Optimising detection limits in whispering gallery mode biosensing

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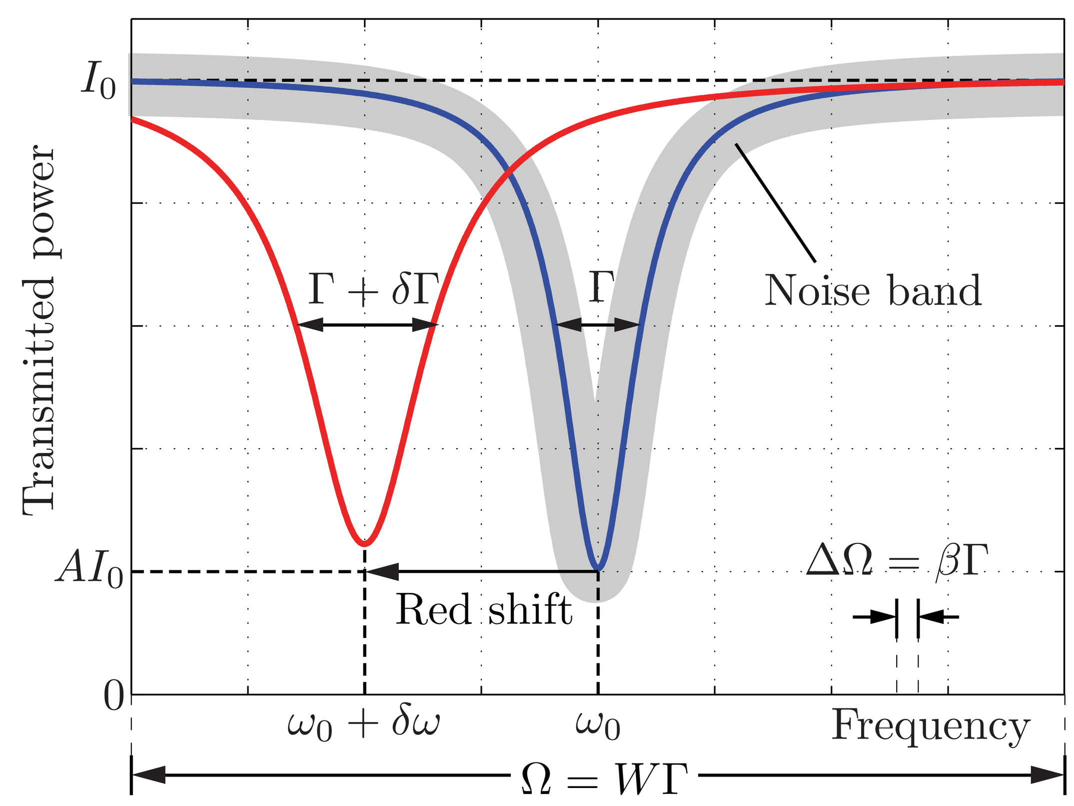
Introduction

Whispering gallery mode (WGM) biosensors commonly operate in a swept modality, whereby the transmission spectrum exhibits a Lorentzian lineshape as the laser source is tuned across the WGM resonance. Binding of small bioparticles to such a sensor induces a shift in the resonance frequency, $\delta\omega$, in addition to line broadening, $\delta\Gamma$. Detection of such events, requires precise knowledge of ω_0 and Γ for each frequency scan, which is ultimately limited by noise present in the measurement. Common noise sources include detector noise and laser jitter/thermorefractive noise. Knowledge of such noise imposed detection limits in turn allows for system benchmarking and improved experimental design.

