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Probing the interactions of organic molecules, nanomaterials, and microbes with solid surfaces using quartz crystal microbalances: methodology, advantages, and limitations†

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Quartz crystal microbalances (QCMs) provide a new analytical opportunity and prospect to characterize many environmental processes at solid/liquid interfaces, thanks to their almost real-time measurement of physicochemical changes on their quartz sensor. This work reviews the applications of QCMs in probing the interactions of organic molecules, nanomaterials (NMs) and microbes with solid surfaces. These interfacial interactions are relevant to critical environmental processes such as biofilm formation, fate and transport of NMs, fouling in engineering systems and antifouling practices. The high sensitivity, real-time monitoring, and simultaneous frequency and dissipation measurements make QCM-D a unique technique that helps reveal the interaction mechanisms for the abovementioned processes (*e.g.*, driving forces, affinity, kinetics, and the interplay between surface chemistry and solution chemistry). On the other hand, QCM measurement is nonselective and spatially-dependent. Thus, caution should be taken during data analysis and interpretation, and it is necessary to cross-validate the results using complementary information from other techniques for more quantitative and accurate interpretation. This review summarizes the general methodologies for collecting and analyzing raw QCM data, as well as for evaluating the associated uncertainties. It serves to help researchers gain deeper insights into the fundamentals and applications of QCMs, and provides new perspectives on future research directions.

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Environmental impact

The interactions of organic molecules, nanomaterials, and microbes with solid surfaces are relevant to critical environmental processes such as organic–mineral interactions, biofilm formation, nanomaterial mobility, fouling in engineering systems and antifouling practices. Quartz crystal microbalances (QCMs) provide a new analytical opportunity and prospect for the characterization of these interactions and have found extensive applications in the past decade. Researchers in this field should have an adequate understanding of the fundamentals of QCMs, appropriate methodologies for specific interactions, and a clear awareness of the associated uncertainties, considering the great variety of interactions and conditions being investigated in environmental research. This review addresses these issues with representative findings from previous studies, provides guidance for the future use of this technique, and identifies future application directions.

1. Introduction

Interfacial processes that involve mass transport at solid/liquid interfaces are ubiquitous in the natural environment and engineered systems, such as sorption/desorption of natural organic matter and attachment/detachment of particulates (*e.g.*, nanoparticles and microorganisms) on mineral or man-made material surfaces. These interfacial processes are fundamental to critical environmental processes and engineering practices, such as the biogeochemical cycling of elements,[1] mobility of colloids and microbes,[2] biofilm formation,[3] and water treatment.[4] Traditional approaches for studying these interfacial processes rely primarily on batch sorption and transport experiments using saturated porous media. These traditional approaches can directly measure the change of adsorbate concentration in bulk solutions and derive the amount of adsorbates adsorbed on sorbents/collectors. However, these traditional approaches also have several disadvantages: (1) they involve tedious preparation and *ex situ* analysis steps (*e.g.*, mixing and separation of the sorbent and sorbate, column

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preparation, and instrumental analysis of the adsorbates), (2) they cannot trace the underlying interactions at a fast rate (s^{-1} to min^{-1}), due to their intrinsic *ex situ* nature, (3) understanding the physicochemical properties of the sorbate at the interface requires coupling with other techniques, such as microscopy and/or spectroscopy.

The development of quartz crystal microbalances (QCMs), especially QCMs with simultaneous energy dissipation monitoring (QCM-Ds), provides a new analytical prospect and an opportunity to study these interfacial processes, thanks to their high sensitivity, *in situ* and almost real-time nature, and simultaneous mass and viscoelastic property measurement. These features can overcome the disadvantages of conventional techniques, thus making this technique an excellent supplement to other tools for studying interfacial processes. The term "QCM" used here includes both QCMs and QCM-Ds. QCMs were initially used in materials and life science, and have been expanded to many other fields, including environmental science.[5–9] The past decade has witnessed their widespread applications, results from which have significantly improved our understanding of the abovementioned environmental processes and engineering practices.

Briefly, the QCM technique is an acoustic sensing technique, and its measurement of mass changes on its sensor surface is non-selective (the contribution of the sorbate and hydrodynamically coupled solvent cannot be deconvoluted) and indirect (QCM-measured physical quantities need to be model-fitted to derive interaction-relevant information such as adsorption mass). In addition, applications of QCMs in environmental research encounter sorbates with a broad spectrum of sizes and properties (forming diverse adlayers on QCM sensor surfaces), which produce complex QCM responses. These two factors determine that data analysis and interpretation need to be conducted appropriately.

The objective of this review is to acquaint researchers in the field of environmental science and engineering with the working principle of QCM techniques and the methodologies for data collection, analysis, and interpretation for different types of interfacial interactions, as well as a clear awareness of the associated uncertainties and limitations, based on findings from representative studies.

2. Theory and methodology

2.1 Fundamentals of the operation of QCMs

The operation of QCMs utilizes the piezoelectric properties of quartz. Briefly, a quartz plate is mounted between two metal electrodes, through which an alternating current (AC) is applied. Resonance is excited when the AC frequency is close to the fundamental frequency (f_1) of the quartz sensor. Interfacial interactions can introduce mass loading on the sensor surface, which will change the fundamental and harmonic frequencies of the sensor and the resonant frequencies are continuously monitored (Fig. 1).

Energy dissipation (D) is addressed by monitoring the decay of the oscillating quartz sensor after the driving current is switched off (Fig. 1). The amplitude of the voltage of the oscillating sensor decays as an exponentially damped sinusoid:[10,11]

$$V(t) = V_0\,\mathrm{e}^{t/\tau}\sin(2\pi f t + \phi) \tag{1}$$

where f is the difference between the resonant frequency of the quartz crystal (f_1) and a reference frequency (f_R), V_0 is the amplitude at $t = 0$, τ is the decay time constant, and ϕ is the phase. The dissipation factor (D)[12] is related to the decay time constant as

$$D = \frac{1}{\pi f \tau} = \frac{E_\mathrm{dissp}}{2\pi E_\mathrm{stored}} \tag{2}$$

The specific-cut quartz sensor allows the probing of f_n and D_n at multiple harmonics in addition to the fundamental frequency, where n is the odd harmonic number. The harmonics are monitored in succession and multiple harmonic data are collected simultaneously. A cycle of resonance excitation and decay monitoring is generally completed at the scale of milliseconds; thus monitoring a sequence of harmonics is very fast and interfacial phenomena can be tracked almost in real time (Fig. 1).

Oscillation of QCM sensors generates a lateral shear wave (which propagates in a direction perpendicular to the sensor surface into the liquid phase), whose amplitude decays exponentially:[13]

$$A(z) = A_0\exp(-z/\delta) \tag{3}$$

$$\delta = (\eta_1/\pi f_n \rho_1)^{1/2} \tag{4}$$

here η_l and ρ_l are the liquid viscosity and density respectively, and f_n is the quartz resonator frequency. A_0 is the maximum vibration amplitude at the center of the crystal resonator. δ is the penetration depth, defined as the distance from the sensor surface into the liquid phase where the vibration amplitude has diminished by $1/e$, and z is the distance from the sensor surface. The penetration depth depends on the resonant frequency (thus differs between harmonics), and is affected by adsorbed materials and liquid properties. The penetration depth is ~250 nm in water for the fundamental frequency (5 MHz), according to eqn (4).[14,15]

The historical development of QCMs and fundamentals of their instrumentation and measurement have already been comprehensively documented; the readers are suggested to refer to these publications for more details.[6,10,13,16–18]

2.2 Analysis and interpretation of QCM measured quantities

As described above, quantities directly generated by QCMs are harmonic frequency and energy dissipation that characterize the oscillation behavior of QCM sensors (Fig. 1). Establishing a quantitative relation between QCM response and interfacial reaction changes is complex, which requires an adequate understanding of the mechanical and hydrodynamic processes at play, as well as complementary information provided by other techniques.[17,19]

