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

Quartz crystal microbalance (QCM-D) technology is a surface-sensitive technique of (bio-)layers on a surface with a 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) Monitoring of polyelectrolyte multilayer build-up

2) Tissue engineering of bio-mimetic bone matrix construct

3) Formation and removal of bacterial biofilm layer

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1) Monitoring of polyelectrolyte multilayer build-up

- 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 phenomena or transformations in ‘soft’ cellular layers (3C).

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2) Bio-activation of PLC nanofibers

- Bioactive implants intended for repair 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) (6).

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3) Real time monitoring of biofilm development

Pseudomonas aeruginosa surface adhesion, biofilm formation and removal

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Fig. 1 3T QCM-D technology. 3T qCell T instrument with dual flow cell chamber (A). 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 (respective damping (Γ)). The inset depicts the unique 3T sensor chip.

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 circle), bacterial or immune cells (yellow oval). See text for further details.

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 black, PSS red, PAH blue). PSS/PAH and PGA/PAH film thickness on sensor surface as a function of PE addition (B).

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

Fig. 5 Biofilm formation monitored with QCM-D. Electron microscopy image of P. aeruginosa, http://path.ufl.edu/pa/ images/johnskij/pa2015/160612_06.jpg (A). Adhesion, growth and removal of P. aeruginosa monitored by QCM-D technology (B). Frequency (blue) and 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 (5), growth medium (6) and detergent (D) (6). Modal scheme of biofilm formation (1): (1) Bacteria adhesion, (2) growth of the bacterial biofilm and increase in the hydro-viscos state due to emergence of the extra polysacramic substances; (3) removal of bacterial film from the sensor.