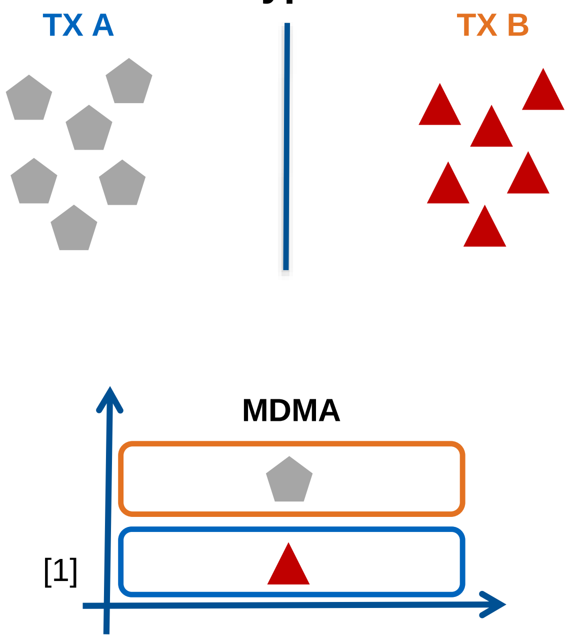
MC Networks need Multiple Access

- Separate different **information sources** and **targets** (locations, biomarkers, vital signs, TX types etc.)



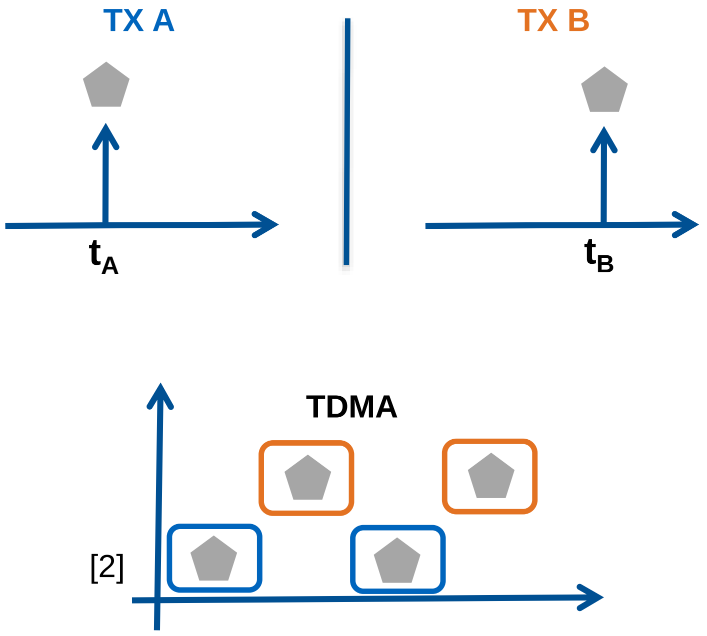
MC Resources for Multiple Access - Overview