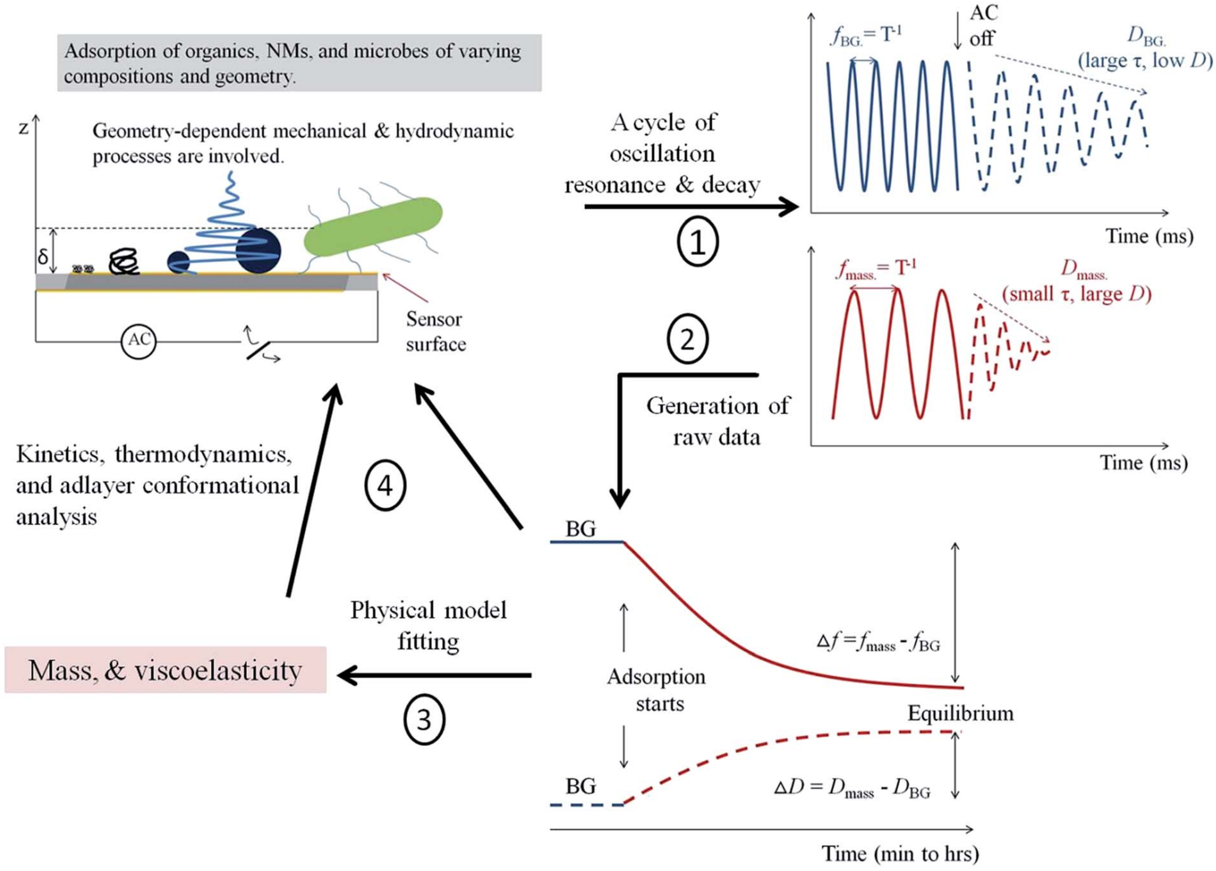

Fig. 1 Illustration of the acoustic sensing of interfacial interactions occurring at the sensor–liquid interface by the QCM-D technique. Both the geometry of the sorbates and their collective presence on the surface affect the mechanical and hydrodynamic processes involved in the acoustic sensing, which has a finite penetration depth. The acoustic sensing is nonselective and the Δf and ΔD collected require appropriate conceptual and physical models to extract meaningful information related to reactions at the interface. T – period of the resonant oscillation; f_{BG} and D_{BG} are background signals prior to interactions; f_{mass} and D_{mass} are signals following interactions with mass change.

The response mechanism of QCMs and methodology used for data analysis depend on a wide range of factors, including the adlayer's geometry (lateral and vertical), adlayer's internal structure, hydrodynamic coupling of the solvent, and contact mechanics between the sorbate and sensor surface.[13,17,20] The importance of the adlayer's thickness lies in the fact that the shear acoustic wave decays at a short distance from the sensor surface (eqn (3) & (4)). This affects how the adlayer is sensed by the QCM, and thickness-dependent QCM response has been extensively demonstrated in the literature.[11,12] For example, as the thickness of the adlayer approaches or exceeds the penetration depth, more significant dispersion of harmonic signals (the difference between $\Delta f_n/n$ and $\Delta D_n/n$) is observed.[21–23] Lateral distribution of the sorbate on the sensor surface affects the coupling of the solvent, mobility of the sorbate, and accuracy of model fitting.[22,24–26] For example, coverage dependent coupling of the solvent was commonly observed for the deposition of particulate sorbates (which affects the contribution of the solvent to Δf or the derived mass).[24,27,28] Slipping of the adlayer or surface-attached particle also contributes to ΔD, which affects its analysis and interpretation.[13,29]

Among all scenarios, the simplest case for data analysis with relatively high confidence is interfacial interactions forming a relatively thin (within the penetration depth) and laterally homogeneous adlayer, which can be modeled with the Sauerbrey equation or viscoelastic models, depending on the dissipation magnitude.[29,30] The Sauerbrey equation is a linear relationship between Δf_n and mass change on the resonator:[31]

$$\frac{\Delta f_n}{n} = -\frac{m_f}{C} = -\frac{\rho_f h_f}{C} \tag{5}$$

where m_f is the areal mass density of the adlayer (which is not necessarily equivalent to the dry mass of the adsorbed sorbate) and ρ_f and h_f are the wet density and thickness of the adlayer, respectively. C is the mass sensitivity constant, which depends solely on the fundamental resonance frequency and properties of the quartz crystal (~17.7 ng cm^{-2} Hz^{-1} for a 5 MHz resonator).[10] The Sauerbrey equation is valid when the deposited mass is rigid and evenly distributed on the surface of the quartz sensor.[31]

In the case of adsorptions with significant dissipation change (*e.g.*, $\Delta D_n/\Delta f_n > 10^{-7}$/Hz), the Sauerbrey equation was found to underestimate the mass change.[29,30] Instead, the viscoelastic models (*i.e.*, the Voigt model or Maxwell model) are applied to derive the adsorption mass, thickness, shear modulus, and viscosity of the adlayer, involving several independent fitting parameters including adlayer density, solvent density and viscosity.[21,32] A detailed description of these viscoelastic models can be found in previous publications.[30,33]

The adsorption of nanosized objects (*e.g.*, NMs, proteins, and virus) generally forms laterally heterogeneous adlayers, which may either cause small ($\Delta D_n/\Delta f_n < 10^{-7}$/Hz) or large dissipation change ($\Delta D_n/\Delta f_n > 10^{-7}$/Hz). In cases of small dissipation, the Sauerbrey equation is applicable for adsorption mass calculation. In cases of large dissipation, although the viscoelastic models were commonly used in these cases, the accuracy of results derived from modeling should be scrutinized before reporting because (1) the viscoelastic models are continuum models that assume a uniform adlayer,[17] and (2) multiple dissipation mechanisms may occur, depending on the material properties and geometry of the sorbate, and its contact with the substrate (*e.g.*, rigidness of the sorbate, slipping of the adsorbed objects, or solvent coupling within the adlayer).[13,16]

For adsorption forming thick adlayers or for attachment of large particles (hundreds of nm to microns, such as microbes and cells), the adlayer may not be thoroughly and homogeneously sensed due to the limited range of the acoustic wave. In addition, QCM response is also strongly affected by the contact between the substrate and the sorbate, which varies greatly between rigid and soft particles, and types of microbes (see Section 3.4.2).[20,34,35] Therefore, there are no explicit models to quantitatively analyze Δf_n and ΔD_n for chemically relevant parameters, such as mass and particle numbers, solvent content, and adlayer morphology.

3. Applications in environmental research

3.1 Overview

A wide range of objects have been tested using QCMs, including organic molecules (small and macromolecules), NMs, cells and microbes, and each of these categories represents an independent research field. These objects differ widely in terms of size, shape, and composition, resulting in a broad spectrum of interfacial interaction behaviors and adlayer characteristics. Accordingly, QCM's response to these interactions is different. The information of interest and the methodology used to collect and analyze QCM data are thus dependent on the categories of the sorbate (Table 1). Therefore, we classified the analysis and discussion into organic molecules, NMs, and microbes.

Generally, the real-time monitoring capability of QCMs allows the study of interaction kinetics and thermodynamics by varying reaction conditions, mainly surface and solution chemistry. Coupled dissipation monitoring enables the tracking and exploring of adlayer dynamics and characteristics. With appropriate data analysis and evaluation of the associated uncertainties, in combination with complementary information from other techniques, QCMs can help approach the interaction mechanism.

3.2 Macromolecule–surface interaction

Many environmental processes involve organic molecule–surface interactions, such as organic–mineral interaction,[36] fouling/antifouling in man-made infrastructures,[37,38] and biofilm formation (surface conditioning before microbial cell attachment).[39] The kinetics and thermodynamics of these interactions and the adlayer properties are of fundamental importance to understand many biogeochemical processes and have important implications for many environmental engineering practices. QCMs serve as a convenient tool to comparatively analyze the effects of solution chemistry (*e.g.*, pH, ionic strength, and temperature) and surface properties (*e.g.*, surface charge, polarity, and heterogeneity) on the kinetics, thermodynamics, and adlayer characteristics of macromolecule adsorption, including polysaccharides, proteins, nucleic acids, extracellular polymeric substances (EPS), and natural organic matter (NOM) (as shown in this section). In combination with complementary information from other techniques, their applications have greatly advanced the understanding of organic–surface interaction and improved engineering practices involving organic–surface interactions.

