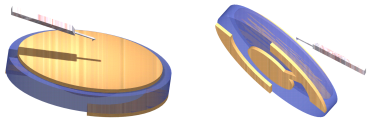
# The metrology of biosensors: a multiparameter approach to characterizing protein layers



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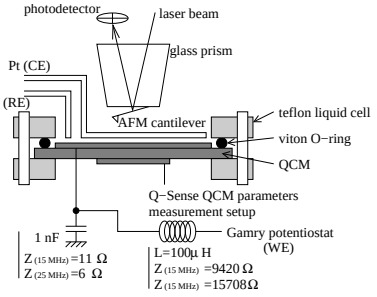
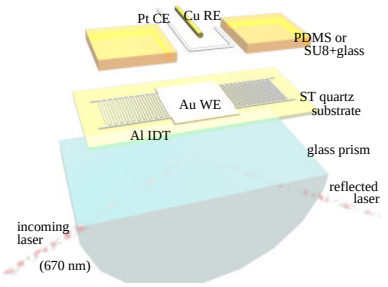
## Objectives of the combination of direct detection methods

• **Mass** detection based on acoustic sensors (QCM, SAW) → provides layer density $\rho$ and thickness $d$
• Dielectric/**optical index** variations (impedimetric sensors, optical sensors) → planar multilayer simulations → ellipsometry/SPR/waveguide sensor provides optical index $n$ of layers and thickness $d$
• scanning probe microscopies → surface morphology, chemical properties when using functionalized tips
⇒ **combine these methods to obtain independent estimates of layer thickness and water content of the protein layers**

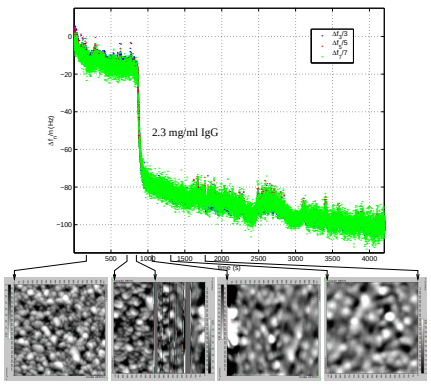



AFM/QCM combination setup



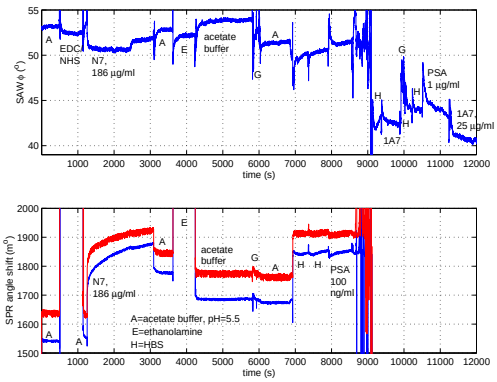

SAW/SPR combination setup

## QCM/AFM combination

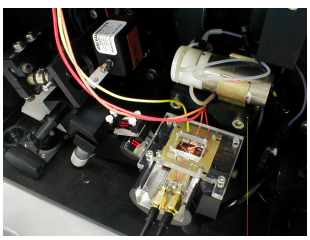



Use of commercial instruments:
• QSense-AB QCM monitoring electronics (frequency overtones and damping) → continuous monitoring of the 3rd, 5th and 7th overtones+quality factor
• Molecular Imaging AFM (moving scanner, fixed sample holder)
• Gamry potentiostat for electrochemistry applications
Problems of viscous interactions, trapped water, QCM/AFM interaction (oscillation amplitude: ≃3 nm ; standing wave pattern disturbs QCM resonance frequency).
Application to electrochemistry (relate QCM behavior to electrodeposited film roughness) and to biology (example presented here: IgG adsorption on hydrophobic-thiol coated gold (data obtained by Z. Cheng).
**Problem:** bare AFM tips provide little information on the surface other than topography (usually only observed for very high concentrations of proteins), individual molecule imaging very difficult on evaporated gold.

## SPR/SAW combination



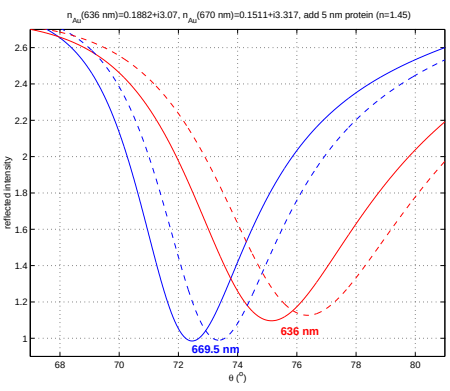

• Development of Love mode SAW devices with improved sensitivity over QCM and open backside for injection of laser
• modified Ibis II SPR instrument
→ limited effect of viscous interactions but problem with birefringence of piezoelectric substrate ⇒ separate SPR dip from interference fringes minima
→ single wavelength SPR leads to uncertainty on optical index and thickness evolution ⇒ reduce the number of variables to water content and thickness (instead of $\rho$, $n$ and $d$). Anti-PSA antibody presented here synthesized at VUB, protocol developed by L. Huang.

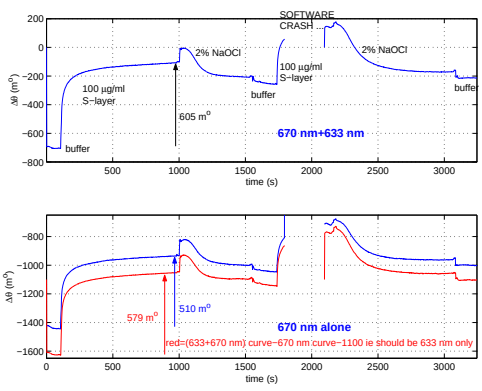


Experimental setup applied to electrodepsotion of copper

## Future improvements

• All three techniques in one instrument ?
• Multiple wavelength SPR by combining lasers using a beam splitter or white light source +diffraction grating ? → issue of interference fringes due to piezoelectric substrate
**Right:** simultaneous measurement of S-layer proteins adsorption on gold coated glass monitored at 633 and 670 nm, and related simulations showing that the angle shift is dependent on the wavelength.

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