Type



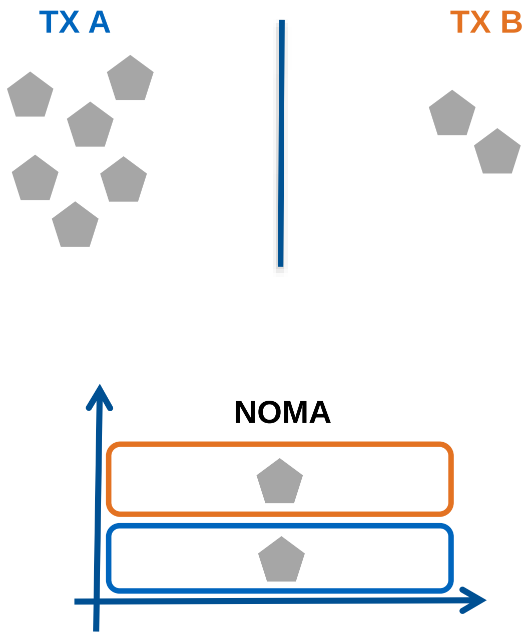
Increases Physical Complexity

Time



Reduces Throughput

Concentration

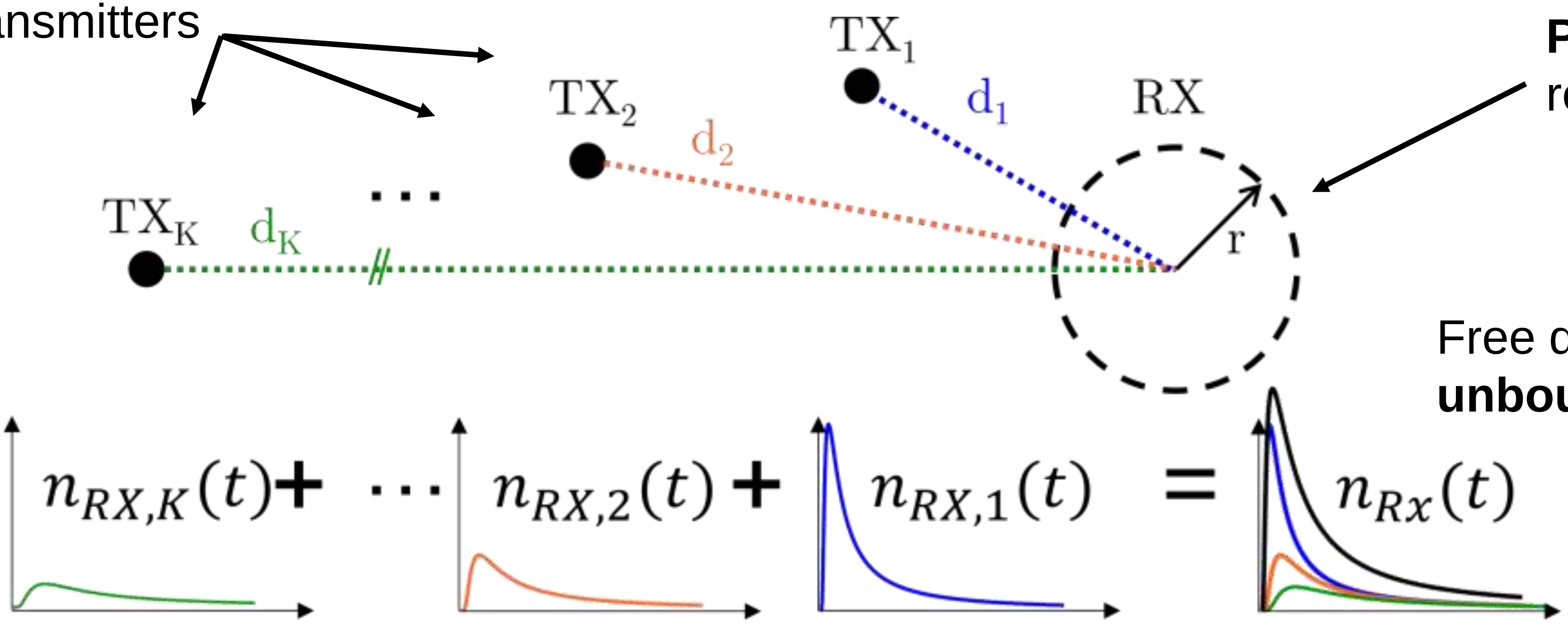


Introduces additional Interference

Simplified Communication Scenario

Point transmitters (TXs)

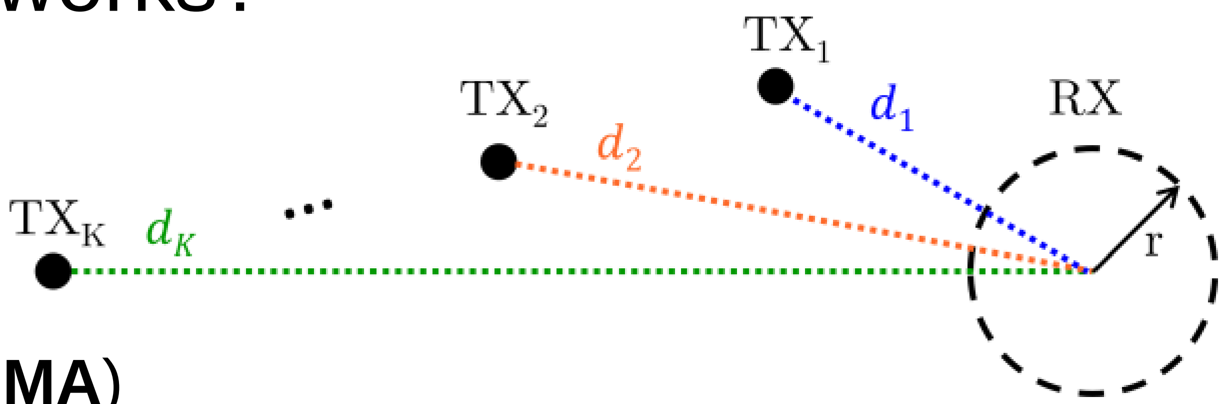
Passive spherical receiver (RX)