3.2.1 Characteristics of QCM response to macromolecule adsorption.

The studied macromolecules generally attach firmly to the sensor surface and form adlayers with a thickness much smaller than the penetration depth of QCM's acoustic wave; thus they are thoroughly sensed by QCMs. Hydration within or between the macromolecules commonly occurs.[40–42] In the non-selective QCM sensing, the entrapped water is sensed along with the organic molecules, contributing to the Δf_n. ΔD_n which is related to the viscoelastic properties of the organic adlayer. Generally, the adsorption of molecules such as humic substances (MW ranges from sub kD to 10 kD)[43–47] and relatively small and rigid proteins (MW < 100 kD)[48–51] were found to cause no or little dissipation change; thus the Sauerbrey equation is applicable for Δf_n-to-mass conversion. The adsorption of relatively large and soft molecules such as polysaccharides,[50,52–54] nucleic acids,[55–59] EPS,[60–62] and large proteins[63] generally forms adlayers that cause significant ΔD_n. In these cases, the viscoelastic models were commonly used to derive the adsorbed mass.

Since the adsorbed amount of organic molecules is the basis of thermodynamic analysis and comparative analysis between adsorption conditions or different molecules, it is critical to evaluate the reliability of QCM measurement for adsorption quantification and the analysis methods. Studies that directly used Δf_{eq} (frequency change at equilibrium) for adsorbed amount comparison between different adsorption scenarios are based on the presumption that Δf_{eq} has the same linear relationship with adsorbed mass under the studied conditions. Studies that derived adsorption mass using either the Sauerbrey relationship or viscoelastic modeling rely on the assumption that the modeled mass approaches the real organic mass. However, these presumptions are not always valid, considering (1) the intrinsic non-selective nature of QCM measurement indicates that Δf is contributed by both the sorbate and hydrodynamically coupled solvent, and (2) Δf-to-mass conversion relied on model fitting with assumptions and uncertainties (Section 2.2).

Firstly, the derivation of "wet" mass from Δf_n relies mainly on the Sauerbrey equation or the viscoelastic models

Table 1 A summary of the methodologies used in QCM data analysis and the associated uncertainties

Sorbate types	QCM response	Analysis approach	Output (uncertainty in parentheses)	Complementary techniques	Reference
Macromolecules	Negative Δf_n	$\frac{\Delta f_n/t}{(\Delta f_n/t)_{\text{fav}}}$	Attachment efficiency for kinetic analysis	OWLS, ellipsometry, and optical surface plasmon resonance	55 and 56
	$\Delta D_n/\Delta f_n < 10^{-7}/\text{Hz}$	Sauerbrey equation	Areal mass density (variable solvent contributions)		49, 65 and 66
	$\Delta D_n/\Delta f_n > 10^{-7}/\text{Hz}$	Viscoelastic model	Areal mass density (variable solvent contribution), viscoelastic properties (estimation of layer density)		55 and 56
Nanoparticles	Negative Δf_n	$\frac{\Delta f_n/t}{(\Delta f_n/t)_{\text{fav}}}$	Attachment efficiency for kinetic analysis	AFM and SEM	81, 83 and 86
	$\Delta D_n/\Delta f_n < 10^{-7}/\text{Hz}$	Sauerbrey equation	Areal mass density (coverage-dependent solvent contribution)		97
	$\Delta D_n/\Delta f_n > 10^{-7}/\text{Hz}$		Direct comparison of Δf_n (Δf_n and mass correlation inconsistent), comparison of $\Delta D_n/\Delta f_n$ for adlayer properties (multiple contributors to ΔD_n)		25, 87 and 88
Microbes	Negative Δf_n		Qualitative comparison of $\Delta f_n/t$ (inconsistent correlation between cell numbers and Δf_n)	Microscopy	105 and 111
	Positive Δf_n	Coupled resonance model	Descriptive explanation of contact mechanics		23, 34, 35 and 106–108
	Any	$\Delta D_n/\Delta f_n$ dynamics	Monitoring and comparison of $\Delta D_n/\Delta f_n$ for the adhesion mechanism (lack validation)		54, 110, 111 and 114

(depending on the ΔD_n value), which are based on specific assumptions (*e.g.*, adlayer uniformity and level of viscoelasticity). In practice, whether these conditions are fulfilled or not was not strictly tested, which may introduce errors during Δf_n-to-mass conversion.

Secondly, the contribution of solvent to Δf or model-derived mass varies between the types of organic molecules and the formed adlayer. This has been substantiated by studies combining QCM and optical techniques such as ellipsometry and optical waveguide lightmode spectroscopy (OWLS).[64] Sander *et al.* quantified the adsorbed dried humic substances and proteins using ellipsometry[47] and OWLS[48,49,65,66] respectively, which were correlated with the QCM-derived thickness and mass (Fig. 2A and B). All these organic molecules were found to have small energy dissipation and the QCM-derived mass was calculated with the classical Sauerbrey equation. Correlation between the wet thickness and dried thickness for humics is linear with a slope of 0.6. In contrast to the relatively linear correlation for humic substances, correlation between "dried mass" and "wet mass" for protein adsorption (at varying pH and IS, and to different solid surfaces) was not linear (a slope of <0.35 if fitted linearly, Fig. 2B). These results suggested that (1) NOM forms adlayers with comparable water contents, regardless of the NOM type, (2) the protein adlayer may have a higher water content than the NOM adlayer, according to the slope value, and (3) the protein adlayers have significantly different water contents, even for the same protein adsorbed under different conditions (Fig. 2B).

The facts that adsorption mass is indirectly measured and has a varying water content significantly affect how QCM data should be analyzed and interpreted: (1) it is evident that when the adsorptions being compared differ significantly in $\Delta D_n/\Delta f_n$, Δf_{eq} should not be directly compared (since Δf is disproportionally correlated to the real adsorbed mass in this case),[21,29] and (2) even for adsorptions with small ΔD_n or with similar $\Delta D_n/\Delta f_n$ ratios, direct comparison of the Δf_{eq} or the derived "wet" mass should still be made with caution (Fig. 2B). Adequate justification for consistent solvent contributions (even for the same sorbate under different conditions) should be provided. Since Δf_{eq} or the derived mass is a "wet" quantity that varies in solvent contribution, the direct use of QCM-derived mass can cause error when the analysis of adsorbed dry mass (*e.g.*, adsorption isotherm analysis) is needed. Even for comparative analysis, researchers need to be careful that possible difference in solvent contribution may cause error in the comparison.

3.2.2 Applications to kinetic and thermodynamic analysis and adlayer characterization. Since the adsorption of organic molecules (relatively small ones) is fast and difference in the adsorption rate is hardly distinguishable by the QCM technique, quantitative kinetic analysis was only achievable for relatively large molecules such as proteins,[48,49] nucleic acids,[55–57,59,67] and EPS.[68] The effects of solution pH, IS, and surface chemistry on adsorption kinetics were quantified and analyzed to explore the interfacial forces governing the adsorption (sometimes in the context of the DLVO theory). Since the methodology is similar to that for NM deposition, we save this subject until the discussion of NMs (Section 3.3.2).

QCMs are primarily used to quantify the adsorption amount of various organic molecules at equilibrium. In practice, direct comparison of the Δf_n at equilibrium or the derived "wet" mass was made between different adsorption conditions (*e.g.*, pH, IS, cation types, temperature, solute concentrations, and types of

