**Supplementary Information**

**Simple and ultrafast resonance frequency and dissipation shift measurements using a fixed frequency drive**

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**S1. Error in resonance frequency shift estimate using FFD method when characteristic impedance is assumed as constant**

The change in resonance frequency due to mass loading or other factors can be modelled by a change in inductance () or capacitance () or both of the equivalent electrical circuit. Since the resonance frequency is given by , and the characteristic impedance is given by , therefore we have

Since is much below 0.1% in most practical cases, therefore we assume to be constant without impacting accuracy or reproducibility in practice. For instance, when the resonance frequency change is purely due to mass loading, i.e. entirely due to change in inductance () of the equivalent electrical circuit, then

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|  | (S1) |

We consider a quartz crystal resonator (QCR) with initial resonance frequency as 14.3 MHz and the initial characteristic impedance () as 400 kΩ (as explained in **Supplementary Information** **§S3**). The drive frequency is also chosen as 14.3 MHz, such that the frequency offset (i.e. the difference between the drive frequency and resonance frequency) gives the shift in resonance frequency as binding progresses. We choose values of reactance from ‑2000 to 2000 in steps of 10. For each reactance value, we evaluate the ‘true’ resonance frequency shift by first estimating the ‘approximate’ using the Fixed Frequency Drive (FFD) method from Eq. 10 assuming , then calculating the ‘true’ from Eq. S1 using the approximate , i.e. , and finally plugging this ‘true’ in Eq. 10. The error between the ‘true’ and the ‘approximate’ , and the percentage of error with respect to the approximate , are given in **Supplementary Figure S1**. We note that the error and % error are ~0.9 Hz and 0.025% for a resonance frequency shift of 3.57 kHz, which is equal to one resonance half-bandwidth for a quality factor of 2000 () in liquid. Since the resonance frequency shift is well within the resonance half-bandwidth for most QCR measurements, we can assume the characteristic impedance to be constant without affecting the accuracy of estimation of resonance frequency in practice using the FFD method.

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**Figure S1**. Error of the resonance frequency shift estimate (assuming the characteristic impedance as constant) with respect to the ‘true’ estimate (considering change in characteristic impedance) using the FFD method

**S2. First and second order series approximation of the resonance frequency offset**

The expression for the resonance frequency offset i.e. difference of the resonance frequency from the drive frequency is given according to Eq.10 of the Main Article as

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|  | (10) |

Here, is the offset of the resonance frequency with respect to the drive frequency , is the characteristic impedance and is the reactance (or imaginary part of impedance). and can be evaluated by fitting the reactance, obtained from a frequency sweep taken at the start of an experiment, to the BVD model. of Eq. 10 is recorded experimentally when the quartz crystal resonator (QCR) is actuated using a fixed frequency drive (FFD). If this drive frequency is set to the resonance frequency at the start of an experiment, then the shift in resonance frequency due to mass or viscous loading can be obtained from the frequency offset derived using Eq.10. The first order Maclaurin series approximation of this offset is given by

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|  | (S2) |

The second order Maclaurin series approximation also evident by neglecting under radical in Eq. 10 is given by:

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|  | (S3) |

Taking the initial resonance frequency as 14.3 MHz, and the characteristic impedance as 400 kΩ (as discussed in **Supplementary Information §S3**), we determined the relative errors of the linear () and second order () series approximations with respect to the exact formula for frequency offset (Eq. 10). This is presented in **Supplementary Figure S2**. The error for the linear expression for frequency offset is ~0.5 Hz for a resonance frequency shift of 3.57 kHz, which is ~one resonance half-bandwidth for a quality factor of 2000 () in liquid. This error may be neglected in practice as the resonance frequency shift is well within the resonance bandwidth in most cases. The second order expression is even more accurate as the error is ~7 µHz for a resonance frequency shift of 20 kHz or 5.6 frequency half-bandwidths in liquid. This formula also allows avoiding calculation of radicals, while keeping excellent accuracy, which can be beneficial for processing by a simple and cheap microprocessor.



**Figure S2**. Error of the expressions for first and second order approximations of the frequency offset with respect to the exact expression (Eq. 10).

**S3. Determination of quality factor of quartz crystal resonator in liquid**

The quality factor for a resonator of mass is given by

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|  | (S4) |

where is the coefficient of viscous damping is the resonance bandwidth. The electrical equivalent form for the expression of quality factor is given by

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|  | (S5) |

where and are resistance and inductance of the electrical circuit and is the characteristic impedance. For a 14.3 MHz QCR that we used in this work, when the impedance from a frequency sweep with one side in liquid is fitted with the Butterworth-Van Dyke (BVD) model (**Main Article** **Figure 1b**), we obtain ohm and ohm. Hence, using Eq. S4, we obtain the quality factor as .

