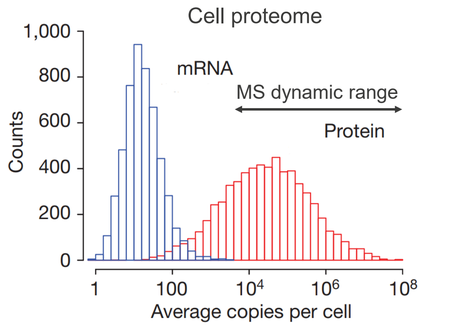
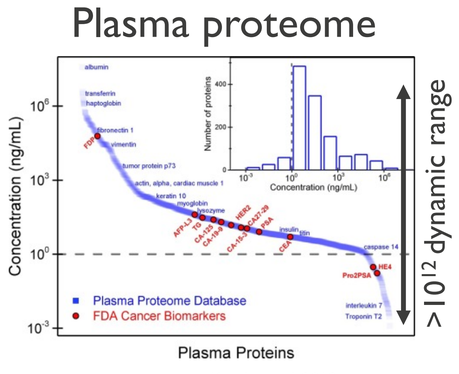
The Nanopore Field Effect Transistor (FET) for Protein Analysis

Koen Martens[1,2], David Barge[1,2], Colin Stocquart[1,2], Sybren Santermans[1], Lijun Liu[1,2], Jacobus Delport[1,2], Bert Du Bois[1], Anne Verhulst[1,2], Simone Severi[1], Pol Van Dorpe[1,2]

Key technology challenge for proteomics-on-chip



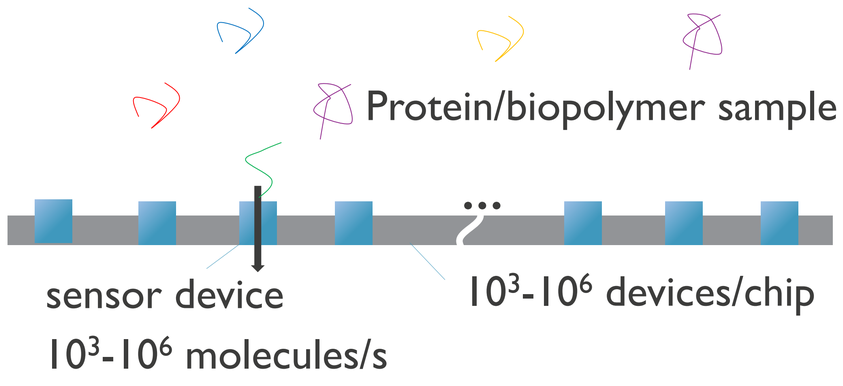
Schwanhausser et al. Nature 2011



Kosaka et al. 2018

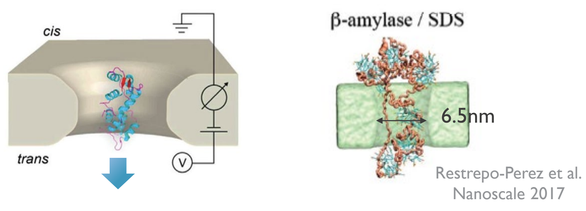
Nanopore FET single-molecule proteomics-on-chip vision

- Proteomics-on-chip favors single-molecule approach
- Enormous concentration differences (= large dynamic range) in proteomes
- To exceed MS dynamic range (10^3-10^5) by multiple orders of magnitude one needs to analyze billions of single molecules
- For 10^{12} dynamic range in an hour, billions of molecules per second need to be analyzed



- NPFET potentially breaks the translocation speed limit currently limiting nanopore technology

Solid-state nanopore

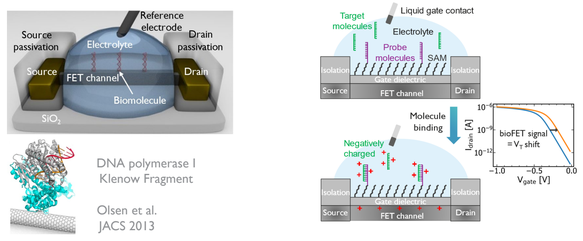


Restrepo-Perez et al. Nanoscale 2017

Translocating molecule modulates the recorded ionic current passing through pore

- ⊕ Chemically robust (vs. biopore)
  Concentration dynamic range
  - misses large part of translocating proteins
  - senses long DNA
- ⊖ Difficult to integrate on chip
- 🎯 Molecular resolution toward sequencing undemonstrated

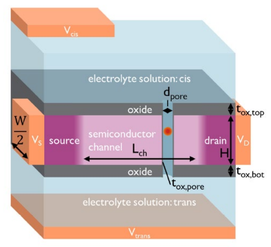
bioFET



Molecule docks close (1-10nm) to FET surface. Molecule's charge modulates channel charge and FET current

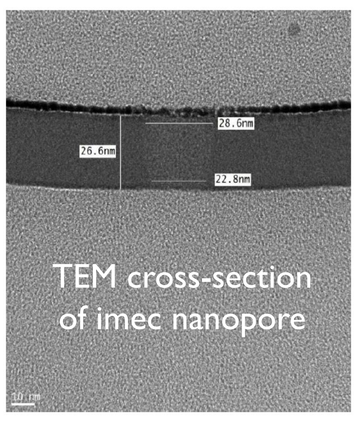
- ⊕ Chemically robust
  Concentration dynamic range
  - surface attachment
- ⊕ Gigascale integration on chip
  - Up to billions per chip
- Molecular resolution determined by biochemistry

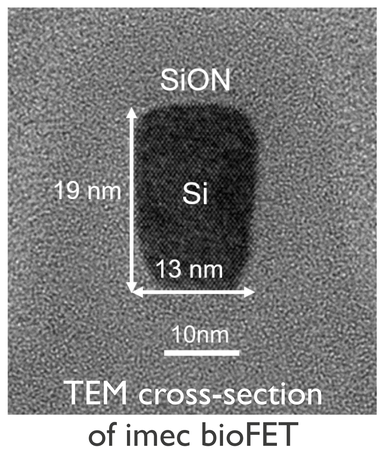
Nanopore FET



A nanopore wrapped by a nanoscale field-effect transistor (FET). The FET senses single molecules translocating through the pore

- ⊕ Chemically robust (vs. biopore)
- ⊕ High concentration dynamic range
  - Potentially orders of magnitude more than MS
  - Chip potentially reads up to billions of molecules/s
- ⊕ Megascale integration on chip
  - Up to millions per chip
- 🎯 Molecular resolution toward sequencing undemonstrated





World's smallest bioFETs