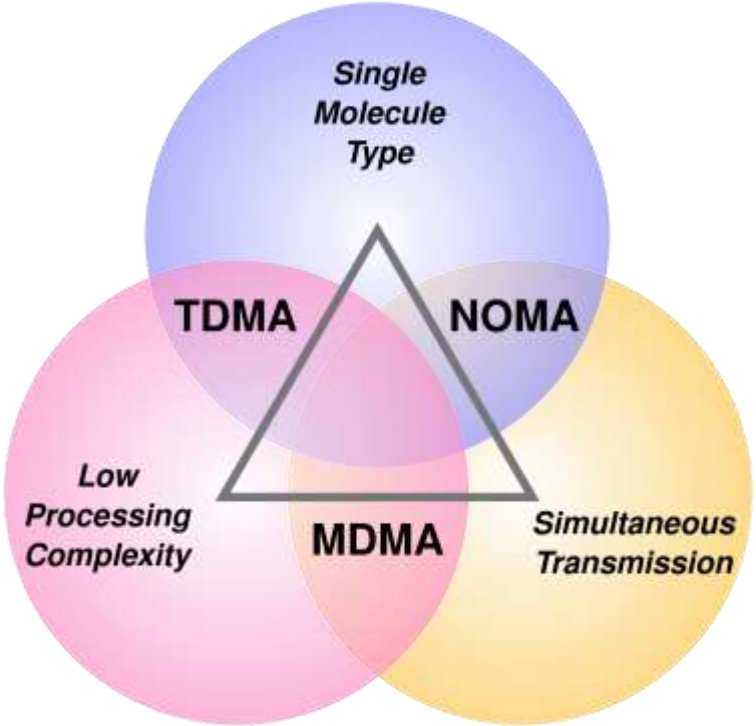
Free diffusion in **unbounded** space

Modelled as mean and variance $\lambda(t)$ of a time-varying **Poisson** distribution

First Step towards MC Networks?

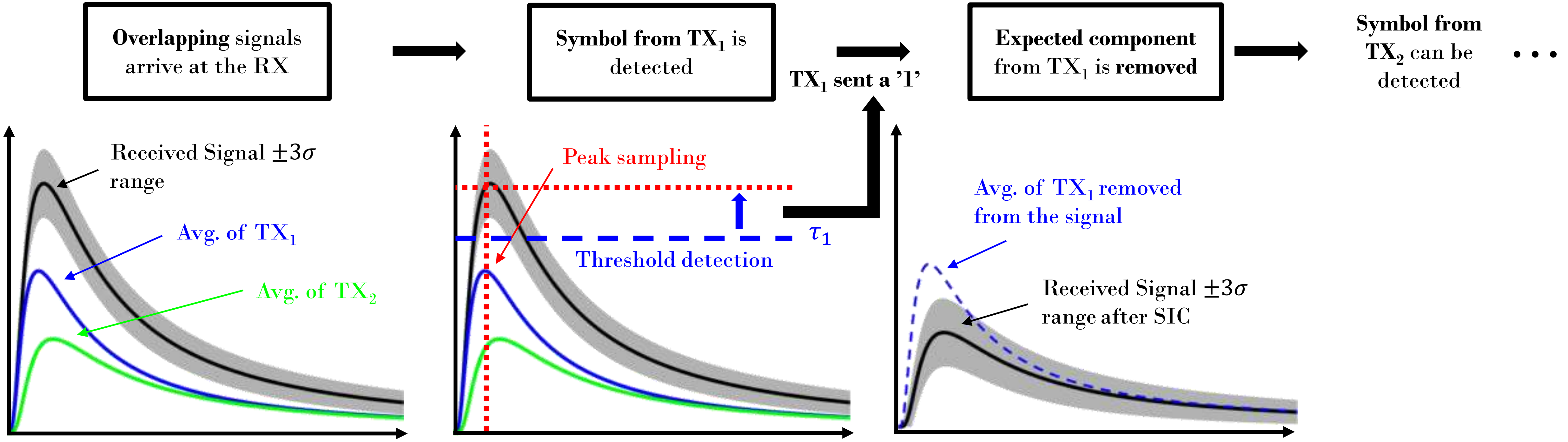


- **Multiple access** is prerequisite
- Time-Division Multiple Access (**TDMA**)
  - Only **one TX** at the same time
- Molecule-Division Multiple Access (**MDMA**)
  - Orthogonal approach ≈ OFDMA
  - **Processing for many molecule types** necessary
- Non-Orthogonal Multiple Access (**NOMA**) based on signal power
  - **Single-molecule-type + simultaneous transmissions**



