Label-Free, Single Molecule Microsensors

Andrea M. Armani, Richard C. Flagan and Scott E. Fraser

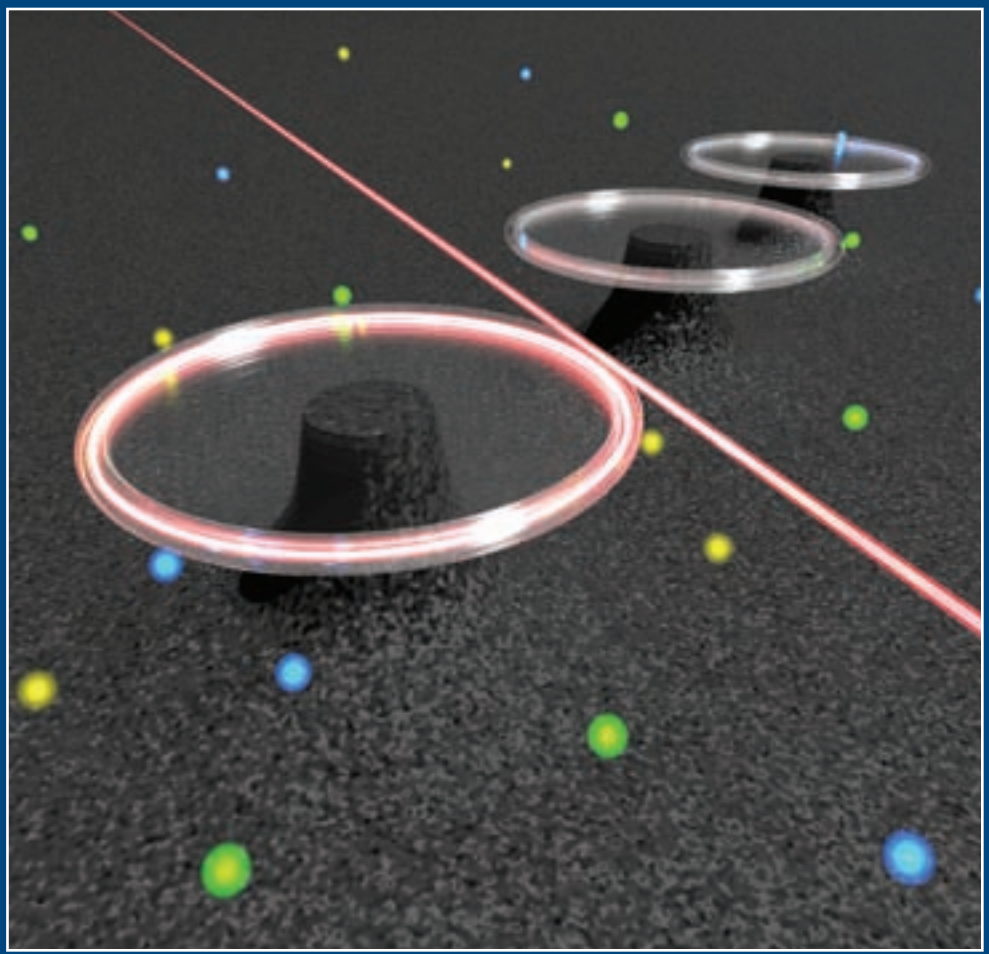
In optical microcavity-based detection, sensitivity is a result of the long photon lifetime inside the cavity; this extended lifetime amplifies small signals. Microtoroid resonators are especially suited for this application because of their exceptionally high Q factors (above 100 million).[1,2]

The detection mechanism is surprisingly simple. The binding of molecules to the surface of the resonant cavity induces a refractive index change, which increases the resonant wavelength of the microcavity. However, both sensitivity and specificity are important characteristics in biosensor design. Specificity is achieved through surface functionalization or the attachment of antibodies to the surface of the resonant cavity.

