Graphene-Based Microfluidics for Serial Crystallography

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Coupling microfluidic technology with advanced protein crystallography techniques for *in situ* analysis is an area of research where significant advances can be made. Microfluidic platforms have the benefit of not only enabling experiments at small volumes, but also of creating an environment free of inertial or convective effects while providing exquisite control over local conditions and gradients. A significant problem in microfluidic-based crystallography is the background scattering resulting from the interaction of X-rays with the device materials, which may reduce the signal to noise ratio obtained from small or weakly diffracting crystals. These challenges can be overcome by decreasing the overall thickness of the microfluidic device. Graphene is an atomically-thin layer that can act as an X-ray compatible window material with negligible contributions to background scattering. Additionally, the remarkable mechanical strength and gas impermeability of graphene further enhance its utility for integration into microfluidic devices for protein crystallography. To facilitate handling and incorporation of atomically-thin graphene layers into a microfluidic chip, we utilize graphene attached to a ~200 nm PMMA supportive film using standard CVD graphene transfer techniques. We have evaluated the ability of various graphene-PMMA films to protect against sample dehydration over time, along with various hydrophilic surface treatments to facilitate surface wetting in microfluidic channels. The potential for these ultra-thin devices to enable data collection from microcrystals was evaluated using serial Laue crystallography of caspase-7, a member of the cysteine aspartate family of proteases that regulate apoptosis, or programmed cell death. This work demonstrates the utility of ultra-thin graphene-PMMA films as a sub-micrometre level barrier against dehydration in microfluidic devices while enabling the collection of high quality X-ray diffraction data on biomedically important proteins. Our ultimate goal is to utilize graphene-based microfluidic technologies and serial crystallography to enable the use of chemical triggering for the time-resolved structural analysis of additional biologically and biomedically-relevant protein targets.