Successive Interference Cancellation for NOMA

- Assumptions: **Channel Information and Synchronization**

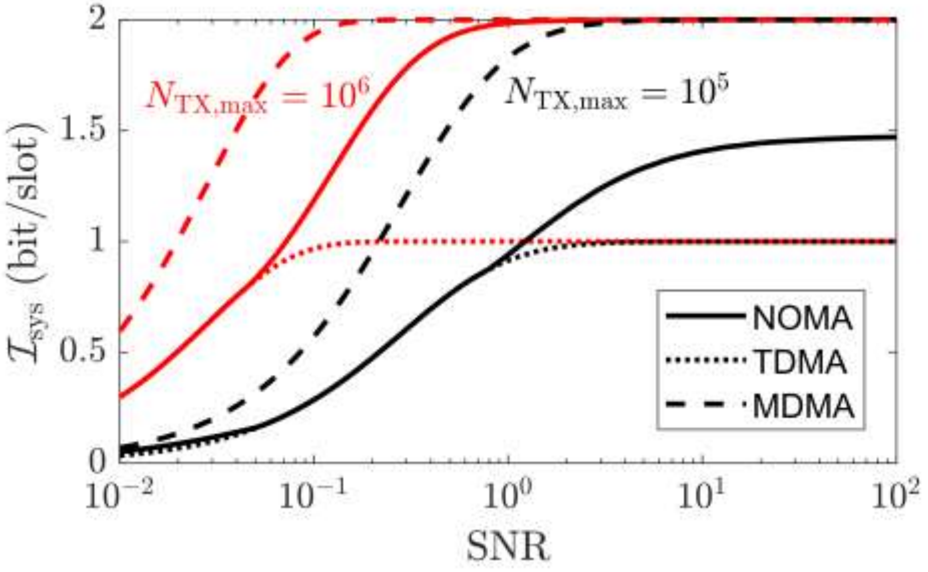


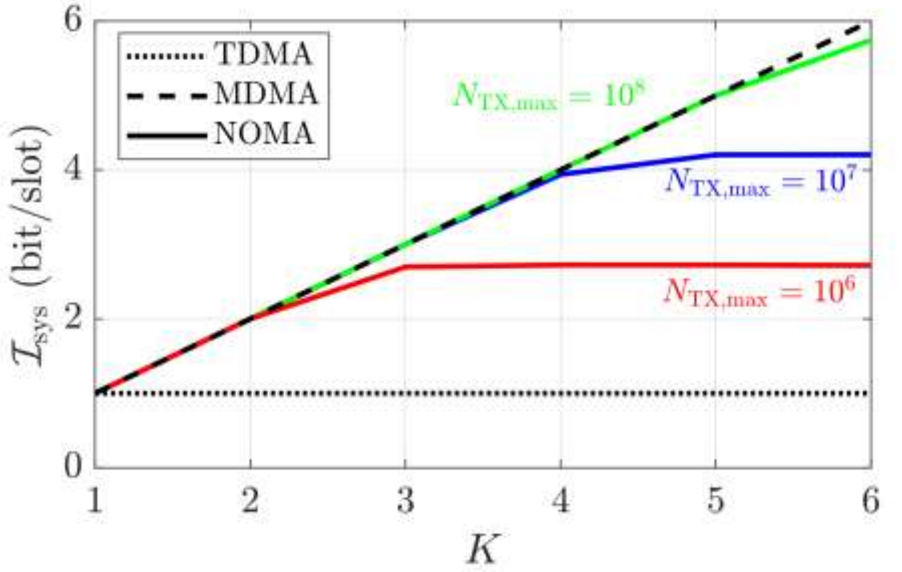
First results - NOMA

- **Performance Comparison** with TDMA and MDMA (= ODFMA)

- Main Results
  1. **TDMA** is **lower bound** and **MDMA** is **upper bound**
  2. **Molecule budget** per TX ($N_{\text{TX,max}}$) **determines** position on the spectrum between upper and lower bound

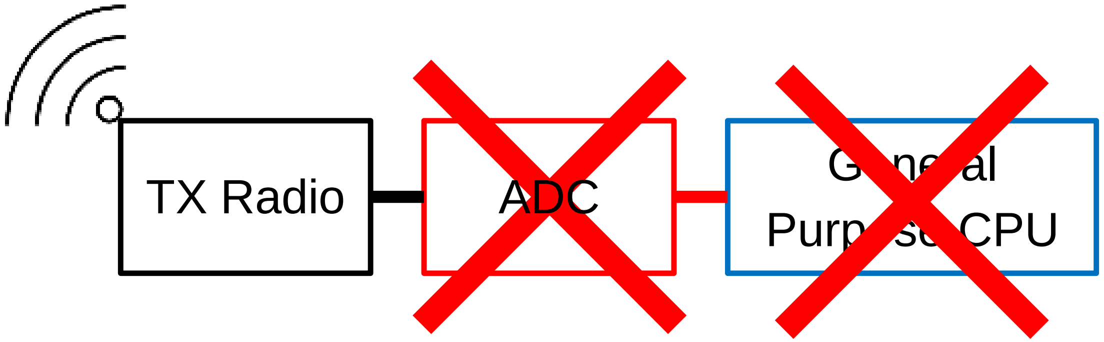
- **NOMA = MDMA** for sufficient molecule budget using **only one molecule type**