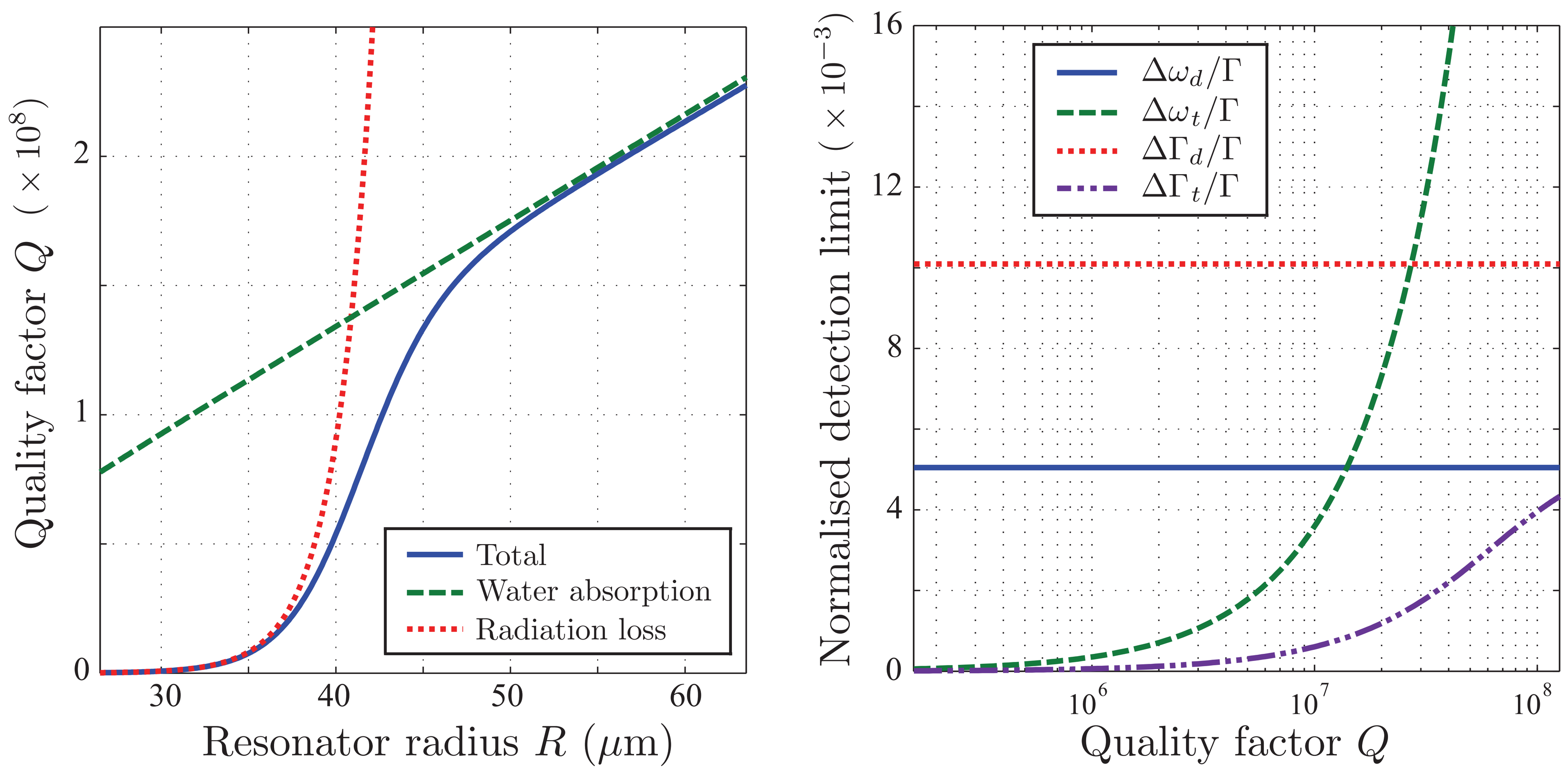


Fisher information and measurement precision

Estimates of the resonance frequency and linewidth, derived from experimental measurements, will randomly vary as can be quantified using the estimator variance $\sigma^2_{\omega_0}$ and σ^2_Γ. The Cramér-Rao lower bound provides a rigorous statistical tool to quantify the best possible measurement precision achievable within any given noise regime and implies $\sigma^2_{\omega_0} \geq 1/J_{\omega_0}$ (and similarly for Γ), where J_{ω_0} is the Fisher information which derives from the probability density function of the noise [1]. For detector and thermorefractive noise we find the minimum detectable change in ω_0 and Γ which are given by:

$$\Delta\omega_d = \frac{\Delta\Gamma_d}{2} \approx \sqrt{\frac{2\beta}{\pi}}\frac{\sigma_d}{I_0 A}\Gamma \quad \text{and} \quad \Delta\omega_t \approx \sigma_t\sqrt{\frac{\beta}{W}}, \quad \Delta\Gamma_t \approx 2\sigma_t\sqrt{\frac{3\beta}{W^3}}$$

respectively. Coloured noise may also be considered when the noise power spectrum is known by employing the asymptotic Fisher information [2].