**S4. Theoretical estimate of resonance frequency shift in streptavidin-biotin binding**

The resonance frequency shift at the nth overtone (resonance mode) is given according to Sauerbrey [1] by

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|  | (S6) |

where is the resonance mode, is the bound mass, , , and are the unperturbed fundamental resonance frequency, density, frequency constant and effective binding area of the QCR respectively. The maximum amount of additional mass due to streptavidin binding can be given by

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|  | (S7) |

where is the molecular weight of streptavidin, is the Avogadro Number and is the cross-sectional area of one streptavidin molecule. Using Eq. S5 and Eq. S6, we have

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|  | (S8) |

Considering (fundamental mode), kDa, MHz, Kg/m3, kHz-mm, and nm2 [2], the estimated resonance frequency shift from Eq. S8 comes as -230 Hz. This theoretical estimate agrees quite well with the experimentally observed value of 148 Hz (SD, 13.65 Hz) obtained from FFD technique when the drive frequency was set to .

**S5. Resonance frequency shift estimates from the Kanazawa theory**

The shift in resonance frequency due to change in liquid phase from methanol to DI water can be estimated using the Kanazawa and Gordon formula [3], which is given by

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|  | (S9) |

where is the unperturbed resonance frequency of a bare quartz crystal, and are the viscosity and density of liquid respectively, and and are the shear modulus and density of the quartz crystal respectively.

Considering, MHz, Pa.s, Pa.s, kg/m3, kg/m3, kgm/s2 and kg/m3, we get Hz and Hz. Hence, the resonance frequency shift due to change in liquid phase from methanol to DI water is Hz. This theoretical estimate agreed satisfactorily with the experimentally observed frequency shift using both the methods (within 0.92% for the impedance analysis method and +0.67% for the FFD method when driven at ).

The shifts in resonance frequency () and dissipation given by the half resonance bandwidth () have the same absolute value due to liquid loading when other losses can be neglected, which is true for methanol-DI water replacement. Hence, . Since , and the relative change in is small, the fractional shift in can be theoretically estimated as . This theoretical estimate agreed satisfactorily with the experimentally observed relative shifts in dissipation using both the methods (within 0.76% for the impedance analysis method and -1.96% for the FFD method when driven at ).

**S6. Needle touch experiment using VNWA 3E from SDR-Kits**

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**Figure S3**. Resonance frequency shifts due to instantaneous needle touches using VNWA 3E from SDR-Kits.

**S7. Electrical noise in our instrument with FFD method**



**Figure S4** Pure electronic noise from FFD method at a data acquisition period of 8.4 ms fits well with the additive normal ‘white’ noise that reduces reciprocally to the square root of the sampling period. One unit of average on the graph’s x-axis corresponds to 4 milliseconds. The rise in the experimental solid line below 10 averages is due to artefacts in the processing algorithm and to be disregarded.

**S8. Theoretical estimate of rise time due to a step-wise transient process on a QCR**

The in-phase sinusoidal signal with a step increase in amplitude after double down-conversion with an intermediate frequency (IF) of 1 Hz is given by Eq. S10. Here, frequency and amplitude are both scaled to unity to have simpler formulae. We have scaled them back to real values later for comparison with experiment. The analog signal is down-converted to IF, digitised, and then digitally multiplied by and . The in-phase component (after multiplication by ) is given by

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|  | (S10) |

where , when , and , when . Laplace transform of this signal is given by

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|  | (S11) |

After applying quadruple moving averaging filter (also known as a type of B-spline) followed by quadruple exponential moving averaging, and taking into account the time transient process of the QCR upon stepwise change of attached mass (time constant ), we have

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|  | (S12) |

where, , is B-spline Laplace Transform, is the time constant of exponential averaging, and , where is the intermediate frequency used in double down-conversion. Here, .

**Figure 5b** of the main article (the graph in bold) shows the Laplace transform transient process of Eq.S12 after scaling back to real units in frequency for , which corresponds to a data acquisition time period of 32.7 µs. The time between 10% and 90% of the step increase in amplitude of the sinusoidal signal is defined as the ‘rise time’ and represents the theoretical estimate for time resolution with the given system. From the theoretical graph, the time resolution (or the rise time) for the quickest data acquisition time period (32.77 µs) was found to be ~112 µs. This agreed quite well with the duration of the “first frequency rise feature” of a representative needle touch experiment (**Main Article** **Figure 5b**).

**References**

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