Improving the Robustness of Microfluidic Networks

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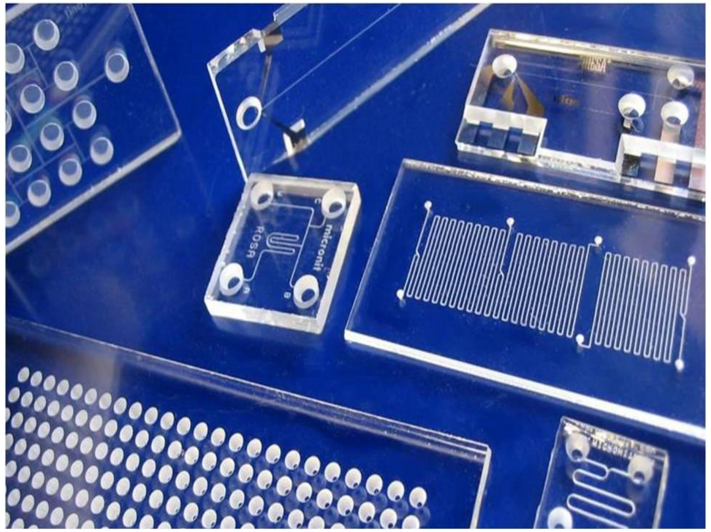
Overview

- Microfluidic Networks and State-of-the-art Design Process
- Defects
- Robustness Metric
- Improvement Methods
  - Sensitivity Analysis
  - Single-Parameter-Variation
  - Downhill-Simplex
- Example
- Conclusion

Microfluidics



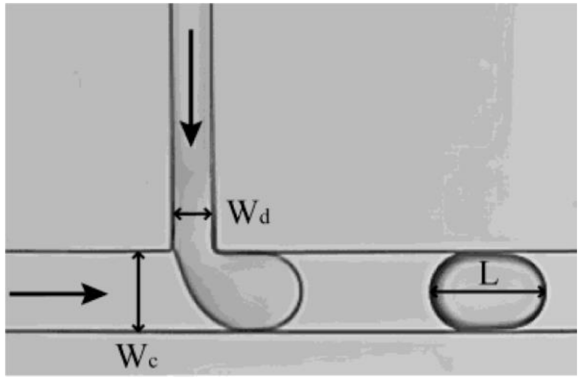
- Reduce sample and reagent volumes
- Increase throughput
- Automate biological/chemical experiments
- Lab-on-a-Chip
- Complex applications: protein crystallization, immunoassays, DNA-synthesizing, etc.

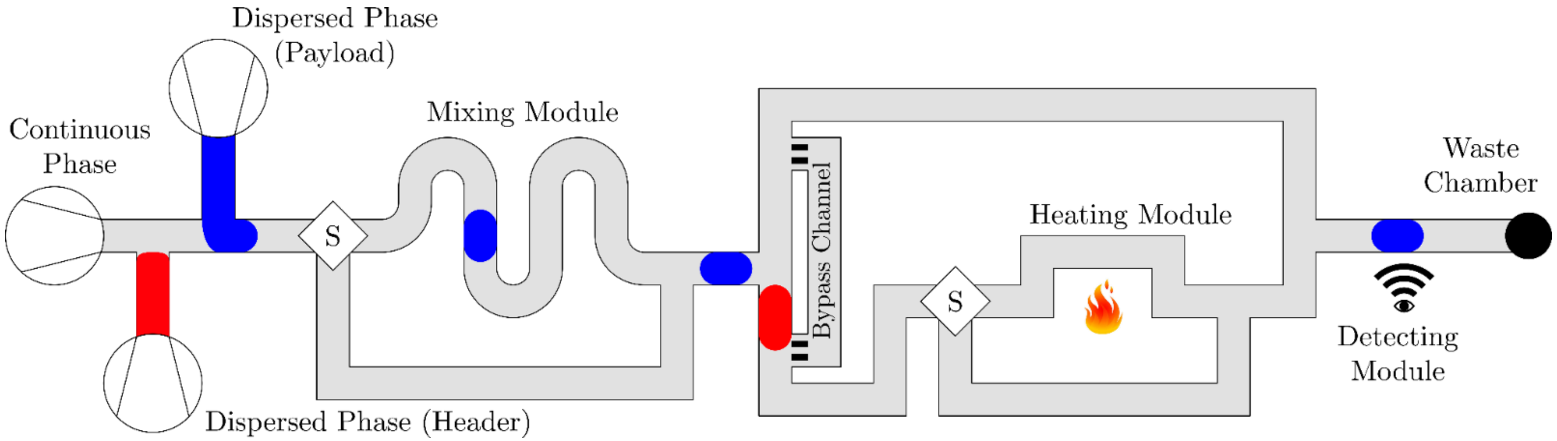
Droplet Microfluidic Networks

- Droplets flow in closed micro channels
- Formation of droplets with T-junctions
- Passive realization (no valves, no electrowetting, etc.)
- Droplets can be routed towards different modules

