S3IC 2020

Design and Modeling of a Nanopore Transistor

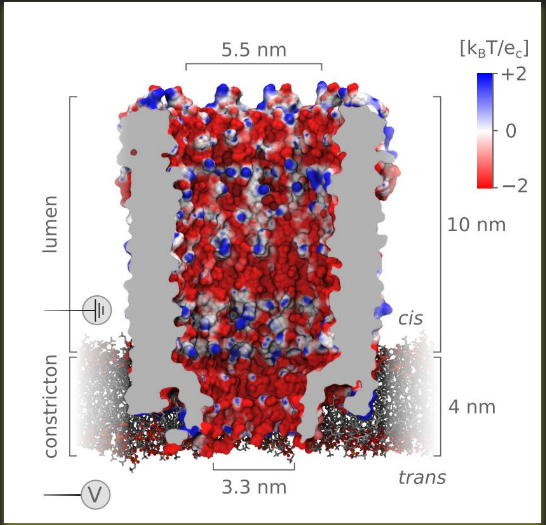
Dino Ruic[†], Kherim Willems, Ashesh Ray Chaudhuri, Chia Ling Chan, Simone Severi, Mihir Gupta, Willem Van Roy, Chang Chen, and Pol van Dorpe*

imec

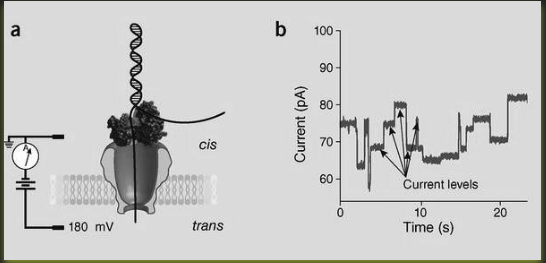
[†]dinoruic@google.com
*pol.vandorpe@imec.be

Overview: Biological Nanopores

- Large pore-shaped proteins suspended in lipid bilayers between two electrolyte reservoirs
- Ion charge current through the nanopore is measured with electrodes
- Presence of molecules inside the nanopore can be measured through changes in current levels
- Signal-to-noise ratio is good enough for commercial DNA sequencing applications
    - see Oxford Nanopore Technologies



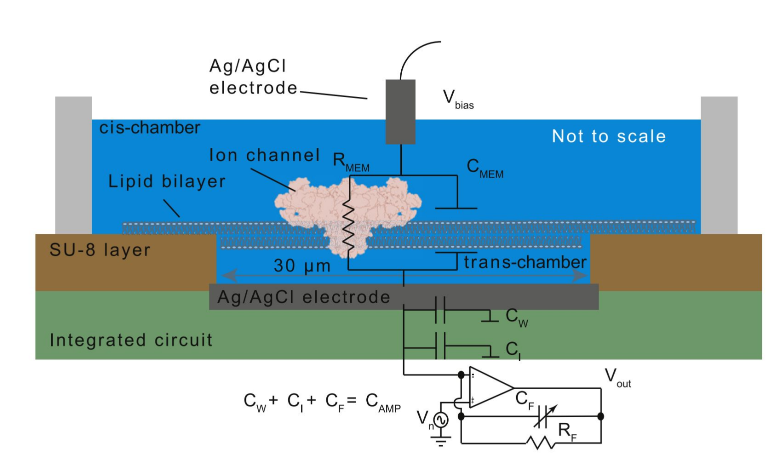
K. Willems et al. (ACS Nano 2019)



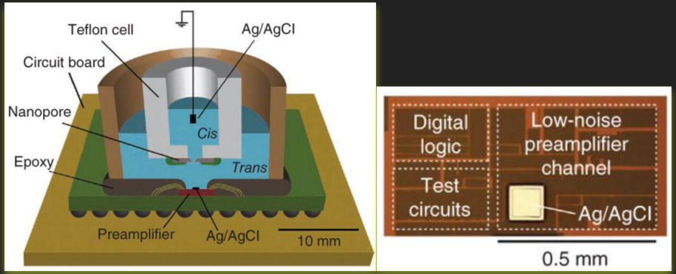
D. Deamer et al. (Nat. Biotechnol. 2016)

Overview: Biological Nanopores

- Nanopore ion current measurements are typically done with low-noise Ag/AgCl electrodes and a patch-clamp amplifier
- A transimpedance amplifier is used to convert the current signal into a voltage signal
- Efforts to increase signal-to-noise ratio and bandwidth typically bring the amplifier closer to the nanopore



