Quartz crystal microbalance technology as a new platform for real-time monitoring in biology, medicine and engineering

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Quartz crystal microbalance (QCM-D) technology is a surface-sensitive technique of (bio)-layers on a surface with regard to adsorption/desorption events, molecular interactions and structural properties. Here, three examples illustrate the versatility of the QCM-D technology in the analysis complex dynamic processes.

1) Build-up of polyelectrolyte multi-layers
2) Tissue engineering of bio-mimetic bone matrix construct
3) Formation and removal of bacterial biofilm layer

Quartz crystal microbalance measuring principle

Fig. 1 3T QCM-D technology. 3T qCell T instrument with dual flow cell chamber (A). QCM-D measuring principle (B). The quartz crystal (grey) is driven by alternating voltage to frequency-stable oscillation (transverse wave, horizontal arrow) and shear vibration (vertical arrow). Changes at the quartz surface (yellow) or in the adjacent medium (blue) affect the frequency (f) - and/or shear vibration i.e. dissipation, (respectively damping (Γ)). The inset depicts the unique 3T-sensor-chip.

- At the heart of the QCM-D technology is the biosensor, i.e. a quartz oscillator (Fig. 1).
- Changes in the QCM-D parameters, frequency and damping of the oscillation, correlate with binding to and/or with changes in the structural properties at the surface layer (1, 2).

Three distinct typical cases illustrate the QCM-D measuring principle (Fig. 2):

- Formation of rigid homogeneous layers leads to a change in frequency, with an unchanged damping change in mass but constant viscoelasticity (2A).
- A change in the viscosity of pure liquids, for example, water compared with glycerol, results in a decrease in the frequency while the same amount is increased in the damping (2B).
- The addition of large ‚soft' molecules, such as immune cells or bacterial cells leads to a frequency and damping change in opposite directions, as yet, with different amplitudes (2C).
- In particular, the damping parameter permits the detection of events or transformations in ‚soft' cellular layers (3) (2C).

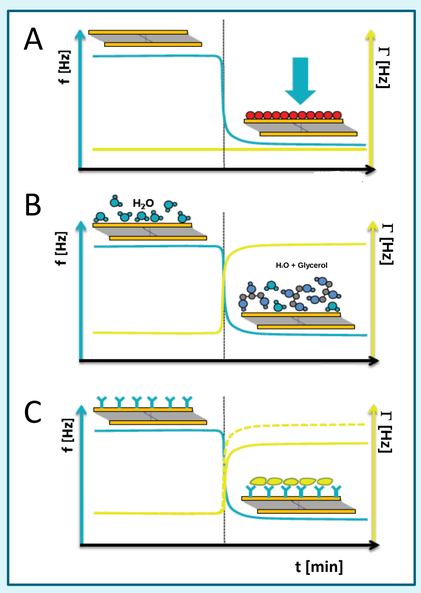
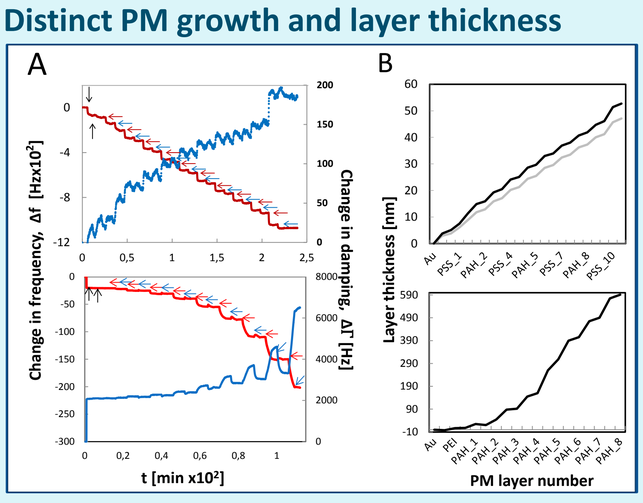


Fig. 2 QCM-D experiment on biological samples. Idealized signal shape of frequency (blue line) and damping (yellow line) during three distinct cases. Rigid globular molecules (red circles). Bacterial or immune cells (yellow ovals). See text for further details.

1) Monitoring of polyelectrolyte multilayer build-up

Distinct PM growth and layer thickness



- Polyelectrolyte multilayers' (PM) widespread potential applications range from implant coating up to filtration devices or specialized optical coatings (4).
- Detailed insights on the PM's growth and physical state is provided by QCM-D monitoring during its formation (Fig. 3).
- The frequency and damping signal progression corresponds to mass adsorption and viscosity changes of the deposited PM film.

Fig. 3. PM build-up monitored by QCM-D. Progression of the frequency (red line) and the damping (blue line) signals of linearly growing (PEI-(PSS/PAH)$_{10}$, top) and exponentially growing (PEI-(PGA/PAH)$_8$, bottom) PMs (A) . The arrows point to polyelectrolyte (PE) addition (PEI black, PSS red, PAH blue). PSS/PAH and PGA/PAH film thickness on sensor surface as a function of PE addition (B). Thickness is determined by applying the Sauerbrey (grey line) or the viscoelastic module (black line) (1,2). PEI, polyethylenimine; PSS, polystyrene sulfonate; PAH, polyallylamine; PGA, poly-L-glutamic acid.

