Smart Transfection: In-flow electroporation with self-learning capabilities using integrated impedance cytometry modalities

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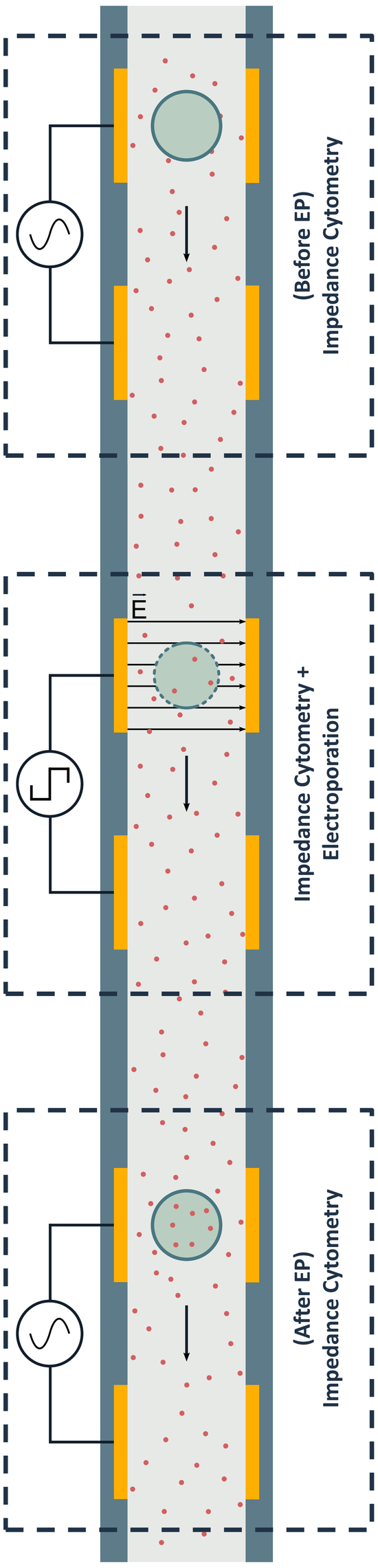
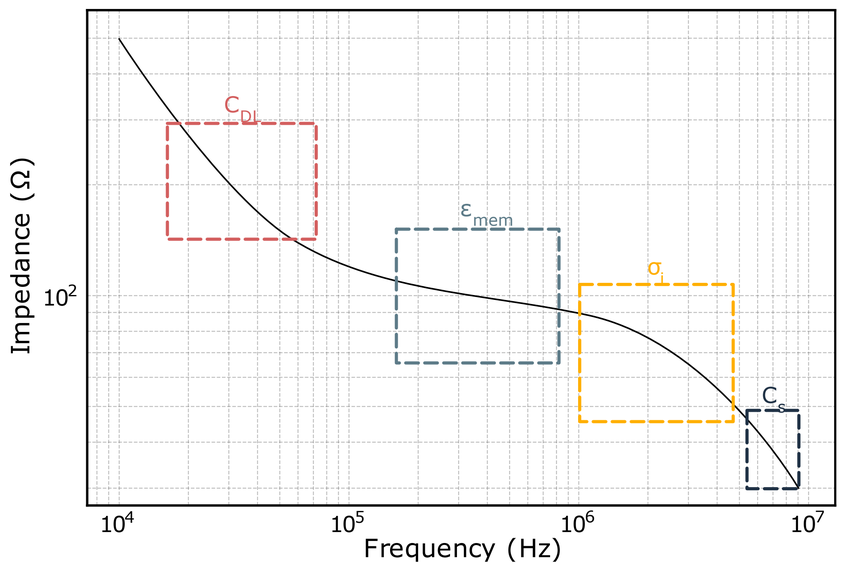
Introduction

Intracellular delivery of exogenous cargo is an essential step in many cell engineering applications. The limitations and stringent safety requirements of viral methods have researchers looking at physical methods. However, the **optimization** remains to be a time-consuming procedure, making the development a **long and costly process**.

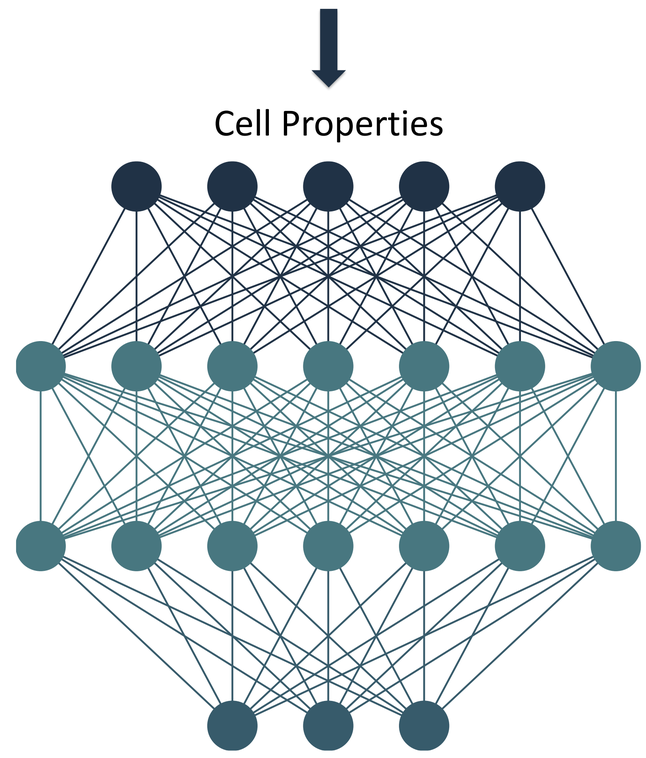
Here we **combine in-flow electroporation and real-time data from impedance cytometry modalities together with machine learning** techniques to enable a **dynamic optimization process**. We envision this device to not only **reduce optimization times**, but also enable **real time in-situ monitoring** of the in-flow electroporation process on an individual cell level.