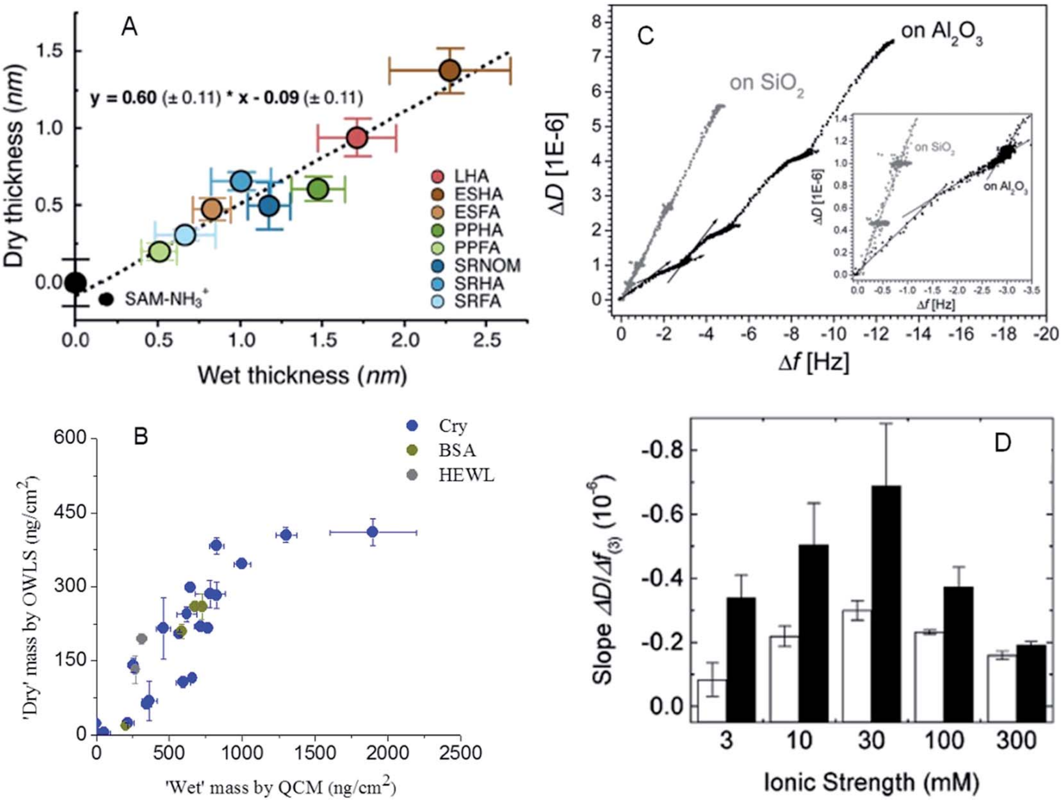

Fig. 2 Cross-validation between the "wet" quantity derived from the QCM technique and "dried" quantity derived from other techniques for humic substances (A) and proteins (B). Data in (B) were compiled from Sander *et al.*,[48,49,65,66] where the proteins were adsorbed to SiO$_2$, and humic or polyelectrolyte coated surfaces at pH from 5 to 8 and monovalent electrolyte concentrations of 10 mM and 50 mM. The $\Delta D_n/\Delta f_n$ ratios for the adsorption of dextran on silica and alumina surfaces (C) and for the adsorption of alginate on silica in the absence (open) and presence of 1 mM Ca (solid) under a wide range of ionic strength (IS) conditions (D). (A) was adapted from Armanious *et al.*,[47] copyright 2014 American Chemical Society. (C) and (D) were adapted from Kwon *et al.*[53] and de Kerchove *et al.*,[52] respectively, copyright 2006 American Chemical Society.

surface) or different sorbates, in order to explore the interaction mechanism and evaluate the affinity of different organic molecules for attachment to solid surfaces.[50,52,53,69] A few studies conducted adsorption experiments at variable adsorbate concentrations to generate adsorption isotherms and calculate quantitative thermodynamic parameters based on the adsorbed mass derived from Δf_n.[70,71] As shown in Section 3.2.1, the use of QCM-derived "wet" mass for absolute analysis may overestimate the adsorption amount, unless the "wet" mass has been corrected for solvent content to give the real sorbate mass. Regarding comparative analysis using either Δf_n or its derived "wet" mass, it is better to estimate the solvent content and evaluate its impact on comparison (*e.g.*, difference in the solvent content between the compared conditions relative to the adsorption difference), by combining optical techniques that measure dry mass (for the reasons presented in Section 3.2.1).[47,65,66,69]

The characteristics of the adlayer formed on sensor surfaces were frequently explored with the help of dissipation monitoring. Two types of studies were frequently performed: (1) comparison of adsorptions of the same organic molecules under different solution conditions or on different surfaces, and (2) comparisons of the adlayers formed by different organic molecules under the same conditions. The research objectives are usually on the influence of solution chemistry and surface chemistry on the molecular conformation, adlayer configuration, and viscoelastic properties of adsorbed organic molecules.

The most common parameter used for this purpose is the $\Delta D_n/\Delta f_n$ ratio (or the $\Delta D_n/\Delta f_n$ plot), and the physical meaning of this parameter is straightforward – dissipation density (dissipation of unit adsorbed mass) of the sorbate under specific conditions, since Δf_n is related to adsorption mass. For organic molecules, two main contributors to ΔD_n are the molecular conformation and hydrodynamic coupling of solvent in the adlayer. Therefore, a larger ratio is considered to be resulted from a "softer" adlayer – molecules are more extended or elastic, or a more "fluidic" adlayer – a higher solvent content (these two factors may be equivalent since a more extended conformation may result in more solvent coupling). This methodology has been used to compare the adsorption of fatty acids,[72] dissolved organic matter (DOM),[45] polysaccharides,[52–54] proteins[50,71] and nucleic acids[57] on different surfaces under different solution conditions (mainly pH, IS, and ion types), to explore the effects of these factors on the molecule conformation at the interfaces (Fig. 2C and D). For example, a larger $\Delta D_n/\Delta f_n$ ratio was observed for dextran adsorbed on silica than that on alumina, and was considered due to a loosely bound conformation and more water entrapment within the adlayer (Fig. 2C).[53]

Since $D_n/\Delta f_n$ does not quantitatively correlate to the water content, molecular conformation and organization at the interface, it mainly serves as a parameter for qualitative comparison between adsorption scenarios. More explicit analysis of the ΔD_n data is primarily through the viscoelastic models, where the Δf_n and ΔD_n data are integrated to derive quantitative parameters such as the thickness, shear modulus, and shear viscosity of the adlayer. This methodology was applied to characterize the adsorption of organics such as DNA[55–58] and EPS[54,60,61,73] on environmentally relevant surfaces.

Dissipation analysis not only helps explore the conformation of organic molecules and the coupling of solvent within the adlayer, but can also provide insights for engineering practices such as membrane fouling and antifouling. For example, the effects of operational conditions (*e.g.*, solution chemistry fluctuations) on the hydration and swelling of foulants and/or membrane polymers were tested, and the results were shown to relate to the performance of the membranes.[61,62,74–76]

3.3 Nanomaterials (NMs)

QCMs have been extensively used to study the deposition and remobilization of a wide range of NMs, such as carbonaceous NMs, metal and metal oxide NPs. The primary application of QCMs is the quantification of the deposition kinetics of NMs and the remobilization of surface-attached NMs under varying solution conditions, in order to explore the interfacial forces involved. QCMs are also used to quantify the adsorption amount at equilibrium and monitor the dynamic changes during NM adlayer formation. These applications greatly improve our understanding of the mechanisms behind NM–surface interaction and help evaluate the mobility of various NMs.

Since the fundamental mechanisms behind the interfacial interactions (*e.g.*, organic adsorption, aggregation and deposition) governing the mobility and fate of NMs have been extensively studied and reviewed (studies involving QCMs also included),[77–79] we focus on reviewing the methodologies used to analyze and interpret QCM results from representative studies and evaluate their validity and effectiveness.

3.3.1 Characteristics of QCM response to NP deposition. Understanding the mechanism of QCM response to NM deposition and the key factors involved (*e.g.*, mechanical and hydrodynamic processes) is a prerequisite for adequate analysis and interpretation of QCM data. Compared to organic molecules, NMs form more heterogeneous adlayers and more confounding factors are involved, rendering the analysis and interpretation of the Δf_n and ΔD_n data challenging. It has been shown that the response mechanism greatly depends on NMs' characteristics (*e.g.*, geometry, rigidity, and surface chemistry), their contact with solid surfaces, and the adlayer characteristics (*e.g.*, coverage, discrete or clustering, and monolayer or multilayer).[13,24,35] We summarize some response mechanisms based on representative results from model systems and evaluate their implications for the analysis of more complex systems.

The simplest case is spherical nanoparticles (NPs) forming a monolayer of discrete NPs on sensor surfaces, in which the NP size and surface coverage were shown to greatly affect QCM response. As the size of NPs increases, significant dispersion of harmonic signals was observed (Fig. 3B).[22] We speculate that the dispersion of overtone signals is likely a consequence of the frequency-dependent response of surface-attached NPs to the QCM's resonant oscillation and the frequency-dependent penetration depth of the acoustic sensing. Since NPs attach to the surface *via* point connection, their loading is not always inertial (they may not rigidly couple to the sensor during oscillation) and their motion relative to the sensor is frequency-dependent. In addition, as the NPs' size approaches or exceeds the penetration depth (harmonic-dependent), what is being detected by the QCM may differ between different harmonics. Further studies are needed to gain a more in-depth understanding of this harmonic dispersion phenomenon. Dissipation in NM deposition was shown to relate to the viscoelastic properties of the NM adlayer, specifically, the rocking and sliding of the adsorbed NMs and the corresponding movement of solvent molecules.[13] Since the contact mechanics is affected by the geometry and surface chemistry of the NMs, and the motion of attached NMs affected by neighboring NMs, these factors have been shown to affect ΔD_n. Deposition of larger NMs of the same material generally produces a larger $\Delta D_n/\Delta f_n$ ratio, most likely due to the NMs' larger momentum and the higher frictional flow of solvent compared to that of smaller NPs (Fig. 3A).[22] Since the motion of adsorbed NMs and amount of hydrodynamically coupled solvent are affected by the neighboring NMs, the dissipation was also showed to be coverage-dependent (Fig. 3C and D, where ΔD_n deviated from the straight line and $\Delta D_n/\Delta f_n$ decreased as NM surface coverage increased).[22,25]