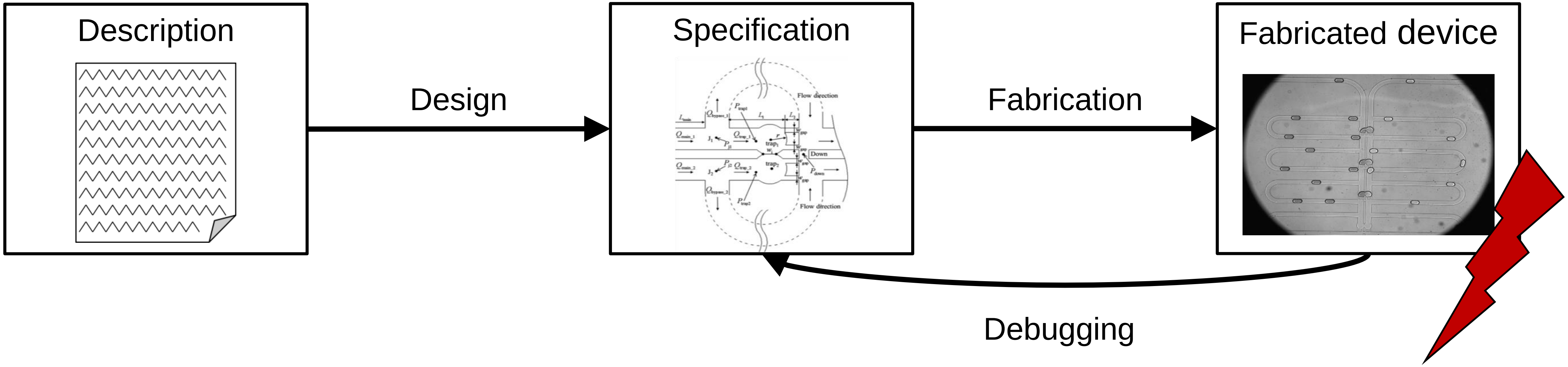
Dispersed phase

Continuous phase



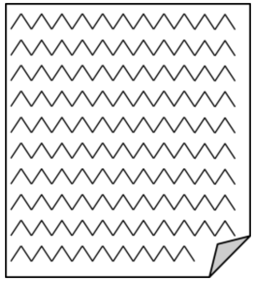


State-of-the-art Design Process



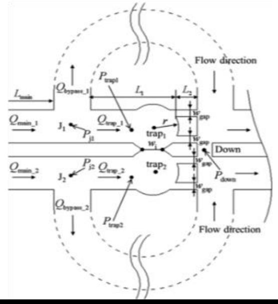
State-of-the-art Design Process

Description



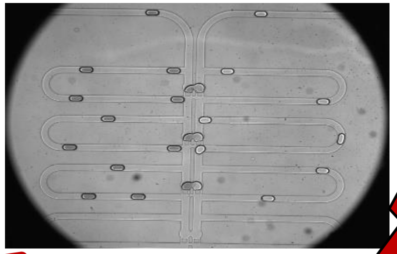
Design

Specification



Fabrication

Fabricated device

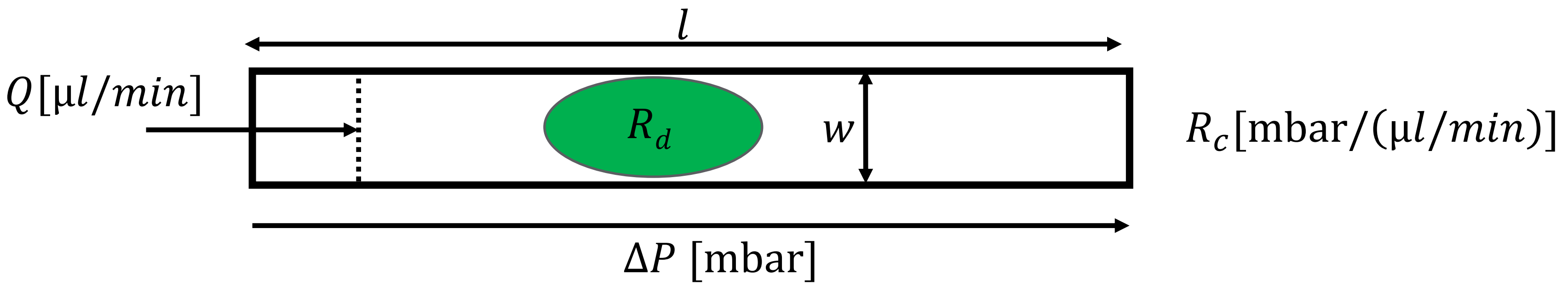


Costly prototyping iterations

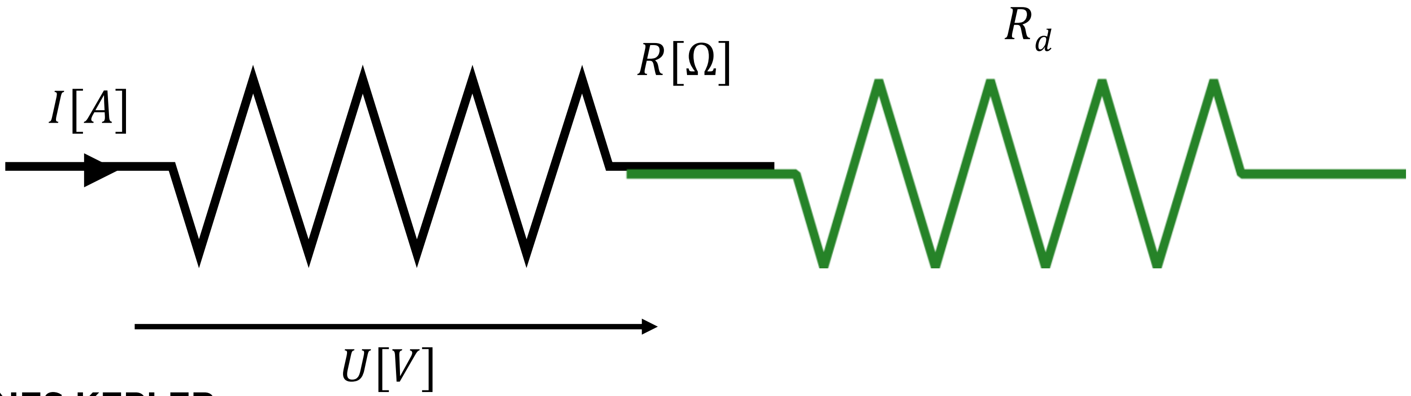
Introduction of methods for simulation and validation

1D Analysis Model

- Conditions: laminar, viscous, and incompressible flow (i.e., low Reynolds number)



$$\Delta P = R_c Q$$



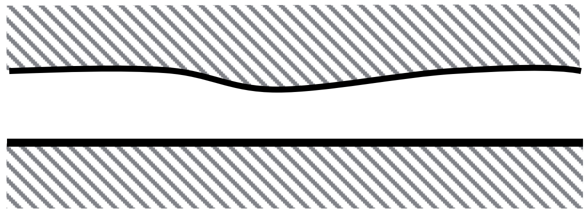
$$U = R\ I$$

Defects

- Neither fabrication processes nor the used materials are perfect

- Fabrication tolerances
  - Fabrication processes always induce fabrication tolerances

- Deformation and Swelling
  - Certain materials (e.g., PDMS) may deform or swell under pressure-driven flows or specific solvents



Goal

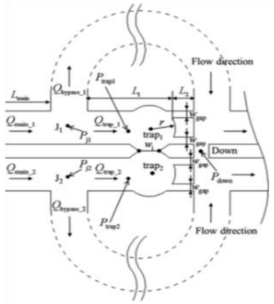
Microfluidic networks should be as robust as possible against such defects

Robustness Improvement Process

1. Obtain a value of a robustness metric for the initial design