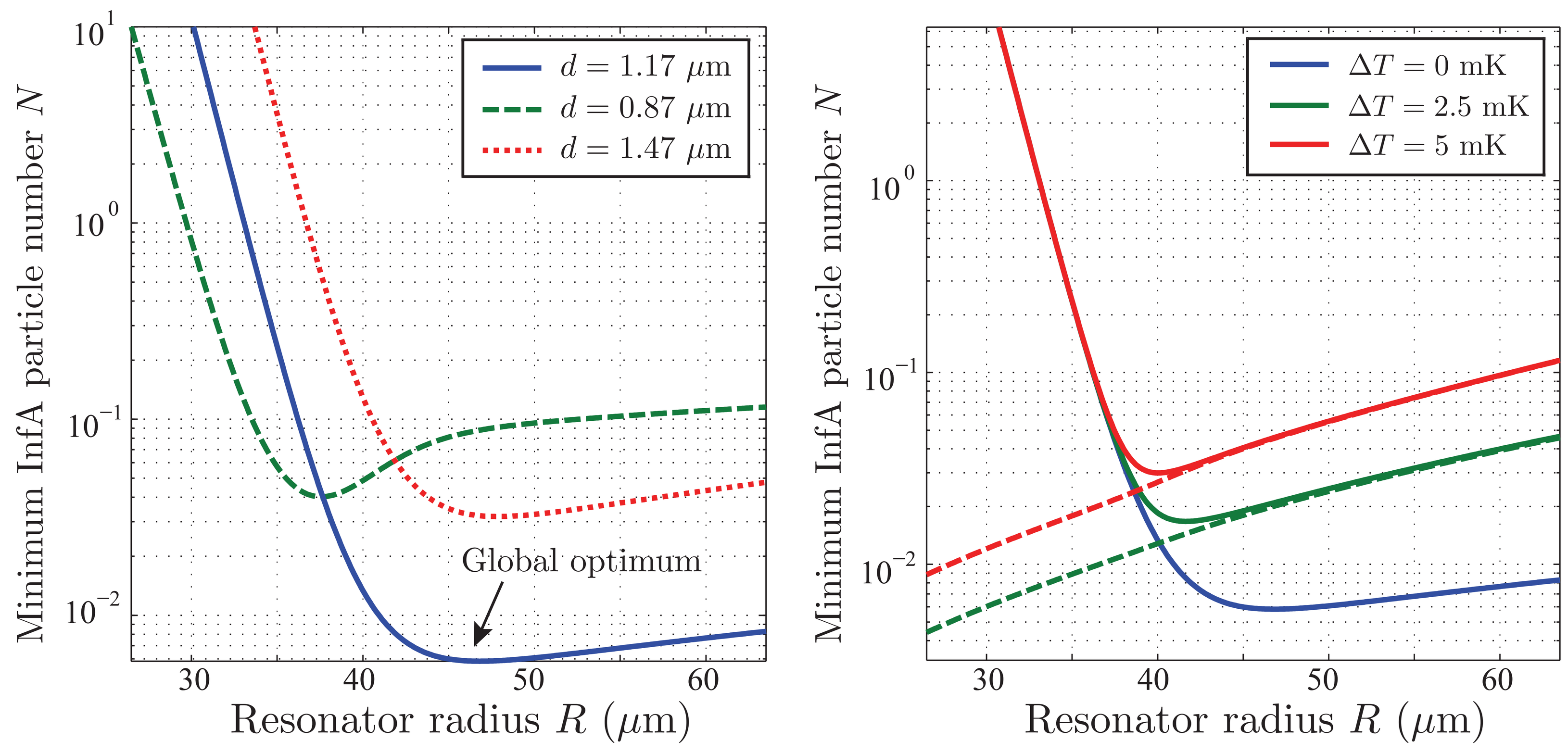
WGM detection limits

Detection limits in WGM sensing derive from a balance between the size of the induced resonance shift or line broadening versus the minimum detectable signal. Taking resonance shifts as an example, the minimum number of detectable (bio)-particles can then be defined as $N = \Delta\omega/|\delta\omega|$, where $\delta\omega$ can be found using perturbation theory [3]. Ultimately we find, for detector noise and laser jitter that

$$N = \frac{(n_c^2 - n_s^2)}{\mathrm{Re}[\alpha]}\frac{R^3}{|Y_{ll}(\pi/2)|^2}\sqrt{\frac{2\beta}{\pi}}\frac{\sigma_d}{I_0 Q_0}\frac{(1+Q_c/Q_0)^3}{4Q_c^2/Q_0^2} \quad (1)$$

where R is the resonator radius, $n_{c,s}$ is the refractive index of the cavity and its surroundings, I_0/σ_d is the measurement SNR, Y_{lm} are the spherical harmonics and $Q_{0,c}$ are the intrinsic and coupling quality factors.