As these results suggested, contributors to QCM signals need to be identified, in order to extract information to understand the NP–surface interaction mechanism. Since the hydrodynamically coupling solvent (including solvent surrounding the NPs and solvent trapped between attached NPs at high coverage) and attached NM mass contribute to Δf_n (the measurement is affected by NP–surface contact mechanics and aggregate structures), the direct use of Δf_n for quantifying the mass of deposited NMs needs to be conducted with caution. At low coverage of NPs that have firm contact with sensor surfaces, Δf_n is proportional to the surface mass density of deposited NPs (with similar water contents, Fig. 3C) and can be used to quantify the mass of deposited NPs, as long as the proportionality constant is known. The proportionality constant is dependent on the types of NPs, aggregation state of NPs, and fractal structure of NP aggregates if formed. At high coverage of NPs which have firm contact with sensor surfaces, the crowded NPs may interfere with each other and affect the solvent coupled to the NPs, resulting in coverage-dependent solvent contribution. The linear correlation between Δf_n and attached NP number (or mass) should be carefully examined using a complementary technique (*e.g.*, SEM) before using Δf_n to quantify the mass of NPs. If one wants to use viscoelastic modeling to derive the mass of NPs, it is critical to examine the proportional relationship between the modeled mass and the actual mass. In the case that NPs have weak contact with QCM sensor surfaces, it is highly doubtable that one can use Δf_n or

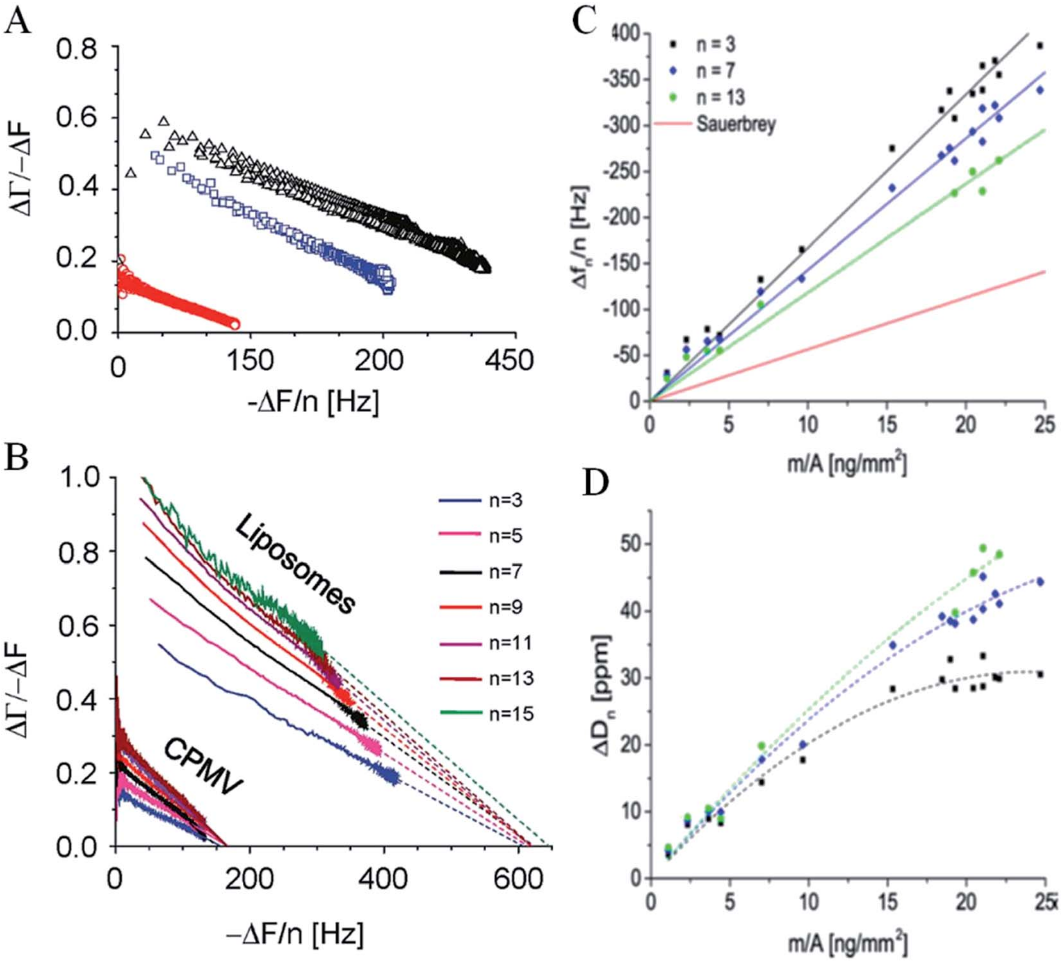

Fig. 3 (A) & (B) The plot of the $\Delta\Gamma/-\Delta F$ ratio *vs.* the frequency shift for liposomes and NPs, (A) showed the 3rd harmonic signal for liposomes (114 nm – black, 86 nm – blue) and virus NPs (28 nm – red), (B) showed the 3rd to 15th harmonic signals for the 114 nm liposome and the virus NPs. Bandwidth (an equivalent measure of dissipation) is related to dissipation by $\Gamma = 0.5fD$.[22] Plot of the normalized Δf_n (C) and ΔD_n (D) as a function of the NP mass density as determined from the SEM images for functionalized silica NPs with a diameter of 137 ± 4 nm. Three harmonic signals are shown and the red line in (C) was the expected Δf_n according to the Sauerbrey equation. (A) & (B) were adapted from Tellechea *et al.*,[22] copyright 2009 American Chemical Society. (C) & (D) were adapted from Grunewald *et al.*,[25] copyright 2015 American Chemical Society.

viscoelastic modeling to quantify the mass of deposited NPs regardless of coverage, because the NP loading is not inertial and different physical models are needed to describe the QCM response.[13,24,34]

A few models have been developed to correlate Δf_n and ΔD_n with NMs' mass and surface coverage, and explain the dissipation behavior. However, these models are phenomenological and only valid in specific cases, since they were based on relatively ideal systems.[17,22,24,27,28,80] As the geometry of NMs and the adlayer becomes increasingly complex, physical description of the adlayer configuration and hydrodynamic coupling of solvent and the dissipation mechanism will be very difficult, if not impossible. For example, carbon-based NMs can exist as spherical fullerenes,[81,82] elongated carbon nanotubes (CNTs),[83–86] and plated graphene oxides (GOs),[87,88] and they could adopt different configurations and form clusters or multilayers on sensor surfaces, depending on surface and solution chemistry.

3.3.2 Applications to kinetic analysis and adlayer characterization.

Early and primary applications of QCMs in environmental NM research were in deposition kinetic analysis. The NM deposition rate is quantified by calculating the slope of the initial frequency shift ($\Delta f_t/t$) or the derived "wet" mass change (ng cm^{-2} t) where the rate change is within the linear range. The rate of frequency shift ($\Delta f_t/t$) was shown to be proportional to the deposition rate of NMs even if when the surface coverage was low and $\Delta D/\Delta f$ was as high as 0.61.[83] Although the deposition rate was frequently used for comparing deposition kinetics under different scenarios,[89–94] it should be noted that the deposition rate is dependent not only on the propensity of NMs to deposit on surfaces but also on the diffusion coefficient of the NMs (which is influenced by the size, shape, and aggregation state of the NMs). Thus, attachment efficiency is more commonly used, instead of the deposition rate. Deposition attachment efficiency is obtained by normalizing the deposition rate under the solution chemistry of interest by the favorable deposition rate under the same solution chemistry conditions.[81,83] Favorable deposition conditions are achieved by using a surface with a charge opposite to that of the deposited NPs, so that the energy barrier between the particles and the surface is absent and the deposition processes is diffusion-limited.[81] Therefore, deposition attachment efficiency excludes the effect of varying diffusion coefficients and allows for direct comparison of the deposition probability of the same sorbate under different conditions or between different sorbates regardless of their size, shape, or aggregation state.

The general methodology used in most studies is to measure the attachment efficiency of NMs on a surface (or different surfaces) under varying solution chemistry conditions (*e.g.*, pH, cation type, and ionic strength) to explore the interfacial forces at play (*e.g.*, electrostatic, hydrophobic, and hydration forces).[82] For example, the attachment efficiency of NMs at increasing ionic strength (IS) was measured to obtain the critical deposition concentrations (CDCs), which, in combination with the surface chemistry of the NMs and solid surfaces, were evaluated in the framework of the Derjaguin–Landau–Verwey–Overbeek (DLVO) theory. This approach has been used to quantify the CDCs of various NMs in different electrolytes and on various solid surfaces, such as fullerenes,[95] CNTs,[83–85] GO,[88] and metal oxides.[96] This approach has greatly improved our understanding of the mechanism governing NM–surface interaction and helps predict their environmental mobility.

Dissipation was frequently used to monitor NM deposition dynamics and explore the characteristics of NM adlayers formed under different conditions and by different materials, and the $\Delta D_n/\Delta f_n$ ratio is the primary parameter used. For example, increasing the $\Delta D_n/\Delta f_n$ ratio during the deposition of silver NPs indicated the formation of NP multilayers or NP clusters at the later stage of deposition.[93] The use of the $\Delta D_n/\Delta f_n$ ratio for comparison between deposition conditions also helped reveal the effects of surface chemistry and solution chemistry on the configuration and contact mechanics of NMs such as GO,[87] metal oxides,[96] and CNTs.[84] As discussed in the above section, the dissipation is related to the viscoelastic properties of the NM–surface interface and those of the NM adlayer if a multilayer was formed. However, a quantitative description of this relationship is missing. Therefore, interpretation of the dissipation data in previous studies was mostly qualitative and inconclusive.