Label-free, single-molecule detection of interleukin-2 (IL-2)—a cytokine released in response to immune system activation by extrinsic and intrinsic stimuli—was demonstrated using a microtoroid resonator. The surface of the microtoroid was sensitized for detection using polyclonal IL-2 antibodies, and detection experiments were performed both in buffer and in serum to verify the sensor's application in a therapeutic situation.

Serum contains many additional molecules that could potentially interfere with the sensor's single molecule detection ability. Several IL-2 concentrations, ranging from 100 aM to 900 aM, were used. The resonant wavelength was monitored in real-time on an oscilloscope and the resonance location was downloaded directly onto a computer. The data acquisition rate, solution injection rate and IL-2 concentration were optimized to allow single-molecule binding events to be resolved.

Ultra-sensitive detection of serum immune agents, such as IL-2, is immediately relevant to the medical community. Additional applications can be found in fundamental studies of single cell signaling and protein folding. ◭



Rendering of an array of tapered fiber waveguide-coupled microtoroid resonators surrounded by spherical biological molecules.

[Andrea M. Armani (armani@caltech.edu), Richard C. Flagan and Scott E. Flagan are members of the engineering and applied science division of the California Institute in Technology, Pasadena, Calif. Additionally, Flagan is a member of the chemical engineering division and Fraser is a member of the biology division.]

References

1. A. M. Armani et al. "Label-free, single-molecule detection with optical microcavities," Science **317**, 783 (2007), published online July 5, 2007 [DOI: 10.1126/science.1145002].
2. D.K. Armani et al. "Ultra-high-Q toroid microcavity on a chip," Nature **421**, 925-8 (2003).

Parallel and Computer-Automated Optical Micro-Assembly

Jesper Glückstad, Ivan Perch-Nielsen, Carlo A. Alonzo, Jeppe S. Dam and Peter John Rodrigo

The parallel assembly of minute components with sizes in the range of 1-100 µm continues to be an exciting scientific challenge within micro-mechanics. Research into real-time, massively parallel and three-dimensional micro-assembly schemes may lead to revolutionary developments of new and reconfigurable micro-opto-electromechanical-systems.

In particular, micro-assembly done within a liquid environment seems attractive to pursue, due to the fact that the undesirable effects of van der Waals and surface interactions can be kept at a minimum. Most contemporary techniques for micro-integration of submerged components rely on self-assembly schemes. However, micro-scale self-assembly in liquid has some constraints, such as the tradeoff between how accurate micro-elements can be positioned to receptor sites and the yield or efficiency of the overall process.

To overcome this, the sample must go through a few recirculations, and the template may require some mechanical agitation. To improve positioning accuracy of micro-components on a template, one may apply suitable matching of the geometrical shapes of the building blocks with their receptor sites.

Real-time reconfigurable arrays of a plurality of interactive optical traps are perhaps a more attractive alternative that can enable precise assembly of freely suspended microstructures. Multiple optical traps are capable of holding, positioning and rotating a plurality of mesoscopic objects in 3D.[1] In the past year, we have demonstrated the first all-optical, directed micro-assembly scheme.[2] We did this by tiling a plurality of microscopic structural elements on a planar substrate using real-time reconfigurable optical traps from a variant of the parallel optical manipulation schemes on which we have previously reported.[3,4]

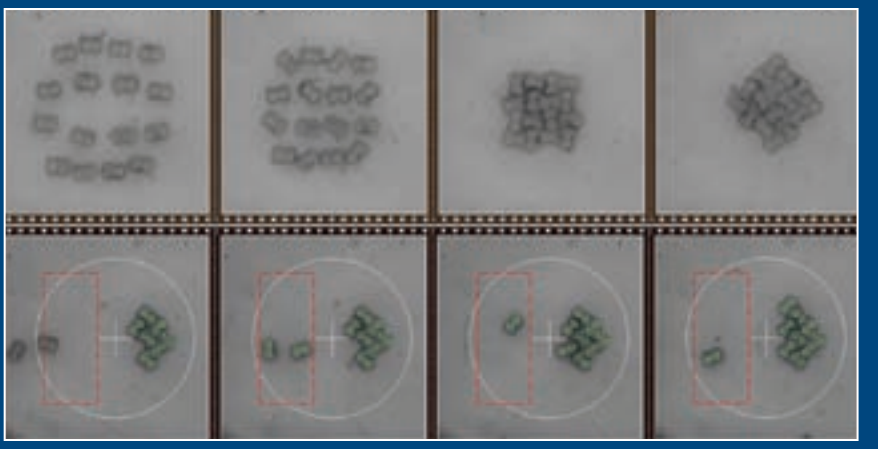
The number of optical traps, their intensity profiles and spatial locations were all controlled either interactively or in an automated way using an advanced computer interface. Under computer-automated control, the system demonstrated the capability for fully autonomous search-and-collect routines without the need for any user intervention.[5]