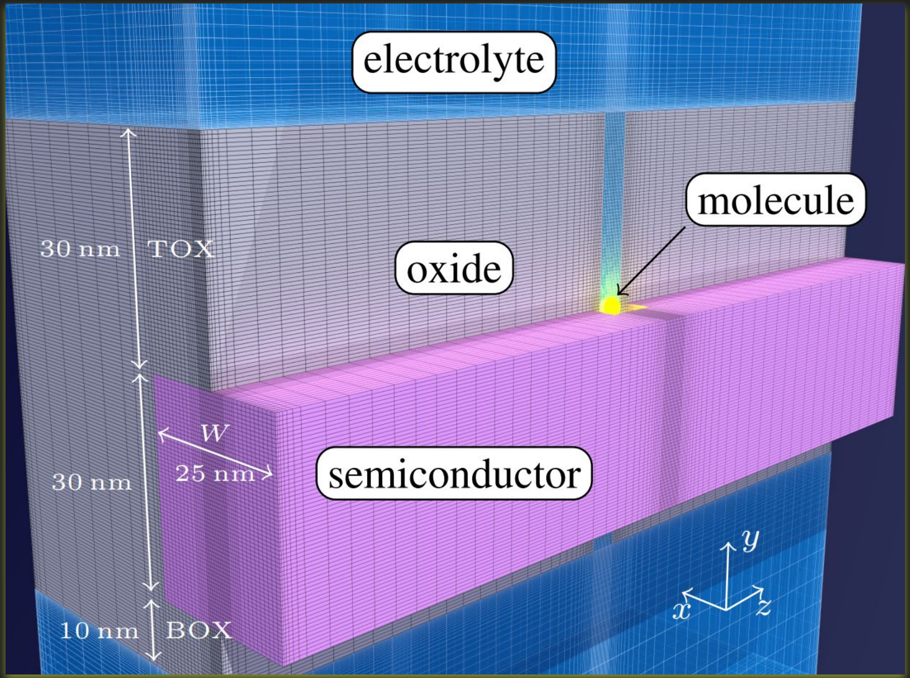
J. W. Hartel et al. (Analytica chimica acta, 2019)



J. K. Rosenstein et al. (Nat. Methods, 2012)

The Idea Behind the Nanopore Transistor (NPFET)

- For the Nanopore Transistor we bring the first transistor of the amp as close as possible by wrapping it around the nanopore
- We can directly sense the electric field in the nanopore
- The transistor is gated by the pore and molecular signals are immediately amplified to a microampere current with >GHz bandwidth



Modeling the Physics with npfetFOAM

- To design the Nanopore Transistor (NPFET), we need to understand
  - The sensing mechanisms
  - The best operating regime
  - Impact of design choices on sensitivity
- There is no trick to reduce dimensionality
  - Need to solve governing equations in 3D
  - This problem is beyond the capabilities of commercial solvers such as Comsol.
- We developed our own (research) solver and it is open source
- Source code of npfetFOAM available at https://gitlab.com/dinoruic/npfet_s3ic2020
  - Finite-volume implementation using OpenFOAM (https://openfoam.com/)
  - VTK-based visualization with Paraview (https://www.paraview.org/)

Electric Potential: Nonlinear Poisson equation

$$\nabla \cdot (\varepsilon \, \nabla V) = -\rho(V)$$

Electrons in Semiconductor: Drift-Diffusion equation for electrochemical potential

$$\nabla \cdot (\mu_n \, n \, \nabla \varphi_n) = 0$$

Ions/pH in Electrolyte: Nernst-Planck equation for electrochemical potential

$$-\nabla \cdot (\mu_c \, c \, \nabla \varphi_c) + z_c \boldsymbol{u} \, \nabla c = 0$$