The deposition amount of NMs at equilibrium is also valuable and was quantified by QCMs in many studies. The Δf_{eq} or the derived mass (from the Sauerbrey equation or viscoelastic models using both Δf_n and ΔD_n) was used for comparison between different deposition scenarios to explore the effects of surface and solution chemistry.[92,93,97] As discussed in the above section, either Δf_{eq} or the viscoelastic model-derived mass does not always correlate linearly with the real NM mass, depending on the surface coverage, aggregate characteristics, and adhesion strength of the NMs.[13,24,34] In addition, the model-derived mass is a "wet" quantity with varying solvent contributions. Therefore, there are potential uncertainties associated with such calculation and comparison of model-derived mass.

3.4 Microbes

Biofilm formation is ubiquitous in the environment and has great environmental, public health and socio-economic impacts.[98] Biofilm formation is a dynamic process that starts with the adhesion of individual microbial cells to solid surfaces, followed by the growth and maturation of the biofilm, and then the detachment of cells at a late stage.[99] The adhesion process, which determines whether a bacterial cell can successfully immobilize on a solid surface or not, is a complex and delicate process. During this adhesion process, the microbe–substratum interface experiences dynamic physical and chemical changes[100] and is influenced by the physicochemical properties of the bacteria and the substrate surfaces[101,102] and solution chemistry.[103] Following initial adhesion, the microbes start to produce EPS and grow to form a biofilm, accompanied with mass and structural changes at the interface. The capabilities of QCMs as described in Section 2 make them a suitable tool to characterize microbial adhesion and biofilm growth, although well defined conceptual models and complementary information from other techniques are needed for the analysis and interpretation.

3.4.1 Characteristics of QCM response to microbial adhesion. Similar to that of organic molecule adsorption and NM deposition, the mechanism of QCM response to microbial attachment determines what information can be acquired and the methodology to be used. Due to the difference in geometry, surface and bulk properties, and adlayer organization, the surface attachment of microbes differs significantly from that of organic molecules and NMs. First of all, the size of microbial cells ranges from hundreds of nanometers to several microns (much larger than the penetration depth of QCM's acoustic sensing), and they generally attach to solid surfaces *via* a point contact.[100] They will have relatively heterogeneous distribution and not have as inert contact as in the cases of organic molecules and NMs. Secondly, they usually have surface components (*e.g.*, EPS and appendages) that form a relatively viscoelastic interface between the cell and the solid surface (which could accommodate contraction, distortion, and compression during resonant oscillation), and this interface may experience dynamic changes over time.[100] With these two features, the behaviors of attached microbial cells (*e.g.*, vibration, sliding, or remaining relatively stationary) in response to QCM's acoustic sensing (lateral oscillation) will be different to those of organic molecules and NMs, requiring different analysis methodologies. The difference between the attachments of microbes and rigid particles is manifested in the comparison between the behavior of silica particles and bacterial cells.[104] Since silica particles are rigid, their contact with solid surfaces does not undergo dynamic changes following surface attachment, resulting in a constant ΔD_n value, while the cell–substrate interface undergoes dynamic change following initial attachment, leading to temporal change of cell-normalized ΔD_n (Fig. 4A).[104]

Regarding Δf_n, it may not be a reliable measure of microbial loading on the surface. As shown in many studies that correlated Δf_n with the adsorbed cell number, the cell-normalized Δf_n

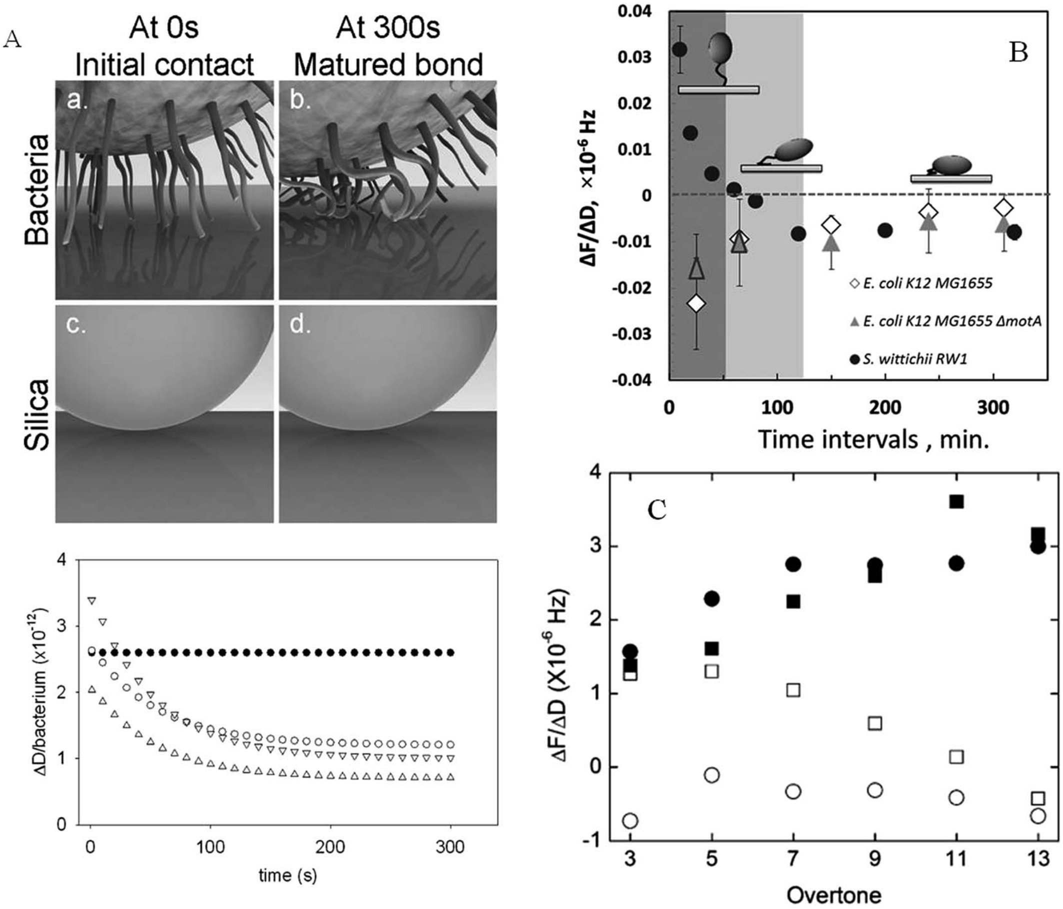

Fig. 4 Comparison of particle-number-normalized ΔD for 1 μm silica (solid circle) and different *S. salivarius* strains (empty symbols), schematic illustration explaining the dissipation behavior of a microbe (a & b) and silica particle (c & d) is also presented (A); dynamic changes of the $\Delta f/\Delta D$ ratio during the adhesion of bacteria with different surface structures to the silica surface (B); the $\Delta f/\Delta D$ ratios of different overtones for the adhesion of relatively hydrophilic (empty) and hydrophobic (solid) *P. aeruginosa* to silica (circle) and PVDF (square) surfaces (C). (A) was adapted from Olsson *et al.*,[104] copyright 2010 American Chemical Society. (B) and (C) were adapted from Gutman *et al.*,[106] and Marcus *et al.*,[105] respectively, copyright 2013 and 2012 American Chemical Society.

differed significantly between bacterium strains and overtones.[23,105] In addition, positive Δf_n was frequently observed during the adhesion of cells with elongated surface structures such as flagella and fimbria, and when these structures directed the contact.[23,106–108] In contrast to conventional QCM theory assuming inert loading of sorbate and simultaneous oscillation with the QCM sensor, a coupled-oscillator model was developed to explain the response (where the cell-loaded inertia may be counteracted because of the elastic connection between the microbial cell and the surface).[34,35,107] Results from these studies suggest that although Δf_n is sensitive to microbial attachment events, it is not always a reliable mass or attached cell indicator (mass cannot be derived with the Sauerbrey equation or viscoelastic models).

The physical meaning of ΔD_n is not as explicit as in organic molecule adsorption, as microbial attachment could be inertial, elastic, or viscous loads (the dominance of which depends on the types of interaction),[105] and the subsequent interplay between the solid surface, microbes, and solvent.[16] Due to the relatively large size of microbial cells and the elastic surface components, the contact mechanics between microbes and the substrate strongly affects the response of attached microbial cells (and the hydrodynamic coupling of solvent) to the resonant oscillation of the QCM sensor.[20,109] Thus, ΔD_n was primarily used to help envision the role of surface components during microbial attachment (details in Section 3.4.2).