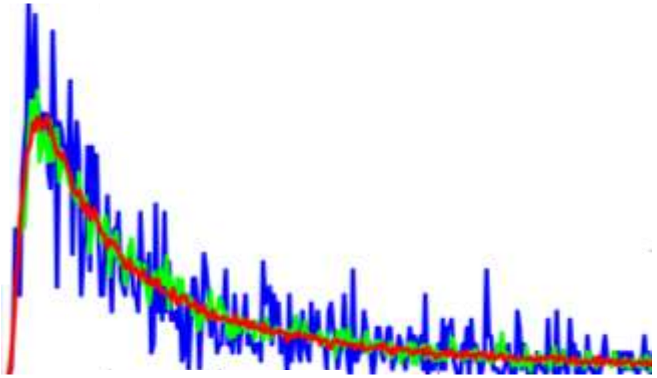
Number of transmitters

Bigger Picture - Challenges



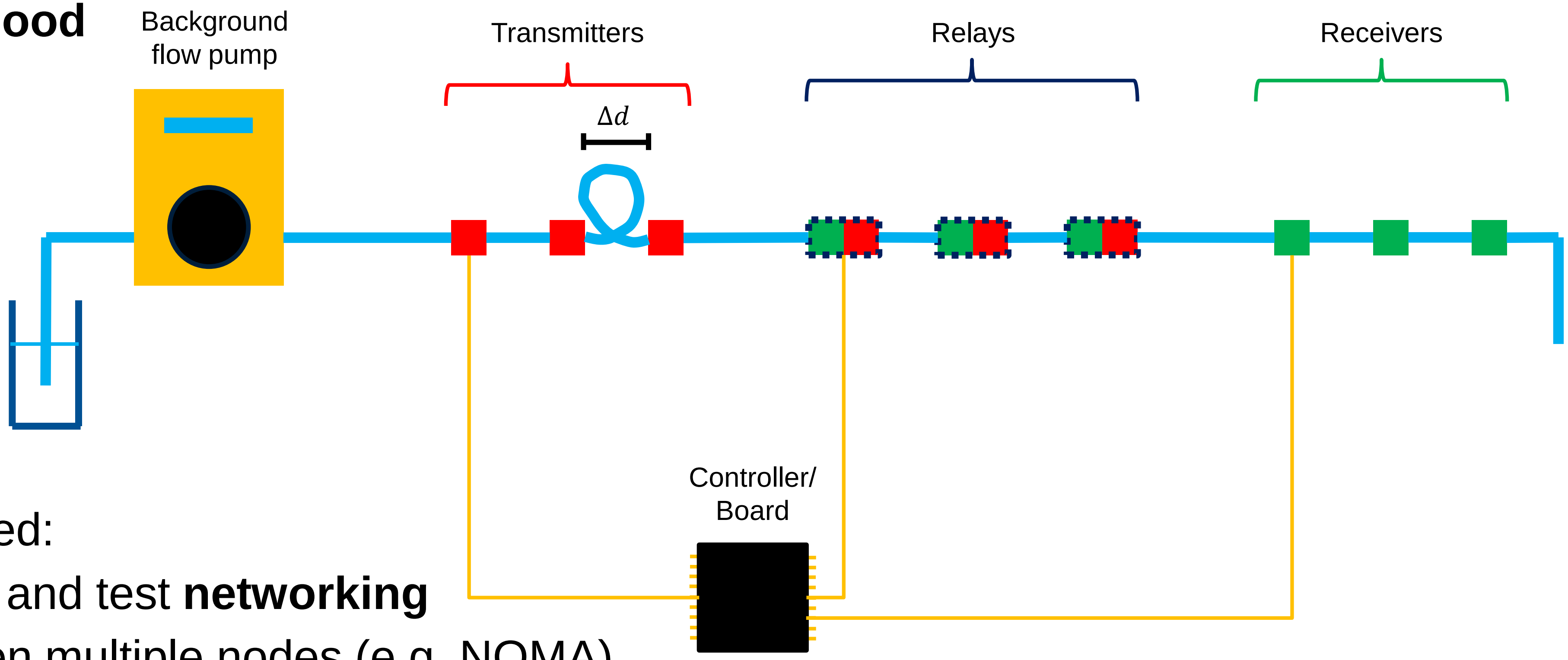
1. **Lack of digital abstraction**

2. **Highly constrained** systems
   - Extremely high **delays**
   - Intrinsic **stochasticity** of biological processes
   - **Uni-directional** channels