2) Monitoring biomimetic bone cell-matrix synthesis

Bio-activation of PLC nanofibers

- Bioactive implants intended for rapid, and durable bone tissue regeneration are generated based on nanofibrous 3D-scaffolds of bio-resorbable poly ε-caprolactone (PCL) mimicking the architecture of bone matrix (5).
- The frequency and damping shifts reflect the gradual stepwise coating of the PCL-nanofiber with linker peptides, poly-lysine (pLys) and –glutamate (pGlu) and at the final coating stage, replenishment of the nanostructures' cisterns with fibroblasts growth factor for bio-activation (Fig. 4, red arrow) (5,6).

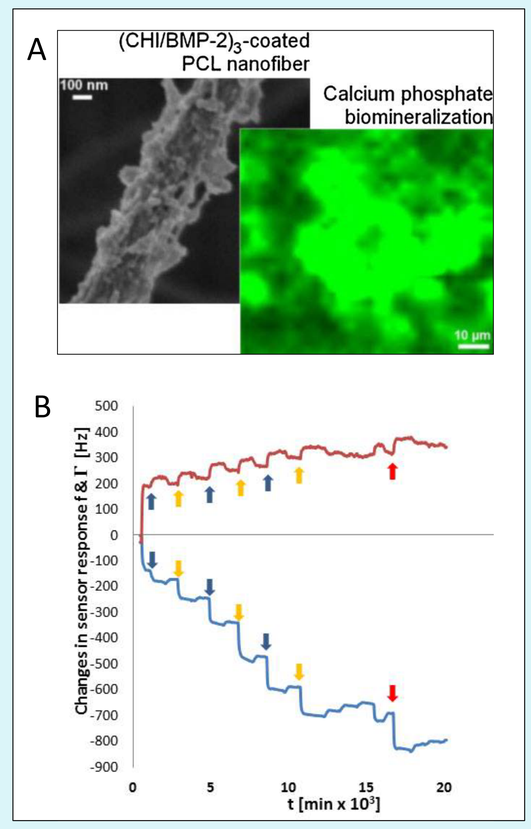
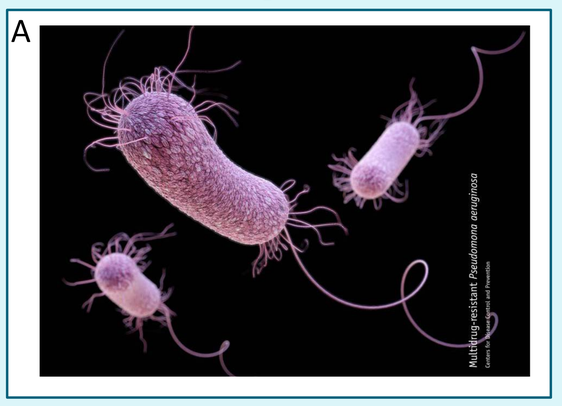


Fig. 4 Tissue engineering with QCM-D. (A) High resolution imaging of PCL polymer, coated with the osteogenetic growth factor bone morphogenetic protein 2 (BMP-2). (B) QCM-D frequency signal progression during the stepwise coating of the nanofiber scaffold with, pLys (blue arrows), pGlu (yellow arrows) and the final bio-activation by addition of fibroblast growth factor, FGF2 (red arrow) (6).

3) Real time monitoring of biofilm development

Pseudomonas aeruginosa surface adhesion, biofilm formation and removal



- A portfolio of effective measures is much needed to contain the medically significant biofilms of e.g. multi-drug resistant *Pseudomonas aeruginosa (P. aeruginosa)* (7).
- Key information about the function, community diversity, assembly and disassembly, as well as the resistance to disinfectants is obtained by QCM-D monitoring of biofilm maturation (8,9; Fig. 5).

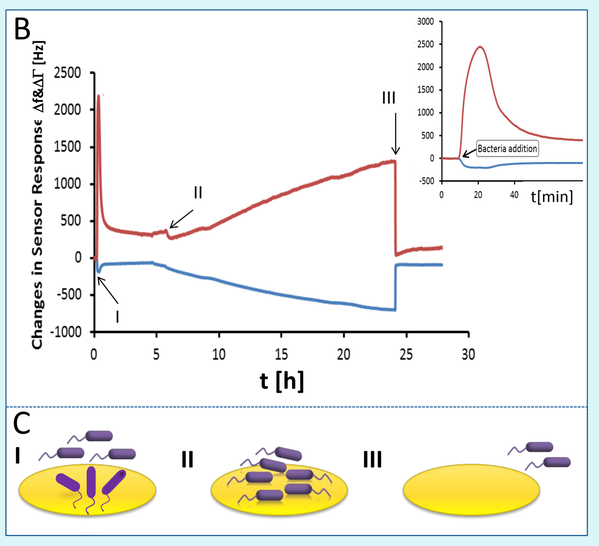


Fig. 5 Biofilm formation monitored with QCM-D. Electron microscopy image of *P. aeruginosa,* http://phil.cdc.gov/phil/details_linked.asp?pid=16876 (A). Adhesion, growth and removal of *P. aeruginosa* monitored by QCM-D-technology (B). Frequency (blue) und damping signal (red) progression. The Inset shows the process of adhesion after bacteria inlet (black arrow) during first 60 min. Arrows mark the addition of bacteria (I), growth medium (II) and detergent (SDS) (III). Model scheme of biofilm formation (C): I) Bacteria adhesion, II) growth of the bacterial biofilm and increase in the hydro-viscous state due to emergence of the extra polymeric substances; III) removal of bacterial film from the sensor.

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