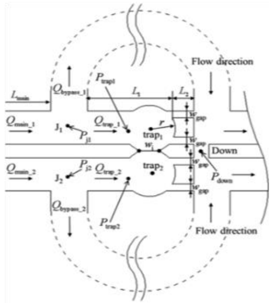
2. Apply methods that are able to improve the robustness of the initial design

3. Validate the improvement by comparing the robustness metric value of the initial and the improved design



Initial Design
Robustness = 50%

Robustness Improvement Methods



Improved Design
Robustness = 70%

Robustness Metric

1. Define the behavior of the network (objectives that must be fulfilled)
   - Certain flow rates inside specific channels
   - A droplet must follow a desired path
   - etc.

Robustness Metric

1. Define the behavior of the network (objectives that must be fulfilled)

2. Randomly “inject” defects into the network
   - The defects are based on a normal Gaussian distribution with a certain standard deviation
   - Width, height, length of a channel

Robustness Metric

1. Define the behavior of the network (objectives that must be fulfilled)

2. Randomly “inject” defects into the network

3. Simulate the network and check if all objectives are fulfilled
   - If yes, mark the corresponding simulation as “Success”

Robustness Metric

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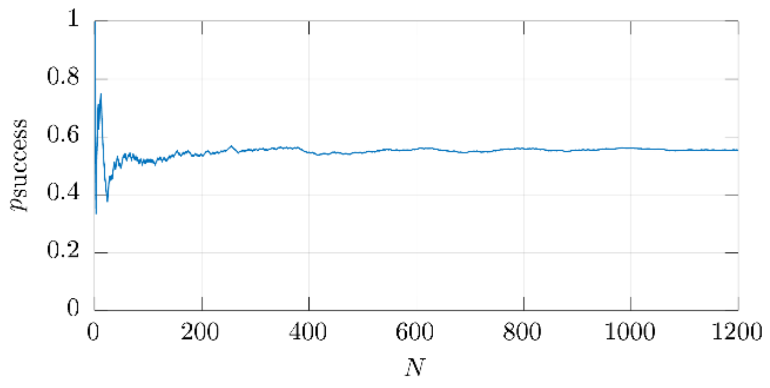


