Synthesis of laser-generated gold nanomarkers by delayed bioconjugation

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Due to their high quantum yield, bioconjugated gold nanoparticles form excellent nanomarkers which show an enhanced bleaching stability and biocompatibility compared to organic dyes and quantum dots. For these applications they need to be functionalized with biomolecules e.g. aptamers to specifically bind to the surface of a cell and e.g. cell-penetrating peptides to cross the cell membrane. Fabrication of these bioconjugates by laser ablation is a promising technology, as it enables a well-defined surface coverage with ligands and particle size control, avoiding application of contaminating precursors as used during conventional chemical synthesis. The bioconjugation of gold nanoparticles can be performed in situ while ablation and conjugation occur simultaneously, achieving a 5 times higher surface coverage and a four times higher conjugation efficiency compared to chemical synthesis. A defined size up to 8 nm can be attained by in situ conjugation, however larger conjugates (> 8 nm) are hard to synthesize [1].

As cell and particularly nucleus penetrating properties are mainly depended on the size of the bioconjugates and the detection by light-microscopic methods is limited to larger particles (>50 nm) we present an alternate method for the fabrication of bioconjugated gold nanoparticles by delayed conjugation in liquid flow ablating a wire. As nanoparticles are generated they grow on ms to s time scale, while the presence of biomolecules quenches that growth (Figure 1) [2]. Using a thiol-functionalized oligonucleotide for conjugation, the size of achieved nanomarkers was tuned by altering both the flow-rate of the carrier stream and the biomolecule concentration. Applying this method, as illustrated in Figure 2, it was possible to generate bioconjugates in a size range between 15 and 50 nm, which are not accessible by in situ conjugation. Additionally the method is well-suited for the generation of multi-conjugates carrying different functional biomolecules which are added consecutively. Preliminary studies were successfully exercised by generating bi-conjugates composed of oligonucleotides and alkanethiols.

Figure 1: Delayed conjugation setup
Figure 2: Particle diameter of nanomarkers with varying conjugation time delay (Δτ) synthesized by delayed conjugation with oligonucleotides (1 µM)