Since the response of attached microbes (and solvent) to sensor oscillation and penetration depth of QCM's acoustic wave are frequency specific (thus harmonic-dependent), overtone-dependent behavior was also frequently analyzed in microbial attachment.[23,105,106] It seems that whether $\Delta f/\Delta D$ varies between overtones or not depends on the contact mechanics between microbes and the substrate surface, with inertial contact showing smaller variation between overtones than elastic contact.[105]

Based on previous studies on microbial adhesion, although QCMs are not a reliable tool for quantifying the number of attached microbes, their sensitivity to contact mechanics between microbes and the solid surface makes them an excellent tool to study the adhesion process.

3.4.2 Application in characterization of microbial initial adhesion. The initial adhesion is a relatively fast process, where the impacts of metabolism are negligible, and involves only physical and chemical interactions between cells and the substrate surface. The important questions of microbial adhesion are the role of cell surface components (*e.g.*, EPS and flagella) in the adhesion and the interplay between the surface properties of microbes and the substrate. The methodology used in studies targeting these questions consists in comparing the adhesion of microbes with distinctive surface properties onto substrate surfaces of different properties (mostly surface charge and polarity), under varying solution conditions.

First of all, the real-time monitoring capability of QCMs allows them to trace the dynamic changes of the adhesion process. Cell-number-normalized Δf_n and ΔD_n or the $\Delta f_n/\Delta D_n$ ratio (or its reciprocal) was predominantly used as the tracking parameter. Stabilization of these parameters indicates the maturation of cell–substrate bonding.[104] For example, the adhesion of bacteria with elongated surface structures (*e.g.*, flagella) usually showed dynamic changes in QCM response during the initial attachment, while strains without these structures showed little change, similar to the behavior of rigid silica particles (Fig. 4A and B).[104,106,108]

In addition to adhesion kinetic analysis, QCM was also applied to the analysis of adhesion thermodynamics, particularly the interplay between the surface properties of cells and substrate surfaces on microbial adhesion, and the effects of solution chemistry. The $\Delta f_n/\Delta D_n$ ratio was commonly used to characterize and compare the properties of different microbe–substrate interactions. Different $\Delta f_n/\Delta D_n$ ratios have been observed for different types of microbes on the same substrate or the same microbe to substrates with different properties.[23,105] The use of this ratio also helped identify the effects of solution chemistry and surface functionality on microbial adhesion.[108,110,111] For example, the hydrophobicity of both the microbe and substrate surface was shown to affect the contact mechanics between them, with hydrophobic cells to hydrophobic surfaces seeming to be more elastic and hydrophilic cells to hydrophilic surfaces more viscous (Fig. 4C).[105]

Due to the intrinsic complexity associated with QCM's response to microbial adhesion, the physical meaning of Δf_n and ΔD_n is relatively ambiguous and inconsistent between microbial adhesion scenarios, compared to that of organic molecules and NMs. Therefore, they primarily serve as parameters to qualitatively track the adhesion dynamics and compare different adhesion scenarios. Despite this, results from QCMs help develop conceptual models of microbial adhesion and identify the role of surface properties and solution chemistry, provided that the studied systems are well constrained (*e.g.*, surface properties of microbial strains have been characterized).

3.4.3 Application in monitoring biofilm growth. The early applications of QCMs in biofilm research were on the long term monitoring of biofilm growth on a solid surface.[112] The idea behind these studies was to identify biofilm growth events from characteristic QCM responses, and study the effects of factors such as substrate surface properties, nutrient conditions, and flow conditions.

As presented above, QCM response gradually stabilized once the microbe achieves irreversible attachment and developed mature bonding with the substrate surface (Fig. 4A and B). Without continuing microbial attachment, subsequent changes in Δf_n and ΔD_n could be caused by the excretion of metabolites or microbial proliferation.[113] Because of the complex response mechanism of QCMs to microbes, although Δf_n cannot be quantitatively related to microbial cell mass (and number), its change (increasingly negative) can be semi-quantitatively attributed to increasing mass loading. Similar to the adhesion study, $\Delta f_n/\Delta D_n$ serves as a parameter to compare the contact mechanics between the biofilm and the substrate surface. For example, after deposition of a certain amount of diatom cells, the decrease of frequency and increase of dissipation suggested the spreading of EPS on the surface, and the growth kinetics and viscoelasticity (semi-quantified by $\Delta D_n/\Delta f_n$) of the biofilm were shown to be species-dependent and surface-dependent.[111,114] Similarly, a QCM was used to monitor long-term biofilm formation from wastewater, and Δf_n was used to compare the growth kinetics on different surfaces and identify the effects of biocide.[115] The versatility of the QCM setup allows the studying of the effects of a wide range of factors on biofilm formation. For example, by monitoring Δf_n and $\Delta D_n/\Delta f_n$ over 20 hours, the growth rate for a "continuous flow" generation method was shown to be faster than that for an "attach and flow" method, and the former had a larger $\Delta D_n/\Delta f_n$ than the latter, indicating a more viscoelastic biofilm as a consequence of more EPS production.[116] In addition to bacterial types and substrate surfaces, the effects of temperature, nutrient conditions, flow rate and pollutants on biofilm formation dynamics can also be conveniently studied.[113,117–119]

As summarized in Section 3.4.2 and 3.4.3, the physical meaning of Δf_n and ΔD_n is relatively inexplicit for microbes; thus data from QCMs should not be over-interpreted. Understanding of metabolic changes during biofilm growth should not rely on QCMs alone; parallel characterization by microscopy and other techniques may be necessary.[120,121]

4. Uncertainties, advantages and limitations of QCMs

4.1 Uncertainties associated with adsorption amount quantification

QCMs were first and primarily designed for quantification of mass changes on surfaces. As described above, two processes are involved in adsorption quantification – QCM sensing and model fitting. Therefore, two questions arise: (1) what is being detected by QCMs in the Δf_n, and (2) is the Δf_n-to-mass conversion performed by the right model and what is the solvent content in the Δf_n-derived mass? These questions affect how we should analyze and interpret the data.

First of all, the response mechanism of QCMs to different sorbates varies greatly, and the physical meaning of Δf_n may not be explicit and consistent (Table 1). For sorbates that are relatively small and have tight contact with the QCM sensor surface, the sorbate and hydrodynamically coupled solvent oscillate with the sensor and contribute to Δf_n. Although the Δf_n can be fitted to derive the adsorbed mass with certain physical models, the mass is a "wet" quantity that consists of both sorbate and solvent. Thus the key to accurate use of QCMs is how QCM-derived mass is analyzed and interpreted and whether the contribution of solvent can be estimated. Therefore, during data analysis and interpretation, there are two questions that need to be considered: (1) is the most appropriate model used to approach the accurate "wet" mass? (2) What is the fraction of the "real" sorbate mass and whether the adsorptions being compared have the same solvent content? The first question is about the accuracy of QCM data conversion, which is partly discussed in Section 2.2.1. The second question determines how the QCM data should be analyzed and interpreted.

As presented in Section 3.2, the contribution of solvent depends on a wide range of factors, such as the size and shape of the sorbate, surface coverage, and organization of the adlayer. Therefore, direct comparison of Δf_n or the derived "wet" mass between different sorbates (even for the same sorbate under different conditions) should be done with caution. The key to reduce the uncertainty resulting from solvent coupling is to estimate its contribution. There are two ways to achieve this objective: (1) theoretical modeling that incorporates the adlayer organization and geometry to estimate the coupled solvent mass,[17,80] and (2) experimental determination with complementary techniques, such as OWLS,[48,49] ellipsometry,[64,122] and optical surface plasmon resonance.[19,123] Model fitting has limitations since it is based on relatively ideal systems, while very complex and heterogeneous adlayers are commonly encountered under most realistic conditions.

For sorbates with sizes close to or larger than the penetration depth of QCM's acoustic wave (*e.g.*, large NPs or microbes), QCM's response to their attachment is greatly affected by the contact mechanics between the particle and the solid surface. For example, particles can be rolling or sliding during the sensor's resonant oscillation, which will affect the hydrodynamic coupling of solvent trapped between the particles (thus the contribution of solvent to Δf_n). The microbe–substratum interface can be very diverse and dynamic, due to the surface properties of microbes. Microbial attachment can be inertial, viscous, or elastic, and may vary during the adhesion process. Thus a nonlinear and inconsistent relationship between Δf_n and the number of attached microbes was frequently observed in studies with simultaneous cell measurement.[23,105,110] These results suggested that Δf_n cannot be reliably related to the attached microbial number, but only serves to semi-quantitatively monitor microbial attachment. Simultaneous microscopy counting of the attached cell number is needed to complement the analysis of Δf_n.