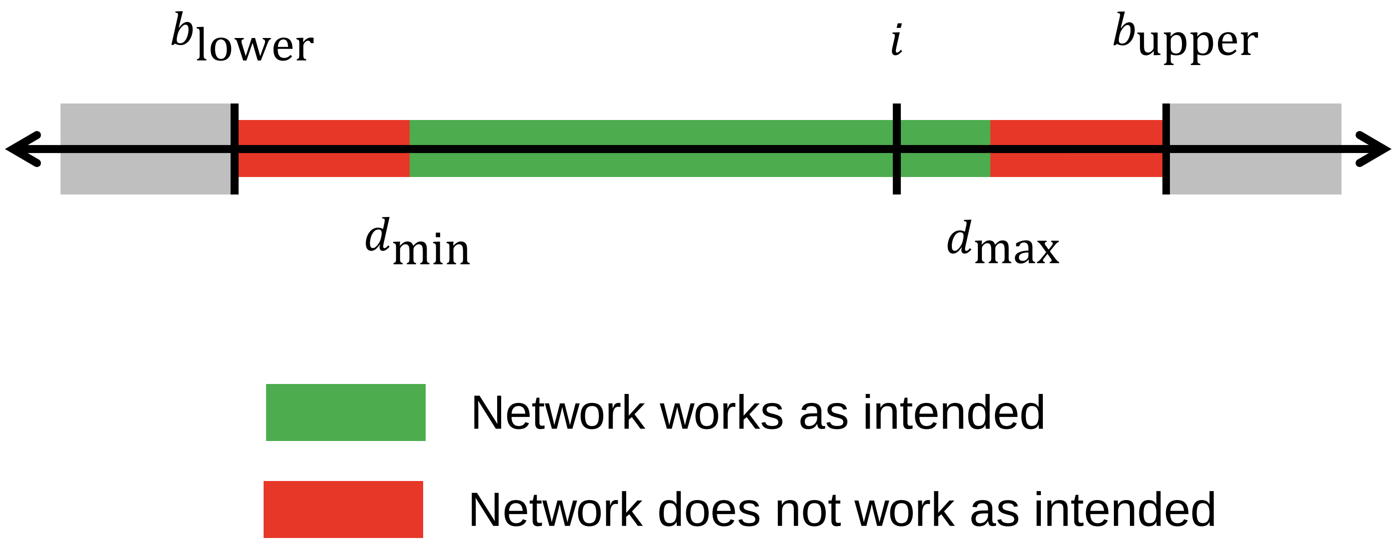
4. Repeat the second and third steps N times
   - This will result in $N_{success}$ simulations marked as success
   - The ratio $\mathrm{p}_{success} = {}^{N_{\mathrm{success}}}/_{N}$ indicates how likely it is, that the network works as intended
   - In order to get a trustworthy value for $\mathrm{p}_{success}$ the number of simulation N must be quite high

Sensitivity Analysis

- Improvement process works by changing certain parameters (channel lengths, width, etc.)
- Considering all channels for the improvement can lead to complex multi-dimensional optimization problems
- Limit focus on these parameters that tend to increase the robustness the most

Sensitivity Analysis

- Parameter
  - i … initial value
- Bounds
  - b_{lower} … lower bound
  - b_{upper} … upper bound
- Defects
  - d_{min} … minimal defect
  - d_{max} … maximal defect
- Sensitivity
  - The closer i lies to d_{min} or d_{max} the higher the sensitivity
  - $S = \frac{i}{i - d_{\text{min}}} + \frac{i}{d_{\text{max}} - i}$