Flow of Electrolyte: Incompressible Navier-Stokes equation for laminar flow

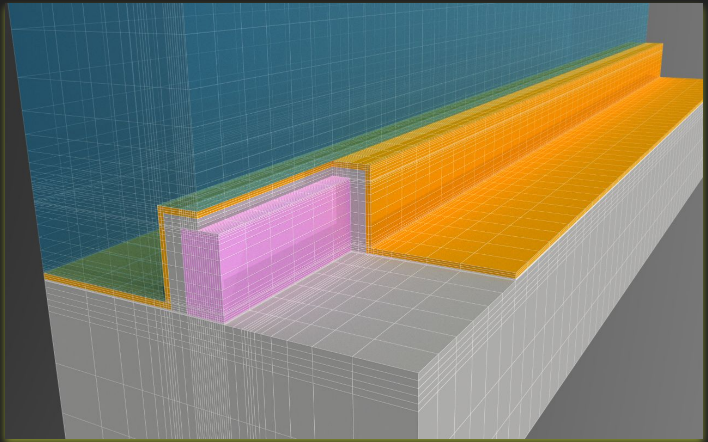
$$\nabla \cdot (\boldsymbol{u} \otimes \boldsymbol{u}) - \nabla \cdot (\nu \nabla \otimes \boldsymbol{u}) = -\nabla p + \boldsymbol{f}$$

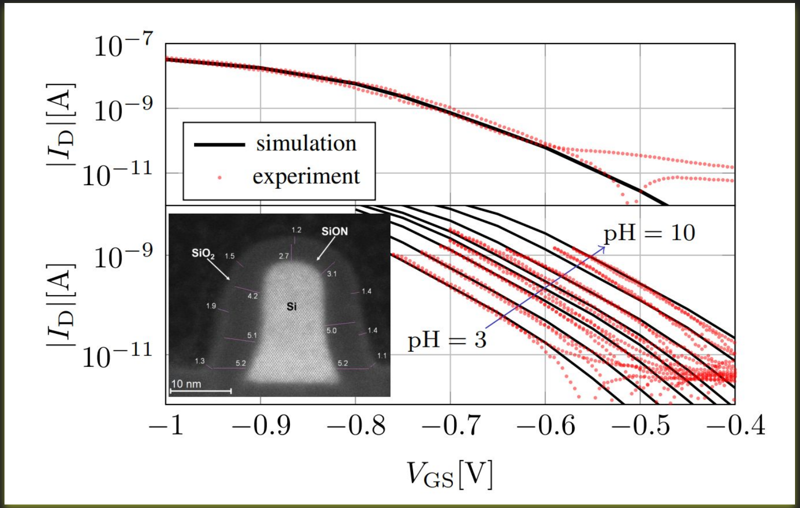
$$\nabla \cdot \boldsymbol{u} = 0$$

npfetFOAM

Calibration of `npfetFOAM`

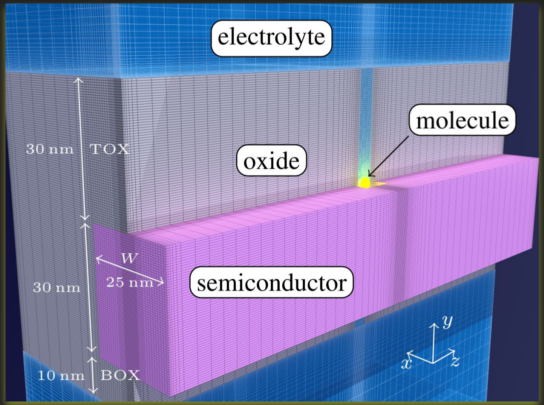
- SiO_2 forms pH-sensitive silanol surface states
  - Surface charge determined by local pH determines sensitivity
  - Use the two populations of silanol states as shown in S. Ong et al. (Chemical Physics Letters, 1992)
- Semiconductor performance will be suboptimal in experimental process
  - Expect worse mobility and degraded subthreshold slope due to oxide traps
- Calibrate these models with IMEC's real FinFET biosensor data from M. Gupta et al. (IEEE Sensors Journal, 2019)
  - We demonstrated the first ever full output curve simulation for a semiconductor-based pH-sensing device matching experiments across the whole pH range
- Use electrolyte mobilities similar to K. Willems et al. (ACS Nano 2019)