4.2 Evaluation of dissipation analysis

Although energy dissipation monitoring is a great feature of QCM technology that helps boost its wide applications, the analysis and interpretation of dissipation for understanding adlayer characteristics remain mostly qualitative and inexplicit. According to the fundamentals of dissipation monitoring, any factors that damp sensor oscillation following AC cutoff could contribute to ΔD_n. The analysis and interpretation of ΔD_n are thus dependent on identifying the contributors and establishing a model (conceptual or physically explicit) that connects D response and the contributors. A wide range of factors have been identified to contribute to ΔD_n, such as the characteristics of the sorbate, its contact with the surface, its distribution and organization on the surface, and the coupling of solvent. Many of them are interrelated.[13,16,26,35,124]

For relatively homogeneous adlayers (such as those formed by organic molecules), the main contributors are the strained deformation of the viscoelastic adlayer (since they may not rigidly couple to the QCM oscillation) and hydrodynamic solvent coupling during sensor oscillation.[16] A higher degree of solvent coupling and a greater thickness of the same materials at the interface generally lead to a larger dissipation and $\Delta D_n/\Delta f_n$ ratio.[21,125] Therefore, the $\Delta D_n/\Delta f_n$ ratio has been used to compare the relative "fluidity" and "softness" of different adlayers. However, "softness" and "fluidity" are not quantitative concepts, with which the $\Delta D_n/\Delta f_n$ ratio does not explicitly correlate. For example, the adsorption of different molecules or the same molecule under different solution conditions shows different $\Delta D_n/\Delta f_n$ ratios, which however, can not reveal the solvent content and the exact conformation and organization of the adsorbed molecules.[50,57] Therefore, the comparison of the $\Delta D_n/\Delta f_n$ ratio for evaluating solvent coupling and sorbate conformation (or softness) is mostly semi-quantitative. Compared to the interpretation of the $\Delta D_n/\Delta f_n$ ratio, more explicit analysis is achieved by the viscoelastic models, through which the thickness, shear and viscosity of the adlayer can be derived.

The analysis of heterogeneous adlayers is more complex, since there are great variations in particle distribution and organization (laterally and vertically) on the surface, as well as the presence of multiple dissipation mechanisms.[13,24,80,126] For example, NMs being tested differ widely in their geometry and surface chemistry, and may form complex and diverse adlayers under the broad range of conditions tested. In these systems, the relative roles of different dissipation contributors may vary, for example, the rolling or sliding of adsorbed NMs at the interface (which contributes to ΔD_n) is affected by both surface coverage and the particle-surface contact mechanics.[13,22] In addition, the complex NP adlayers (*e.g.*, those formed by carbon-based nanomaterials) will also affect how solvent is coupled during QCM oscillation. All these factors make it challenging to establish an explicit relationship between ΔD_n and dissipation contributors of these heterogeneous systems.

The analysis of energy dissipation in microbial adhesion is much more complex than that of organic molecules and NMs, because of the limited penetration depth of QCM's acoustic sensing and the relatively large size of microbial cells, as well as the dynamic cell–substrate interface (contact mechanics depend on a range of factors and change over the course of adhesion). On the one hand, the contributors of ΔD_n are difficult to deconvolute (including the viscoelasticity of both the cell and cell–substrate interface, and hydrodynamically coupled solvent). On the other hand, Δf_n does not consistently relate to microbial loading on the sensor surface.[34] This inhibits an explicit interpretation of the $\Delta D_n/\Delta f_n$ ratio (or its reciprocal) that is commonly used to characterize and compare different microbe–substrate interactions. Furthermore, microbial adhesion usually shows complex overtone-dependent responses, which are related to frequency-dependent response to the attached microbes.[23,105,127] The intrinsically complex QCM response to microbial adhesion or biofilm growth determines that Δf_n and ΔD_n from QCMs serve mostly as semi-quantitative parameters for understanding the adhesion mechanism.

4.3 Strengths and limitations of QCMs in studying interfacial interactions

As analyzed in the previous sections, QCMs possess great capability, versatility, and potential in studying environmental interfacial processes at the solid–liquid interface. However, in addition to the uncertainties associated with data analysis and interpretation, QCMs also have intrinsic limitations that prevent their wider application.

First of all, although technically almost all interfacial reactions involving mass change at solid/liquid interfaces can be characterized by the QCM technique, they are not sensitive to atoms and small molecules. In addition, their mass quantification is neither selective (can not differentiate water or different sorbates) nor direct (mass is not directly quantified but modeled). Therefore, they are not good at studying element and small molecule adsorption, and not suitable for studies that require accurate concentration information (such as adsorption isotherm). Because of their non-selective mass measurement, they can not be used for monitoring competing adsorption. In these cases, batch sorption and column experiments, which commonly use mass spectroscopy (and other techniques) to accurately measure sorbate concentration, may be a better choice than QCMs.

Secondly, although a broad range of surface materials (*e.g.*, SiO_2, Fe_3O_4, Al_2O_3, gold, stainless steel, polystyrene, *etc.*) are commercially available and can be further modified *via* various chemical surface modification techniques (*e.g.*, vapor deposition, spin coating, and surface adsorption),[128] these surfaces are generally flat and uniform (with a constant surface area), compared to the complex and heterogeneous environmental surfaces. Therefore, QCMs are more suitable for studying interfacial phenomena on model surfaces and the effects of surface chemical properties (*e.g.*, charge, hydrophobicity, and polarity), but not some realistic interfacial processes, such as adsorption on porous sorbents (which also involves the physical properties of the sorbents, such as particle sizes, porosities, and roughness) or crystalline minerals.

In addition to the conveniently modifiable surfaces, QCMs also have other unique features: (1) the QCM technique is an *in situ* and almost real-time technique, capable of capturing signals within seconds, (2) the energy dissipation monitoring capability of QCMs makes it possible to explore the adlayer characteristics (*e.g.*, solvent coupling, relative compactness, thickness, and contact mechanics) and track their dynamics in addition to mass changes,[53,106,108] (3) the flow-through setup with the flow rate and temperature control makes QCMs suitable reactors to simulate different environmental scenarios, such as sorption and desorption,[59,60,86,88,129] dissolution and degradation,[130] and changes in flow, solution chemistry, and temperature.

Overall, QCMs excel in testing the effects of surface chemical properties on interfacial interactions, and monitoring interfacial interactions whose real-time kinetics, molecular conformation, or adlayer properties are invaluable. They have unique features that make them an incomparable tool in studying certain interfacial interactions, and providing information that can not be obtained by batch sorption or column experiments. Researchers are suggested to take all their technical advantages and limitations into account, in order to decide if QCMs are applicable to their systems and make the best use of them. Moreover, mainstream QCM instruments (and the consumables such as crystal sensors) that can measure both frequency and dissipation shifts at multiple harmonics are still very expensive. Improvement in cost reduction would promote future applications of QCMs.

5. Other environmental applications of QCMs

The versatility and capability of QCMs are reflected in their broad applications, in addition to studies involving organic molecules, NMs, and microbes.

QCMs can be used to detect and monitor various pollutants, by functionalizing their sensor to specifically adsorb the pollutants from gas or liquid phases.[131–137] For example, QCM gold sensors can be functionalized with a monolayer of aminothiols with an ionically bound anthracene group, which preferentially adsorbs polycyclic aromatic hydrocarbon (PAH) anthracene *via* π–π interaction, which showed a detection limit of 2 ppb.[131]

QCMs are also an excellent tool for studying surface mineralization.[138–142] One major challenge in studying surface nucleation and crystallization is their relatively fast reaction rate and the small size of the nuclei and crystals, and few techniques are capable of *in situ* monitoring. QCMs have been used to study the effects of surface properties and solution chemistry on the mineralization kinetics of various minerals, which improved our understanding of biomaterial formation[138,139,143,144] or scale formation in many engineering facilities.[141,145]

Another QCM feature with promising prospect in environmental research is electrochemical QCM (EQCM).[146,147] Many natural or environmental engineering processes such as corrosion are electrochemically driven, which can be conveniently studied by EQCM with high sensitivity in real-time.[148,149]

6. Future perspectives

As analyzed in previous sections, future studies are needed to gain in-depth understanding of the response mechanism for different sorbates, especially for NMs and microbes that have diverse physicochemical properties and complex QCM response. This is necessary for definite and accurate analysis of the QCM responses. Future applications of QCM techniques are encouraged to collect complementary information from other techniques and cross-validate the results, in order to reduce the uncertainty associated with QCMs and obtain more accurate and in-depth understanding of the studied interfacial processes. In the future, the applications of QCMs in environmental research can be expanded in several directions. Firstly, the applications of QCMs can be broadened by utilizing other instrumental features (*e.g.*, modules that allow the coupling of other analytical techniques, and EQCM) and sensor surfaces that may include important environmental features (*e.g.*, physical and chemical heterogeneity). Secondly, following the advancement of QCM technology, new interfacial reactions suitable for QCM application need to be identified, in addition to interactions involving model organics, NMs and microbes as summarized above. Thirdly, adsorption/deposition studies using QCMs can be combined with other studies to further understand the subsequent behaviors or effects of the adlayer, and to identify any discrepancies during the scaling up (*e.g.*, when results from QCM studies are correlated with results from studies on larger scales) and the causes of any discrepancy. Finally, new theories and methodologies for better understanding of the response mechanism and analyzing QCM raw data for more quantitative results are needed, considering the diverse interactions and broad conditions encountered in environmental research.

Conflict of interest

The authors declare no competing financial interest.

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