Next Steps – Practical Implementation in a Testbed

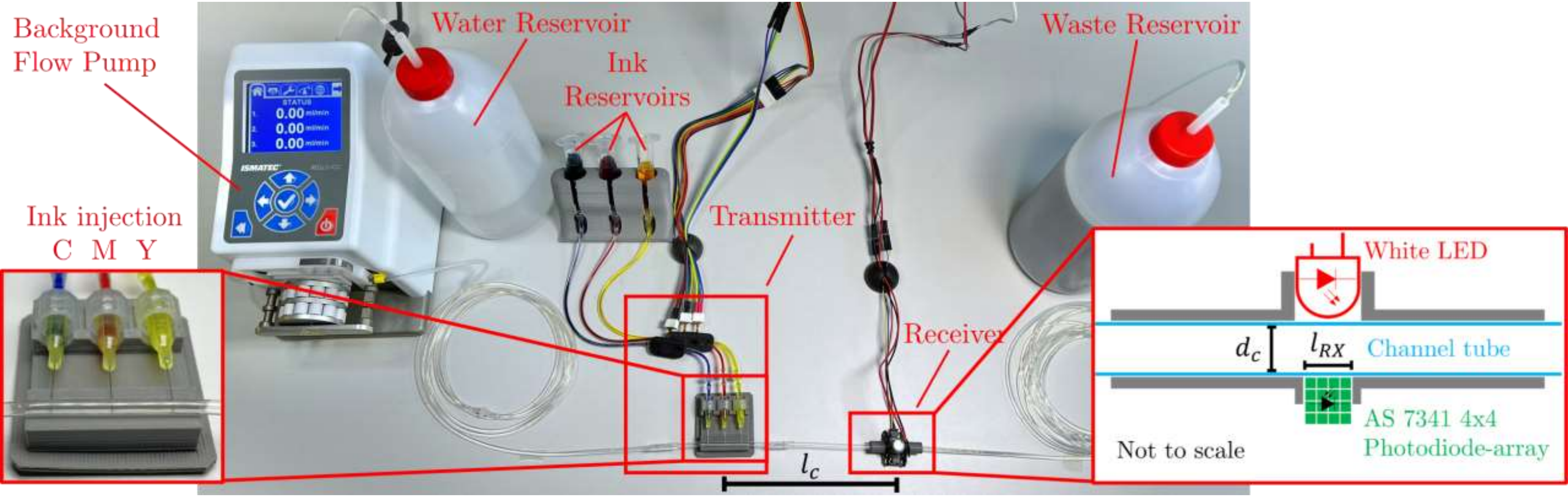
- Based on existing liquid-flow tube testbeds, extended for **multi-node** and **multi-hop** networks
- Oriented on in-body **blood vessel** use cases