Sensitivity Analysis

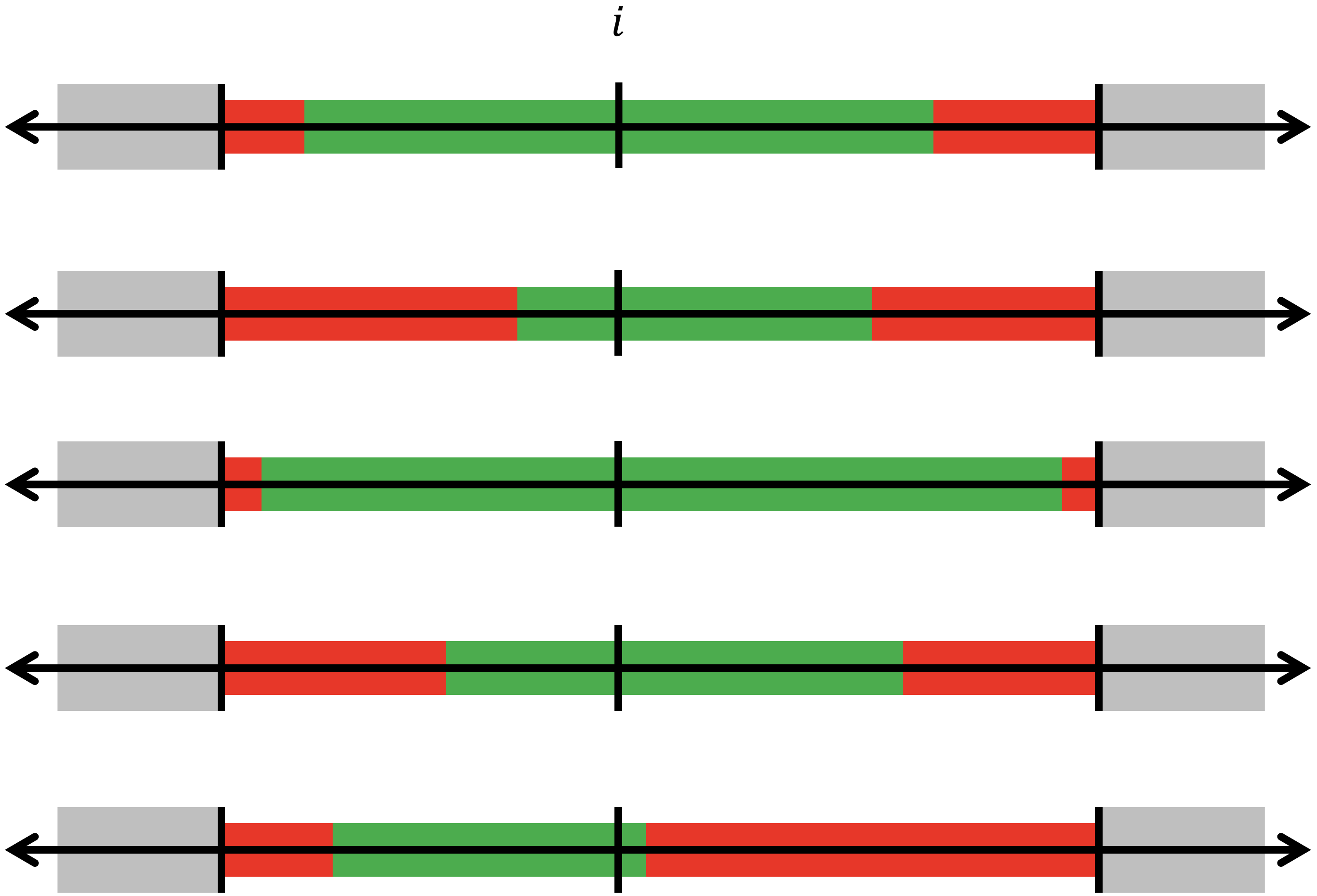
1. Parameter: $S = 2$

2. Parameter: $S = 4$

3. Parameter: $S = 1$

4. Parameter: $S = 3$

5. Parameter: $S = 5$



Sensitivity Analysis

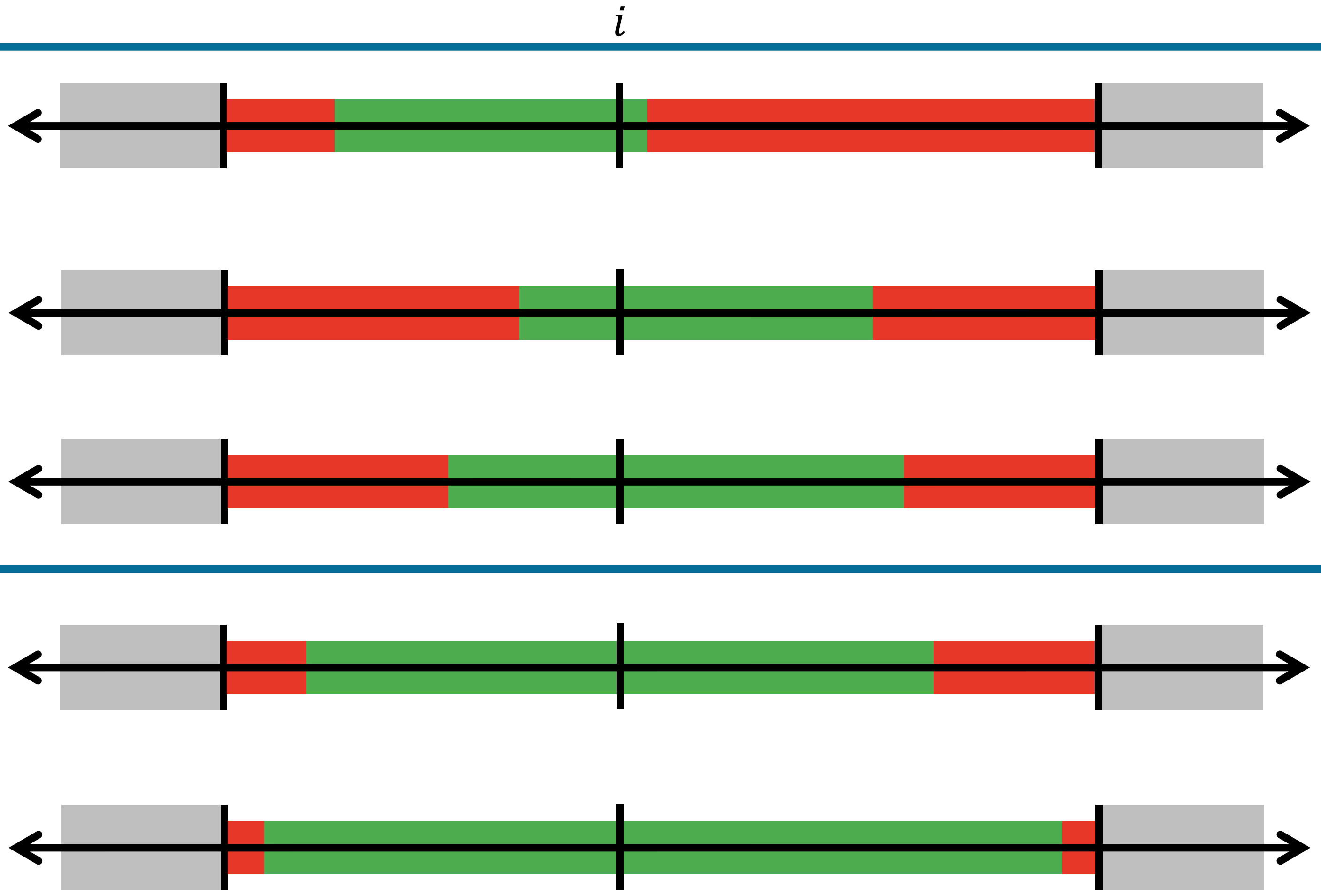
5. Parameter: $S = 5$

2. Parameter: $S = 4$

4. Parameter: $S = 3$