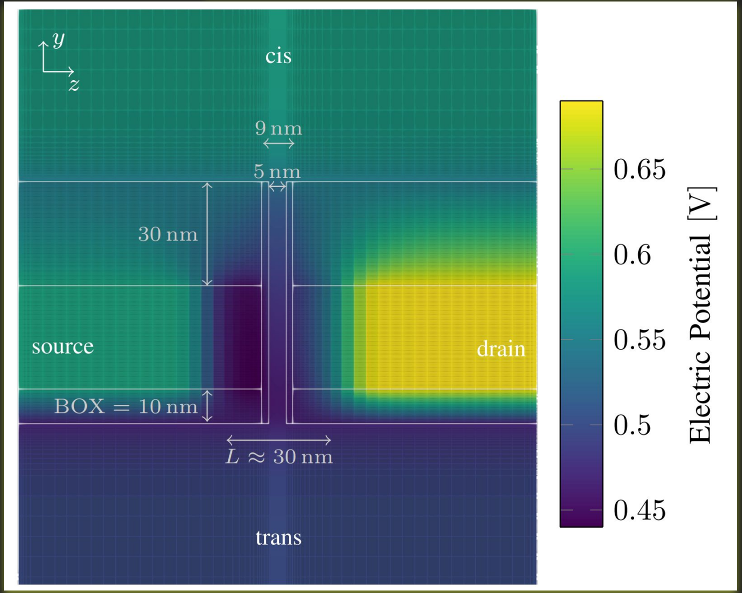




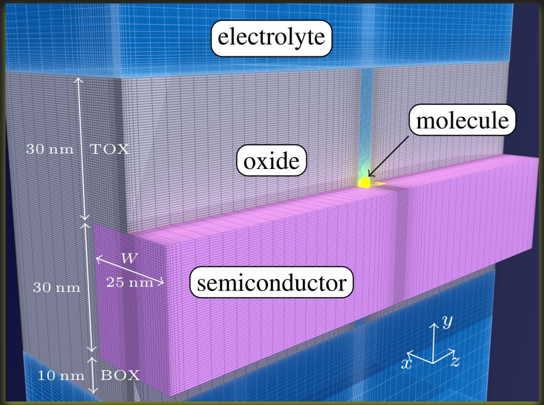
Operation of the Nanopore Transistor

- A bias is applied from the top to bottom electrolyte reservoirs
  - Ion electromigration & electroosmotic flow through the pore
  - Molecules are captured and translocate from top to bottom
- A bias is applied from source to drain of the Nanopore Transistor
  - Electron current flows from source to drain around pore
  - Undoped channel region around pore is gated by pore potential and sensitive to changes in the pore