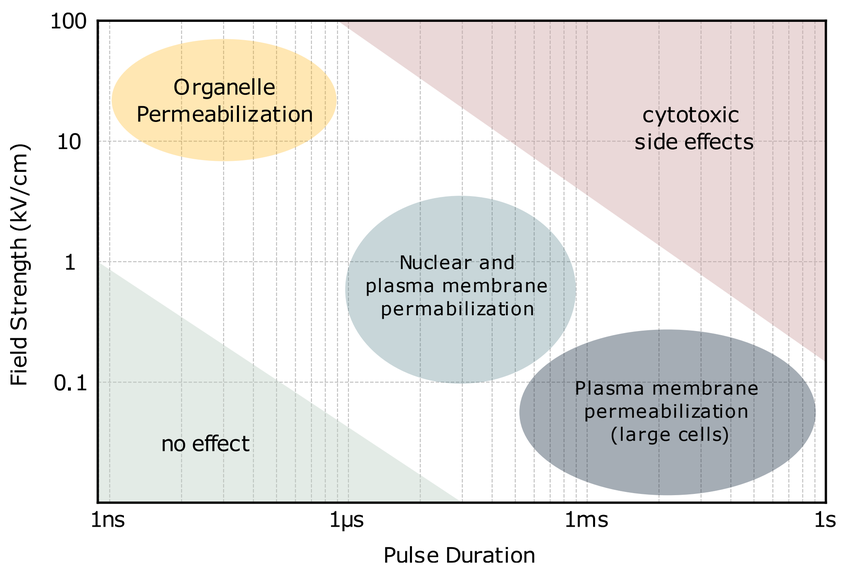
Impedance Cytometry

- Impedance Cytometry (IC) **measures cell properties** by detecting the **change in impedance** caused by a cell.
- By **probing at different frequencies**, different properties can be measured simultaneously.



Feature Extraction

- Cell **properties vary between populations** and **inside a single population.**
- Electroporation uses **a single set of parameters** for an **entire population.**
- AI techniques (e.g. Neural Networks) will be used to **extract (higher dimension) features** and **determine suitable electroporation parameters** on an **individual cell level.**

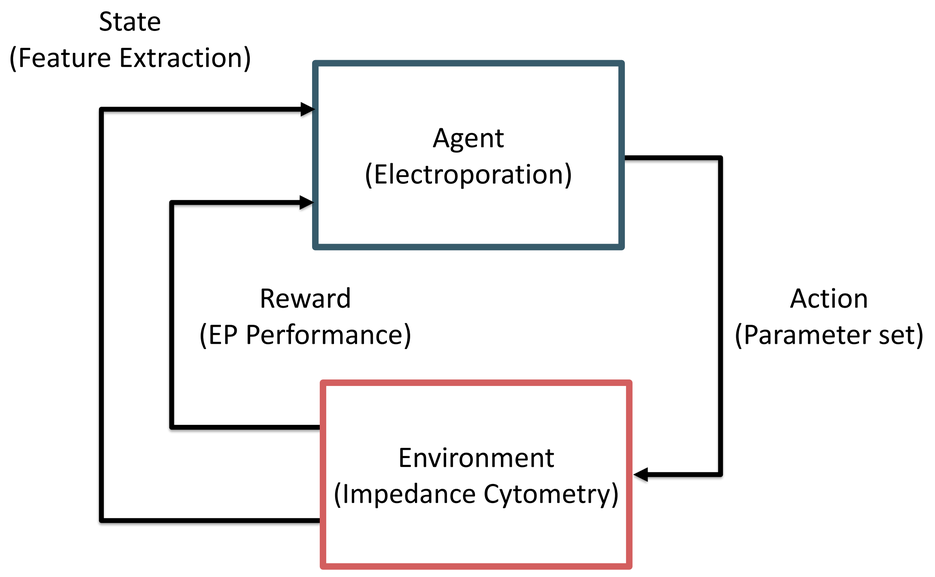


In-Flow Electroporation

- Electroporation (EP) is the **formation of nanopores** in a cell membrane **due to the exposure of an external field**.
- In-flow electroporation is **performed in a microfluidic channel** and can be done on the **individual cell level.**
- Defining and delivering the **optimal electric pulse to each cell** is of critical importance for **efficient transfection** while **avoiding cytotoxicity**.

Optimization

- Finding the **optimal parameter** set is a **time-consuming process.**
- Implementing **additional Impedance Cytometry** steps **during and after electroporation** allows to **quantify the electroporation degree.**
- **Combining IC data** from different moments in time of the electroporation process opens the possibility of a **dynamic optimization process – e.g. Reinforcement Learning.**



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