1. Parameter: $S = 2$

3. Parameter: $S = 1$



Single-Parameter-Variation Method

1. Conduct sensitivity analysis for all parameters
   - Sort them according to their sensitivity

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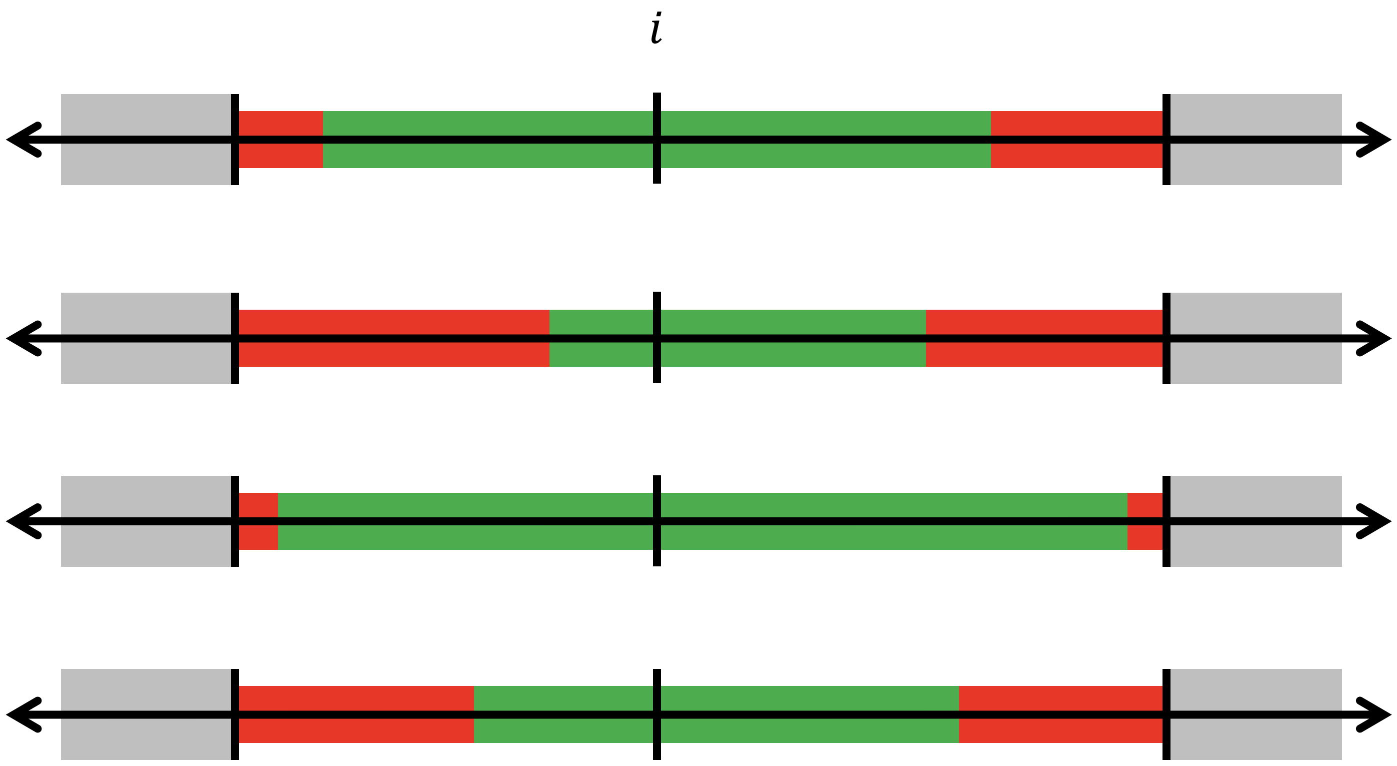
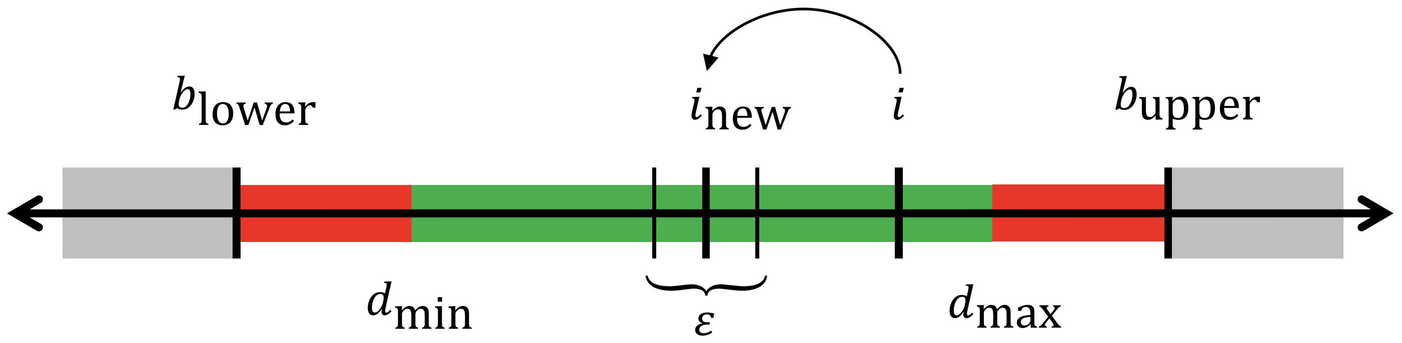