Optimal WGM biosensors



Equation (1) can be optimised in a number of ways. Firstly, the resonator radius can be adjusted to improve detection sensitivity, due to its effect on cavity losses. An optimum exists for detector based noise since radiation losses exhibit a differing size dependence to absorption losses. Thermorefractive noise/laser jitter, is however found to be independent of coupling and cavity losses, such that $N \sim R^3$. Realistically, any experimental setup will be subject to both technical and fundamental noise sources. Accordingly the experimental detection limit and optimal microcavity size is set by competing requirements of both noise sources. Stam's inequality allows detection limits to be found in this case.

Furthermore, since cavity loss mechanisms play a critical role in determining optimal resonator geometries a strong wavelength dependence is seen. Dispersion of water and water absorption dominate the behaviour, such that clear improvements are seen when blue light is used. The transmission window of water implies blue light gives globally optimal detection limits.

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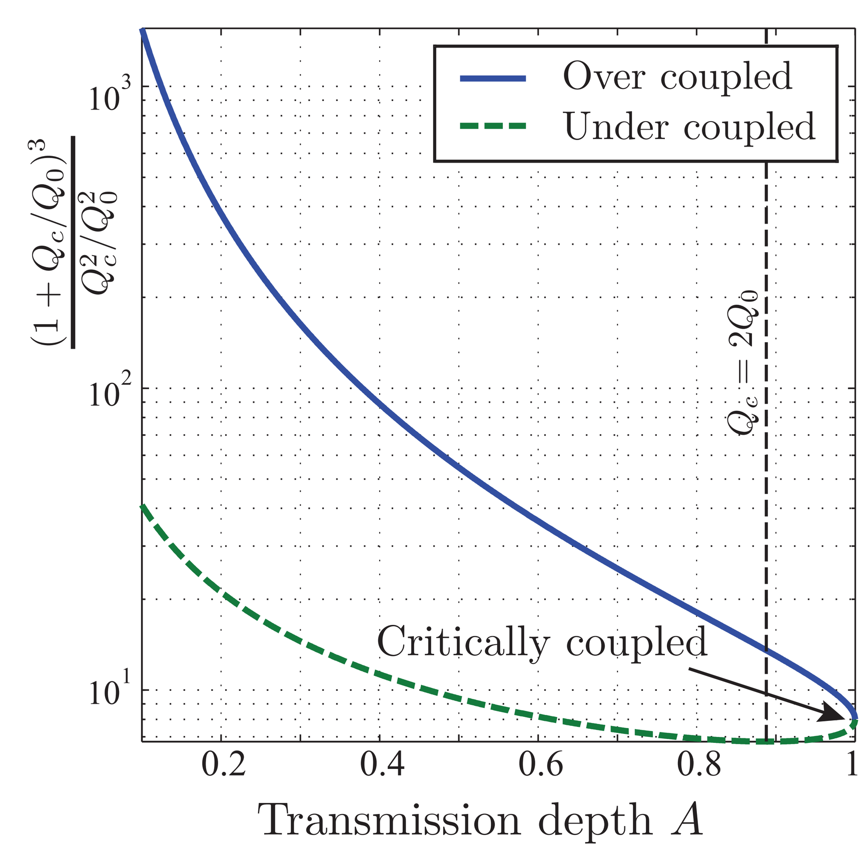
λ (nm)	Q_0	R_{opt} (μm)	d_{opt} (μm)	$\log_{10} N_{opt}$
1550	1.30×10^5	60.64	0.972	1.23
1300	1.79×10^5	53.07	0.866	0.92
780	1.51×10^8	46.80	1.169	-2.23
633	1.52×10^9	41.18	1.127	-3.41
410	7.95×10^9	26.63	0.799	-4.65

Finally, the $(1+Q_c/Q_0)^3/(4Q_c^2/Q_0^2)$ factor can be maximised by varying the coupling losses Q_c such that $Q_c/Q_0 = 2$. This can be done in a prism coupled system, for instance, by adjusting the coupling distance d. In contradiction to common wisdom optimal detection is thus seen to be achieved when the microresonator is slightly under coupled rather than critically coupled and holds since optimal detection simultaneously requires both a large transmission depth, A, and a narrow linewidth.



References

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