Design of Matched Optical Pulses for Coherent Raman Imaging

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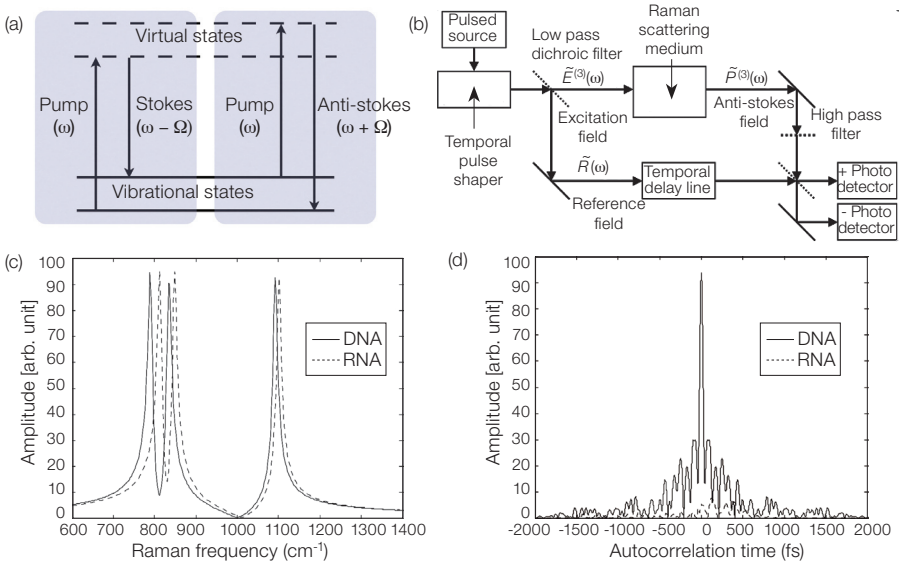
One objective of nonlinear microscopy is to image endogenous properties of samples, particularly biological ones. Coherent anti-Stokes Raman scattering (CARS) can provide information on the Raman spectrum of a sample at greater signal strength than incoherent Raman scattering. Scientists have invented methods to map the presence of molecules at one vibrational frequency and over a bandwidth of such frequencies.[1,2]

The techniques expose the sample to two or more narrowband optical pulses whose carrier frequencies differ by the frequency of the vibrational mode to be probed (or one double-chirped pulse of sufficient bandwidth). By varying the gap in carrier frequencies, and the location of the focus of the pulse beams, we can map the sample's Raman spectrum. Nonlinear interferometric vibrational imaging allows the Raman spectrum to be recovered without tuning the carrier frequencies of the pulses.[2]

The complexity of biological tissue poses a problem. With so many chemical species present, the fingerprint spectral region is crowded, and it can be difficult to determine what combination of species gives rise to a spectrum. Moreover, signal nonspecific to the vibrational modes of the molecules in the sample—which originates from electronic four wave mixing processes (often called nonresonant CARS)—can overwhelm the resonant signal.

Typically optical pulses are used to induce CARS and then infer the presence of a certain species among the plurality of those present in the sample. Instead, using a priori knowledge of the Raman spectrum of a certain species, we designed shaped optical pulses to generate a large CARS signal from a chemical of interest, while only generating a small or no signal from others.[3,4]

The idea was to use a single broadband optical pulse to excite all vibrational modes of the molecules in the sample over a given bandwidth. But the pulse was conceived so that only a subset of modes would generate CARS signals that interfere constructively at a detector. The signals from other modes will interfere destructively and produce a much weaker signal. The subset can correspond, for example, to the vibrational modes of a single chemical species. Moreover, pulse shaping leads to a longer duration, reducing nonresonant background signal. We shape the pulse so that its intensity envelope approximates the matched filter of that susceptibility.



(a) Energy diagram of CARS. (b) Schematic of instrument. (c) Raman spectra of DNA and RNA phosphodiester vibrational modes. (d) Predicted autocorrelation signals from instrument with pulses designed to coherently excite vibrational modes from DNA.

Although an analogue of the matched filter concept has been applied to CARS in the frequency domain,[5] our pulse design algorithm explicitly constructs an approximation to the matched filter of a given third-order nonlinear susceptibility in the time domain, subject to constraints of finite time support and realizability given an initial laser pulse spectrum. We also propose a heterodyne detection method to further increase the instrument's sensitivity. A reference pulse is specifically shaped to have the form of the emitted CARS signal of a chemical species. The peak of the photodiode response used to detect the combined sample and reference signals will then be found when the relative time delay between the sample and reference arms is adjusted to zero.

We performed a calculation to predict the output of the instrument in distinguishing DNA and RNA based on slight differences in the vibrational stretch frequencies of their phosphodiester backbones. We used our algorithm to design a pulse to coherently excite stretch vibrations of the DNA backbone. The spectra of the vibrations modeled were similar. Nevertheless, the autocorrelation signal predicted from DNA was more than 10 times that of RNA. Hence, even closely related biochemical species could be distinguished.

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References

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