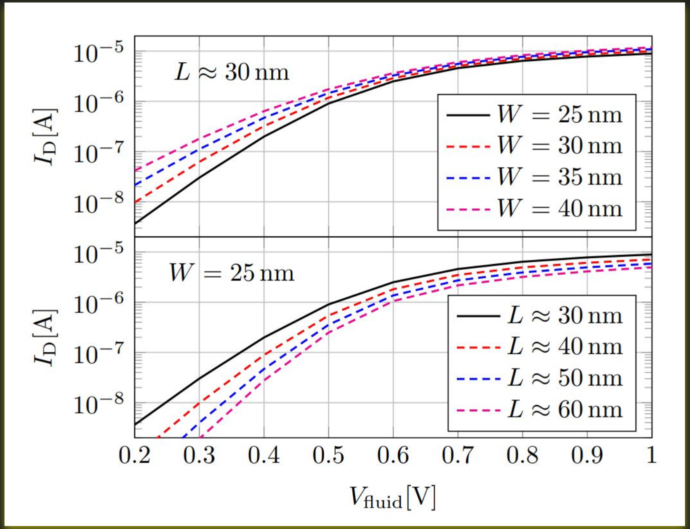




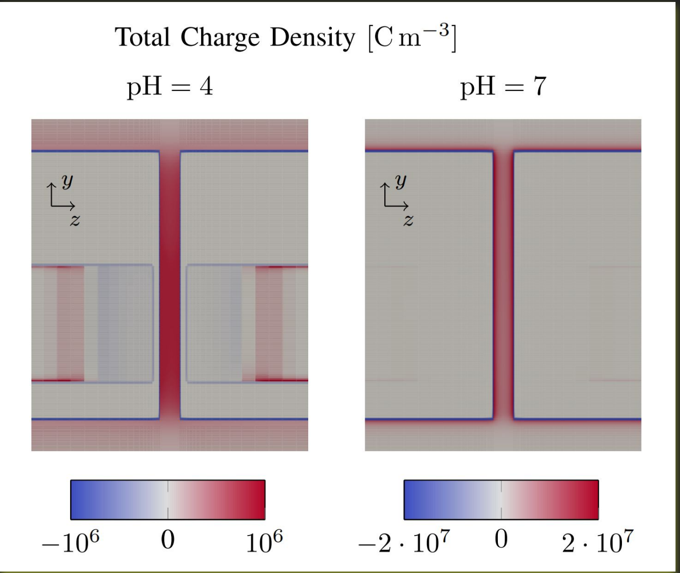
Operation of the Nanopore Transistor

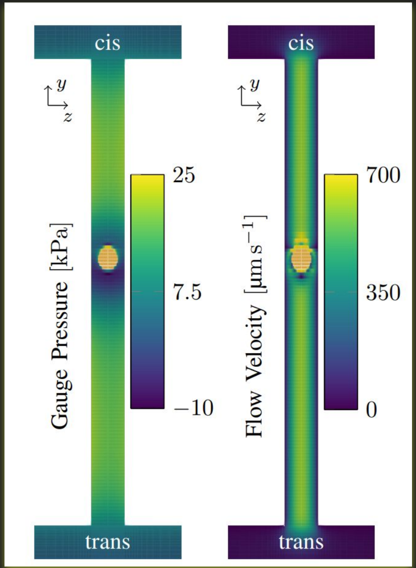


- Current-voltage curves for symmetric cis/trans potential V_{fluid} reveal gate control problems
  - In wider devices channel regions far away from the pore cannot be controlled anymore
  - In shorter devices drain-induced barrier-lowering appears
  - Transistor performance is not directly related to the sensitivity
- Optimal operating point likely $\max(g_m)$ or V_T



Charge distribution and molecule model

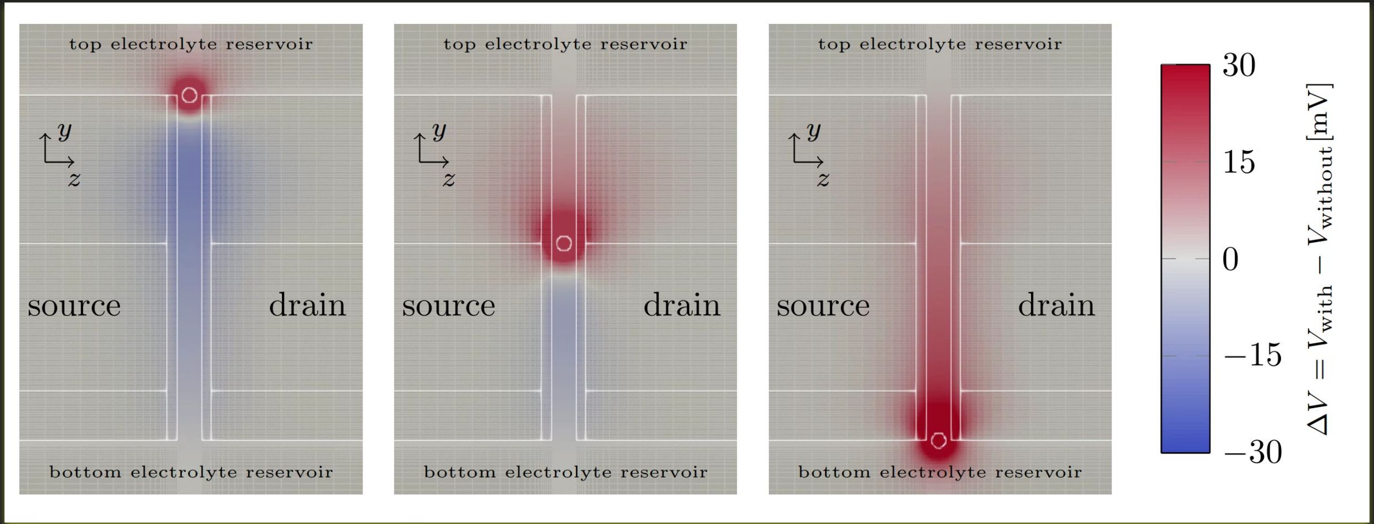




- Use calibrated model to understand charge distribution and screening
- For smaller pH = 4
  - Silanol surface states have small negative charge
  - Nanopore forms a potential well for positive ions
  - Diffusion zones in semiconductor are also visible
- For larger pH = 7
  - Silanol surface states are strongly charged
  - Ions form a double layer of a few nanometers thickness

- Use spherical molecule with 3 nanometer diameter and +10 elementary charges
- Creates notable disruption of electroosmotic flow
- Affects nanopore ion current and potential landscape