Single-Parameter-Variation Method

1. Conduct sensitivity analysis for all parameters
   - Sort them according to their sensitivity

2. Loop through sorted parameters
   - Set new initial value to $i_{\text{new}} = \frac{d_{\text{min}}+d_{\text{max}}}{2}$
   - Or skip parameter if initial value i lies already inside a tolerance range ε



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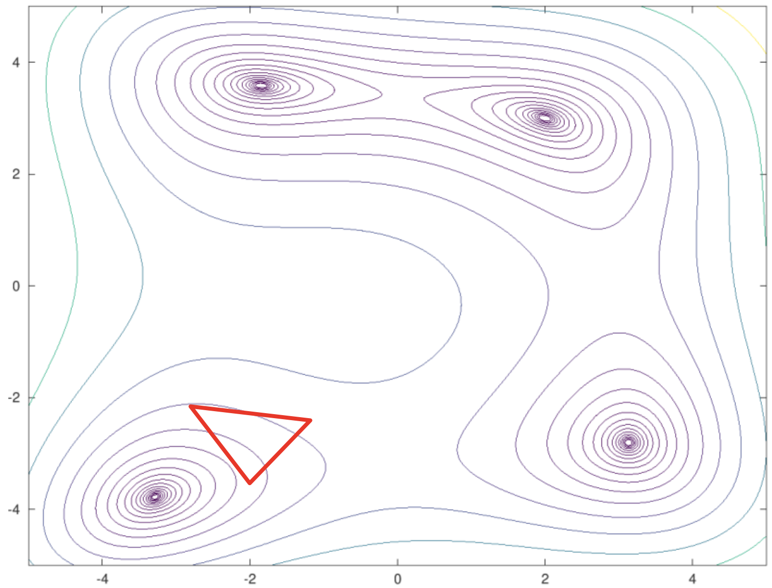
3. Continue with Step 1 until a termination criterion is reached
   - Maximal number of iterations
   - All parameters were skipped (they lie inside the tolerance range ε)

Downhill-Simplex Method

- Method is generally used to optimize n-dimensional cost functions ($f\colon \mathbb{R}^n \rightarrow \mathbb{R}$) where no derivative is known
  - $n + 1$ dimensional simplex moves towards an optimum

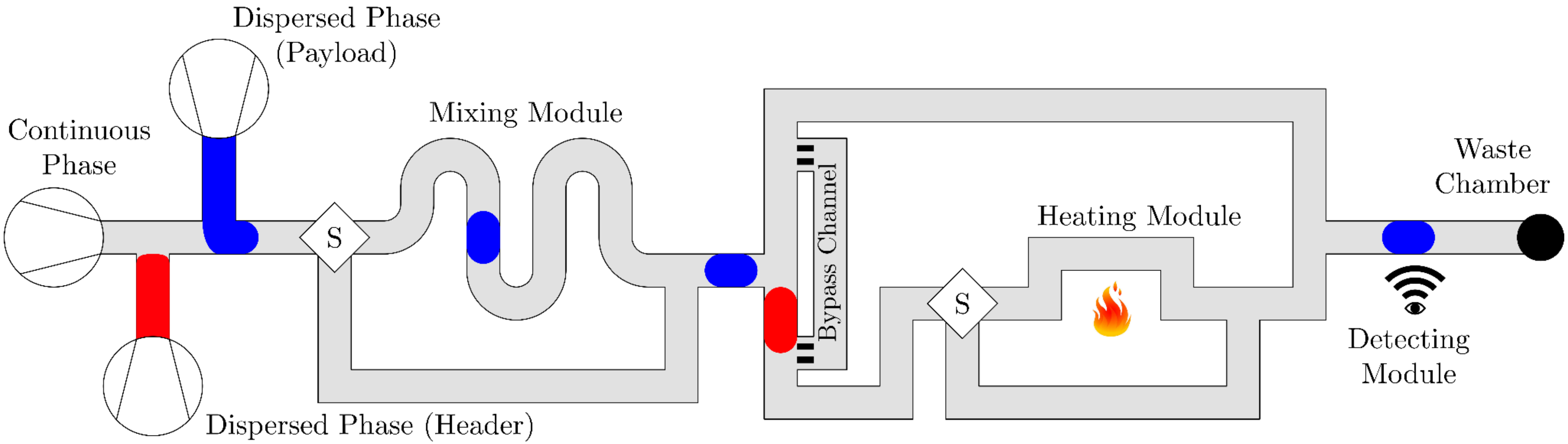
- Tries to improve the robustness metric directly (in contrast to the Single-Parameter-Variation method)
  - High costs due to the computation of the robustness metric

