In situ optical spectroscopy of crystallization: One crystal nucleation at a time

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Understanding the microscopic picture of crystal nucleation is crucial for rational control of crystallization processes and crystal polymorphs. A major challenge for experimentalists to study crystal nucleation is its stochastic and heterogeneous nature at the nanoscale: it is impossible to predict where and when a nucleation occurs. Despite the difficulty, a real-time observation of nucleation dynamics has been long desired as it can provide key information to establishing the microscopic picture. A recent breakthrough on this aspect was the development of cryo and liquid cell transmission electron microscopy (TEM). The presence of morphologically "featureless" or "amorphous" clusters was observed before crystallization in several TEM studies, which suggests that the nucleation process can be more complex than the view offered by the classical nucleation theory [2-3]. While optical spectroscopy has the potential to reveal the details of the nucleation dynamics and the structure of prenucleation aggregates, the stochastic and heterogeneous nature of crystal nucleation has been particularly detrimental for its application. To this regard, there is a well-established powerful concept to deal with a stochastic, complex and heterogenous system: *Single molecule spectroscopy* [1]. The key to bring optical spectroscopy to the field with its full potential is to probe *single* nucleation event at a time, if we can predict precisely where a nucleation occurs.

We developed a method called Single Crystal Nucleation Spectroscopy (SCNS) which spectroscopically probes crystallization process in aqueous solution one crystal nucleation at a time [4]. SCNS is based on an extension of optical trapping Raman microspectroscopy combined with optical trapping induced crystallization. A single focused continuous wave (CW) laser beam serves a dual role as to spatially confine a crystal nucleation and to generate Raman spectrum during the nucleation process. We achieved measuring Raman spectral evolution of a *single* glycine crystal formation in aqueous solution with 46 ms time resolution at room temperature. The spectral analysis by a non-supervised spectral decomposition technique uncovered the Raman spectrum of prenucleation aggregates as well as its critical role as an intermediate species in the dynamics. The kinetical data showed that the spectrum of prenucleation aggregates were replaced by that of β-glycine which then quickly converted to α-glycine. Molecular dynamics simulation was performed on glycine molecules in water at two concentrations, where we observed the formation of clusters and their size growth with increasing concentration. The comparison of experimental and simulated Raman spectra of glycine aggregates suggests that the structure of glycine aggregates could be hydrogen-bonded linear networks which are the likely precursors of crystallization. This work provides a strong impetus for accelerating the investigation of crystal nucleation by optical spectroscopy.

References

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