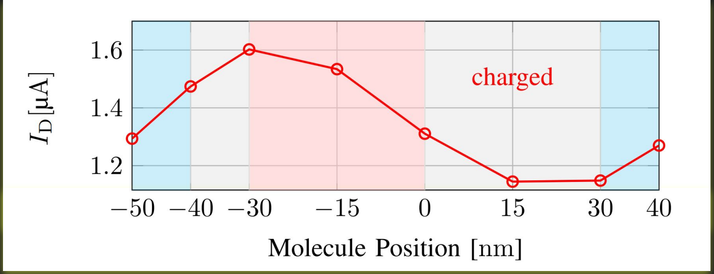
Molecular Potential Perturbations

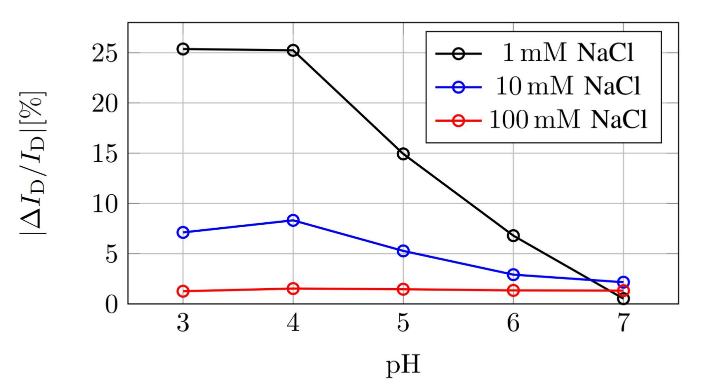


- When the molecule with +10 elementary charges is present in the nanopore, it strongly perturbs the potential
- The potential is perturbed along the whole pore because the ion current adjusts
  - A point-like potential perturbation around the molecule gets turned into a macroscopic volumetric perturbation
- There is a direct field-effect from the molecule's charge and a pore ion current blockage effect
- The potential drops off ahead of the molecule and increases behind the molecule due to the ion current blockage
- The blockage effect is enhanced if the molecule is charged because charge acts as an additional barrier

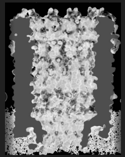
Current Signal and Sensitivity of the Nanopore Transistor

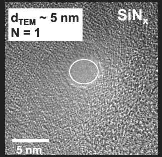
- The signal current is in micro-amperes
  - Far away from equipment noise
- The signal profile exhibits a symmetry
  - Drops when molecule enters and increases on its way out
- Sensitivity is highest at
  - Low salt due to lower screening
  - Lower pH due to less surface charge
- Exceptionally high sensitivities of >25% can be achieved
- A Nanopore Transistor's bandwidth is easily >1GHz
  - Fast enough for free translocation of molecules



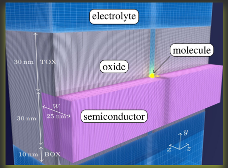


Pros and Cons of Nanopore Biosensors


K. Willems et al. (ACS Nano 2019)



Y.-C. Chou et al. (ACS Nano 2020)



	Biological Nanopores	Solid-State Nanopores	Nanopore Transistor
Signal Amplitude	Low	Low	High
Bandwidth	Low	Low	High
Nanopore Noise	Low	High	High
Biocompatibility	Good	Bad	Bad
Multiplexable	No	No	Yes
Variability	Low	High	High
Scalability/Productization	Bad	Good	Good

Summary

- We developed `npfetFOAM` the first ever fully self-consistent solver for flowing electrolytes and semiconductors
  - Calibrated surface state, electrolyte, and semiconductor models
  - Visit https://gitlab.com/dinoruic/npfet_s3ic2020 for the source code and try it out yourself!
- Our modeling suggests that the Nanopore Transistor could be a paradigm shift in sensing capabilities
- The Nanopore Transistor is in active development at IMEC
  - Fully integrated on the state-of-the-art 300mm semiconductor manufacturing line
  - IMEC's wider goal is to develop scalable fully integrated nanopore/biosensing technologies
- Contact Dino Ruic (dinoruic@google.com) if you have questions about this presentation
- Or directly contact Pol van Dorpe, scientific director at IMEC (pol.vandorpe@imec.be), if you are interested in
  - Fully integrated solid-state nanopores or other biosensors
  - The accurate modeling of biological and solid-state nanopores and other biosensors
  - Research collaborations