- Only consider sensitive parameters so the problem stays manageable



Example

- Experiment: A droplet must be processed by the modules in a certain order



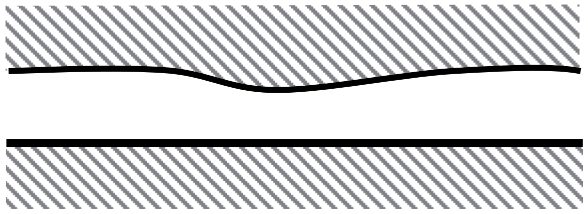
Example

- σ … standard deviation used in the robustness metric
- ε … tolerance range
- n … considered parameters
- I … number of iterations
- t … required time
- $p_{success}$ … robustness metric value

	Networks		
Modules/Channels	8/34	10/67	15/101
σ	0.005	0.002	0.002
$p_{\text{success}}^{(\text{initial})}$	55.42%	40.91%	46.07%
Single-Parameter-Variation:			
ϵ	0.05	0.05	0.05
n	16 (all)	8	8
I	24	30	10
t	31 s	21 min	26 min
p_{success}	64.86%	74.81%	59.10%
Downhill-Simplex:			
n	16 (all)	5	3
I	109	38	22
t	9 min	32 min	96 min
p_{success}	63.86%	53.50%	62.20%

Conclusion

- Fabrication processes and material properties always induce unavoidable defects into microfluidic networks, frequently resulting in costly iteration loops



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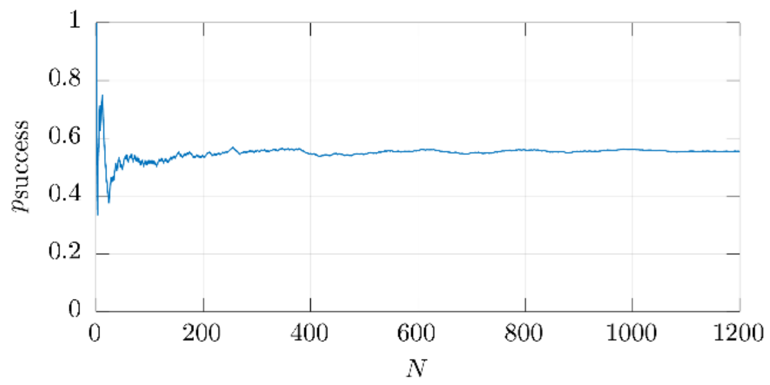
- Robustness metric acts as reference value for comparison between the robustness of an initial with an improved design



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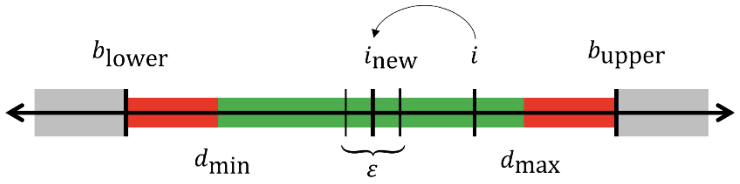
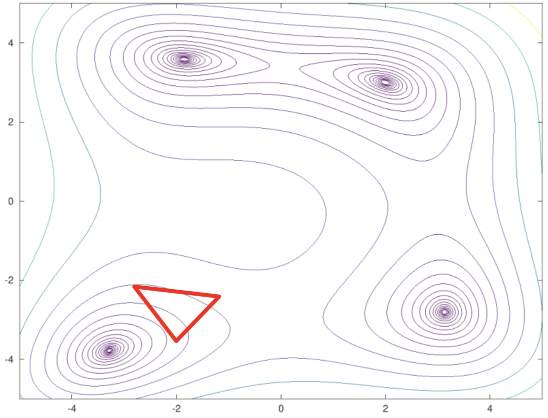


- Different robustness improvement methods
  - Single-Parameter-Variation Method
  - Downhill-Simplex Method



Many thanks for your attention

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