APPLICATIONS OF QCM-D IN PHARMA

nanoScience Instruments

Quartz Crystal Microbalance with Dissipation (QCM-D) is a sensitive and versatile analytical technique used to study thin films, biomolecular interactions, and other surface-related processes. QCM-D can provide valuable insights into the adsorption, interaction, and stability of molecules on a solid surface.

QCM-D monitors the resonance frequency of a quartz sensor as a function of time. The resonance frequency of the sensor depends on its mass, so changes in frequency will reveal changes in the mass coupled to the sensor surface. Energy loss of the system, or dissipation, is also monitored by QCM-D. Changes in dissipation can be used to quantify the viscoelastic properties of soft layers attached to the sensor. Frequency and dissipation changes can be used to analyze molecular interactions with the sensor surface.

Biolin Scientific, a pioneer in QCM-D technology, has commercialized the QSense system and it is the leading QCM-D instrument in the market.

UNIQUE FEATURES OF QSENSE:

- High surface mass sensitivity i.e., <0.3 ng/cm²
- Small sample volume (50-200 µL)
- Wide temperature range (4-150 °C)
- Relatively quick analysis (A few minutes to a couple of hours)
- A variety of sensor coatings mimicking surfaces of production vessels, filtration membranes, container closure, and delivery equipment.

1 DRUG DEVELOPMENT:

The mass sensitivity at the sub-nanogram level offers a promising potential of this tool in drug discovery or drug development. Some of the research activities that have used Qsense for drug development include,

a. Interaction of small molecule drugs with proteins, cell membranes, and RNAs can be precisely monitored in vitro and in real-time under a variety of experimental conditions. [1]
b. Protein-protein interactions [2]
c. Structural changes in RNA upon interaction with small molecule [3]

2 DRUG DELIVERY:

QSense has also been proven to be a cost and time-effective technique for the characterization of Lipid Nanoparticles (LNP) and their drug delivery properties. Several research articles have reported the use of QSense in

a. Analyzing the binding affinities of serum proteins to lipid nanoparticles (LNP) [4]
b.Binding and release of biomolecules such as siRNA and mRNA from LNP [5]
c. Delivery of LNP to the desired organs. [6]
d. Screening of the binding affinity of serum proteins to LNPs in a cell-free environment [7]
e. Analyzing surface modification of LNPs [8]
f. Interaction of lipids with biologically active molecules including drugs, DNA, and siRNA [9]

APPLICATIONS OF QCM-D IN PHARMA

3 DRUG–SURFACE INTERACTIONS:

QSense is invaluable in the characterization of drug formulations – surface interactions during production, purification, storage, and delivery. Selected examples include,

a. Drug interactions with surfaces such as polymers, glass, metals and metal oxides, silicone oil, etc. [10], [11], [12], [13], [14], [15], [16]
b. Effect of excipients in mitigating drug-protein adsorption onto surfaces [17]
c. Effect of other formulation conditions; concentration, pH, temp, etc. [18]
d. Effect of interfaces and interfacial stresses in the development of biologics [19]

LIST OF QCM-D SENSORS FOR DRUG-SURFACE INTERACTION STUDIES		
Plastic Packaging	• Polypropylene (PP) • Polyvinyl chloride (PVC) • Polyethylene terephthalate (PET) • Polymethylmethacrylate (PMMA)	• Polyethylene (PE) • Low density PE (LDPE) • High density PE (HDPE) • Linear low density PE (LLDPE)
Glass Containers	• Borosilicate glass	• Soda-lime glass
Bags	• Cyclo olefin polymer (COP)	• Cyclo olefin co-polymer (COC)
Filter Materials	• Polyvinylidene fluoride (PVDF) • Polytetrafluoroethylene (PTFE) • Polycarbonate (PC)	• Polyethersulfone (PES) • Polyethylene terephthalate glycol-modified (PET-G)
Pre-Filled Syringes	• PDMS (Silicone oil)	
Other Relevant Materials	• Polystyrene • Cellulose • Stainless steel L605 • SS2343 (Similar to US standard 316) • Ethylene-vinyl Acetate (EVA)	• Nylon • Polyurethane • Cellulose Acetate • Polyacrylonitrile (PAN)
**Note: Custom sensor surfaces can be made upon request*		

4 BIOMATERIAL INTERACTION WITH HUMAN TISSUE:

Biocompatibility of implants and biomaterials in the human body is key to their successful performance. QSense provides in vitro analysis of implant surface or biomaterial interaction with human blood and tissues at the molecular level.