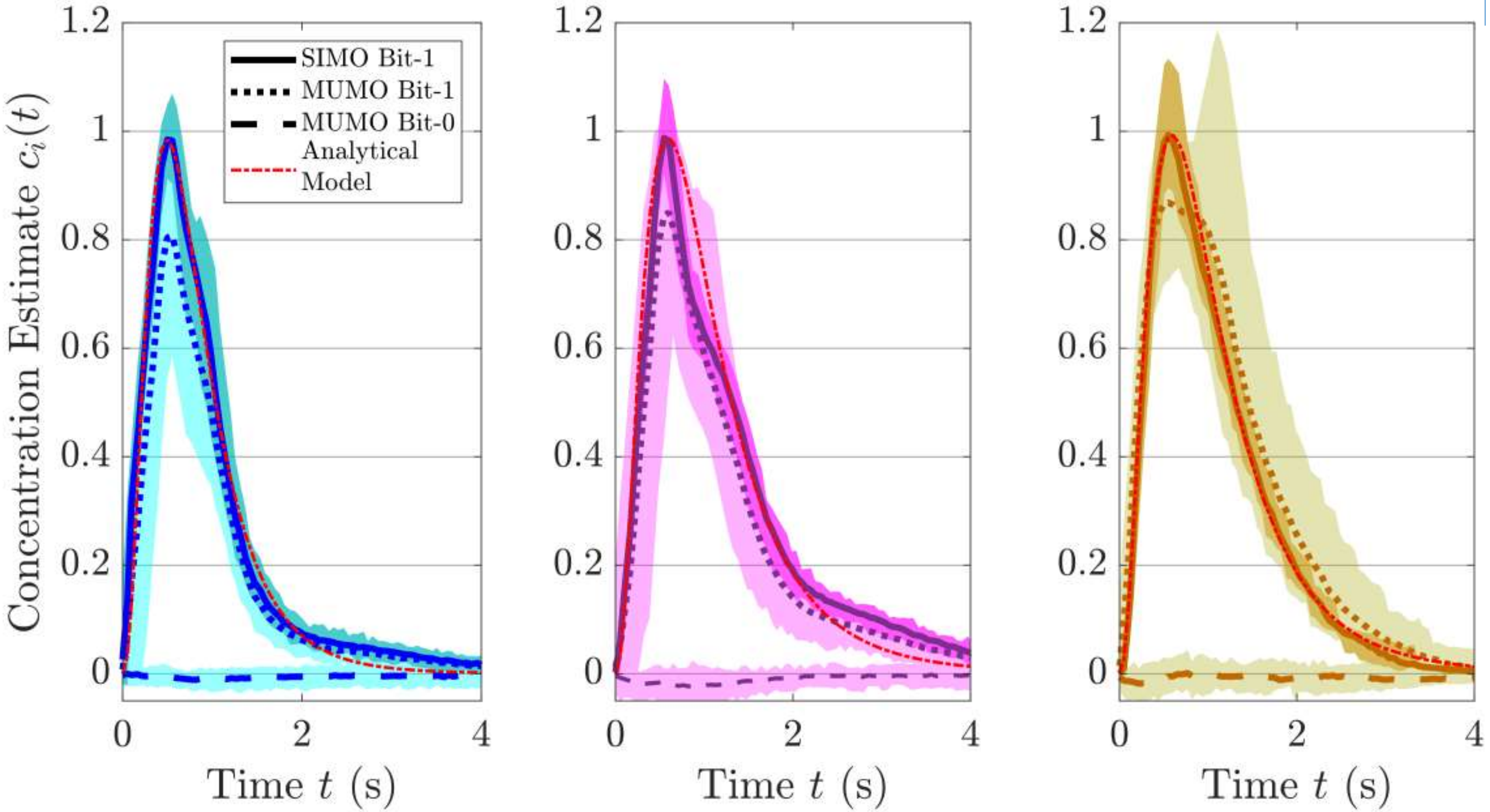


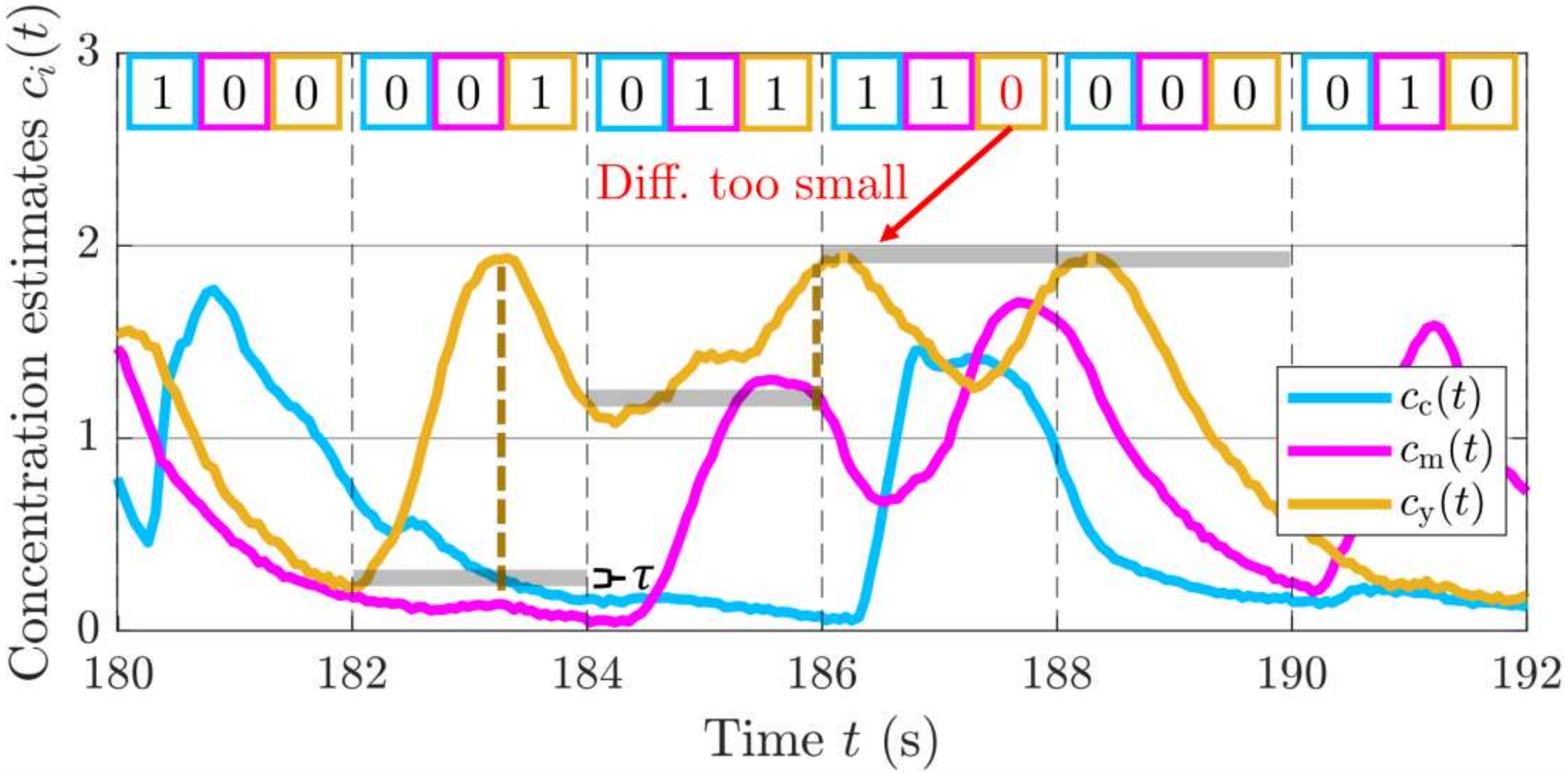
Main **extensions** planned:

1. Ability to implement and test **networking procedures** between multiple nodes (e.g. NOMA)
2. Representation of **multiple different communication resources**, i.e. time, molecule type, and molecule number