a. Interaction of various eye care formulations on mucin/cell membrane surface [20]

5 BIOSENSOR DEVELOPMENT:

QSense has also been reported to be used in the development of:

a. Protein biosensors [21], [22]
b. Point-of-care sensors [23]

REFERENCES:

[1] Small-molecule-mediated control of the anti-tumour activity and off-tumour toxicity of a supramolecular bispecific T cell engager

[2] Genentech - Viscoelastic characterization of high concentration antibody formulations using quartz crystal microbalance with dissipation monitoring

[3] Roche - Reconstitution and Functional Analysis of a Full-Length Hepatitis C Virus NS5B Polymerase on a Supported Lipid Bilayer

[4] A Fast and Reliable Method Based on QCM-D Instrumentation for the Screening of Nanoparticle/Blood Interactions

[5] A QCM-D and SAXS Study of the Interaction of Functionalised Lyotropic Liquid Crystalline Lipid Nanoparticles with siRNA

[6] Helper lipid structure influences protein adsorption and delivery of lipid nanoparticles to spleen and liver

[7] AstraZeneca - Screening of the binding affinity of serum proteins to lipid nanoparticles in a cell free environment

[8] Insights into the mechanisms of interaction between inhalable lipid-polymer hybrid nanoparticles and pulmonary surfactant

[9] On the interactions between RNA and titratable lipid layers: implications for RNA delivery with lipid nanoparticles

[10] Genentech - Adsorption and Aggregation of Monoclonal Antibodies at Silicone Oil–Water Interfaces

[11] Bristol-Myers Squibb - Mechanistic Understanding of Protein-Silicone Oil Interactions

[12] Bristol-Myers Squibb - Adsorption of polypropylene oxide-polyethylene oxide type surfactants at surfaces of pharmaceutical relevant materials: effect of surface energetics and surfactant structures

[13] Bristol-Myers Squibb - Particle Characterization for a Protein Drug Product Stored in Pre-Filled Syringes Using Micro-Flow Imaging, Archimedes, and Quartz Crystal Microbalance with Dissipation

[14] Pfizer - Engineering a ceramic piston pump to minimize particle formation for a therapeutic immunoglobulin: A combined factorial and modeling approach.

[15] Antibody adsorption and orientation on hydrophobic surfaces

[16] AstraZeneca - The Impact of the Metal Interface on the Stability and Quality of a Therapeutic Fusion Protein

[17] Janssen Pharmaceuticals (Johnson and Johnson) - Quartz Crystal Microbalance as a Predictive Tool for Drug-Material of Construction Interactions in Intravenous Protein Drug Administration

[18] Eli Lilly - Surface Interactions of Monoclonal Antibodies Characterized by Quartz Crystal Microbalance with Dissipation: Impact of Hydrophobicity and Protein Self-Interactions

[19] Bristol-Myers Squibb - Overview of the Impact of Protein Interfacial Instability on the Development of Biologic Products

[20] Novartis Pharma - Understanding the adsorption and potential tear film stability properties of recombinant human lubricin and bovine submaxillary mucins in an in vitro tear film model

[21] Dual-mode and Label-free Detection of Exosomes from Plasma Using an Electrochemical Quartz Crystal Microbalance with Dissipation Monitoring

[22] Amplified QCM-D biosensor for protein based on aptamer-functionalized gold nanoparticles

[23] Bioactivated PDMS microchannel evaluated as sensor for human CD4+ cells – The concept of a point-of-care method for HIV monitoring

ADDITIONAL MATERIALS:

WEBINARS:

- How excipients, surfaces, and formulation conditions affect therapeutic proteins
  (Dr. A. Jaiswal, Nanoscience Instruments)
- Assessing the inflammatory responses induced by biomaterials in contact with human blood using in vitro assays including QCM-D
  (Dr. K. Fromell, Uppsala University)
- Adsorption and aggregation of monoclonal antibodies studied by QCM-D
  (Dr. A. Kannan, Genentech)

WHITE PAPERS:

- Effect of Excipients, Storage, and Formulation Conditions on Therapeutic Protein Stability
- Surfactant/Surface Interactions
- Protein adsorption on glass and plastic surfaces
- QCM-D in drug formulation and storage
- Protein Fibrillation
- Viscosity analysis for microliter protein samples