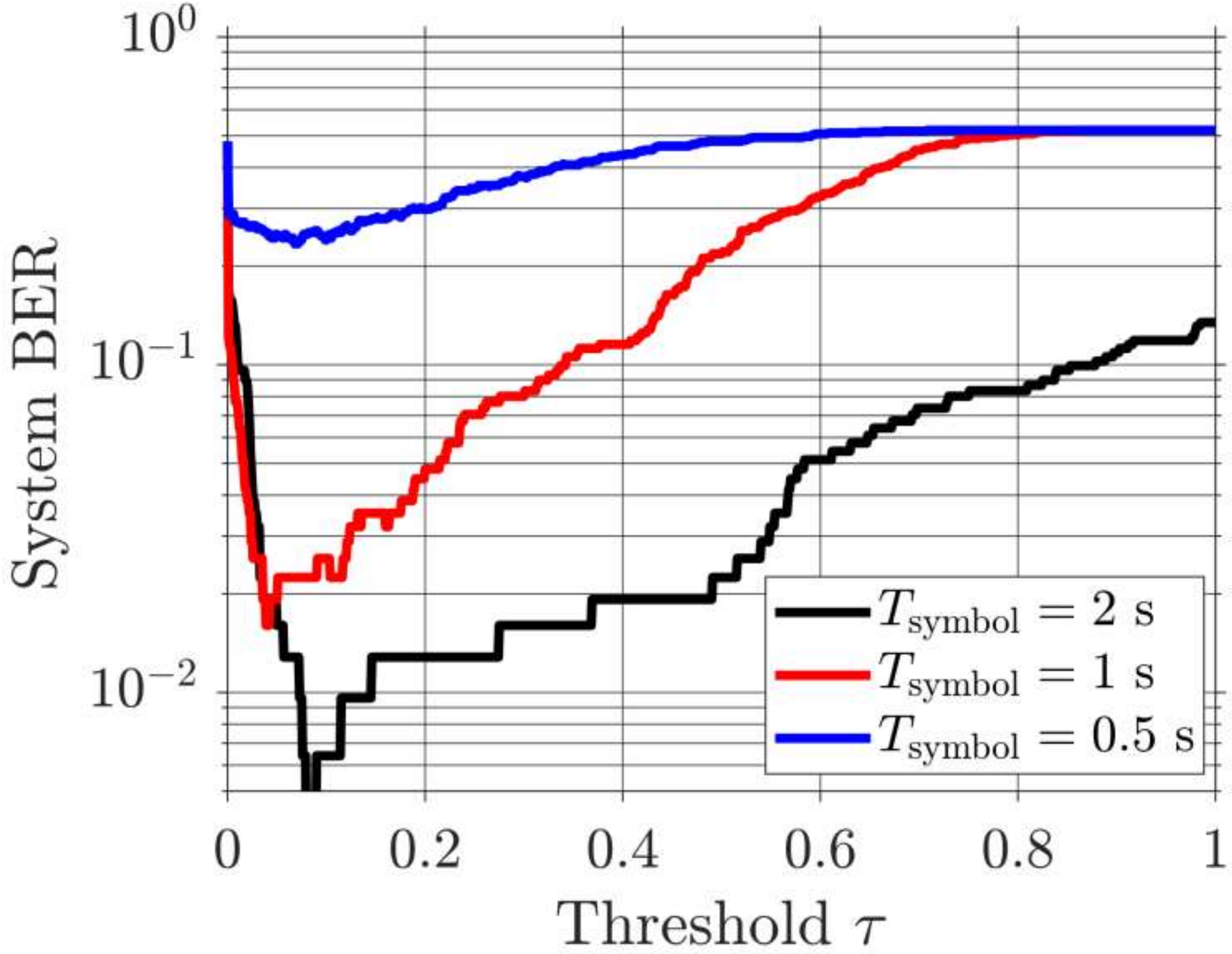
Multi-Molecule Molecular Communication Testbed Based on Spectral Sensing




1.2
1
0.8
0.6
0.4
0.2
0
Concentration Estimate $c_i(t)$
SIMO Bit-1
MUMO Bit-1
MUMO Bit-0
Analytical Model
0
2
4
Time t (s)
Time t (s)
Time t (s)



Concentration estimates $c_i(t)$
1 0 0 | 0 0 1 | 0 1 1 | 1 1 0 | 0 0 0 | 0 1 0
Diff. too small
τ
$c_c(t)$
$c_m(t)$
$c_y(t)$
0
1
2
3
180
182
184
186
188
190
192
Time t (s)



10^0
10^{-1}
10^{-2}
System BER
0
0.2
0.4
0.6
0.8
1
Threshold τ
$T_{\text{symbol}} = 2$ s
$T_{\text{symbol}} = 1$ s
$T_{\text{symbol}} = 0.5$ s

Outlook: MC at LKN and in 6G-life

➡ Towards Molecular Communication Networks

Biocomputing for MC Networking Algorithms

MC protocol **stack**

Continuation of work on **NOMA**

MC **resource management**

MC networking **testbed**

MC network **simulation**

Short Term → Long Term

6G-life

GEFÖRDERT VOM

Bundesministerium
für Bildung
und Forschung