Our experimental demonstrations showed that optical traps of a few milliwatts can achieve good positional and rotational control of the assembled micro-structures. Efficient tiling also benefited from applying shape complementarity among the micro-puzzle pieces that have identical geometrical shapes and in-plane rotational symmetry. Finally, the puzzle pieces had an elongated aspect ratio so that the orientations were conveniently determined by an image analysis subroutine; this made it easy to orient the projected elongated optical traps. The micro-fabrication of the puzzle pieces was achieved by a standard femtosecond laser two-photon polymerization technique.

[Jesper Glückstad (jesper.gluckstad@risoe.dk), Ivan Perch-Nielsen, Carlo A. Alonzo, Jeppe S. Dam and Peter John Rodrigo are with the optics and plasma research department, Risø National Laboratory, Technical University of Denmark.]

References

1. Glückstad et al. "Optical 3D manipulation and observation in real-time (invited paper)," J. Robotics Mechatronics **18**(6), 692-7 (2006).
2. P. J. Rodrigo et al. "2D optical manipulation and assembly of shape-complementary planar microstructures," Opt. Express **15**, 9009-14 (2007).
3. P. J. Rodrigo et al. "GPC-based optical micromanipulation in 3D real-time using a single spatial light modulator," Opt. Express **14**, 13107-12 (2006).
4. P. J. Rodrigo et al. "Three-dimensional forces in GPC-based counterpropagating-beam traps," Opt. Express **14**, 5812-22 (2006).
5. I. Perch-Nielsen et al. "Autonomous and 3D real-time multi-beam manipulation in a microfluidic environment," Opt. Express **14**, 12199-205 (2006).



(Top) Micro-scale tessellation of 16 micro-puzzle pieces optically assembled in a parallel manner into a 4 x 4 tiling arrangement. Once assembled, all elements remain intact in the whole structure, which can also be displaced and rotated by the interactive group of optical traps. (Bottom) Computer-automated "hunt-and-collect" demonstration for joining micro-puzzle pieces. The dashed rectangle highlights the detection area, where incoming pieces from the left are automatically detected. Once detected, trapping beams with appropriate orientations and target trajectories are subsequently created.

The Fundamental Limit to Optical Components

David A.B. Miller

Is there a fundamental limit to how small we could make an optical component—for example, one that separates beams of different colors or gives us slow-light optical delay? For applications such as wavelength-division multiplexers, we would like smaller, cheaper devices. Nanophotonics offers new opportunities to create them.

For traditional devices, such as Fabry-Perot resonators or gratings, we already have good models to predict performance limits. But for some nanophotonic structures, the only way to design them is by trial and error; we cannot logically separate the functions of the different parts. Simply put, we do not know how they work, so no device model can tell us how well they could work. Since designing nanophotonic structures is computationally hard, we want at least an upper limit so we know when to stop optimization. Intriguingly, empirical designs for layered dielectric superprism wavelength splitters hint strongly at just such an underlying performance bound.[1]

Such a bounding limit should be independent of the details of the structure's design, and should work for large contrasts in refractive index, including even the very large dielectric constants of metals. Constructing such a limit is challenging; the mathematics must include multiple strong scattering. Obvious approaches such as summing series typically do not converge, for example.

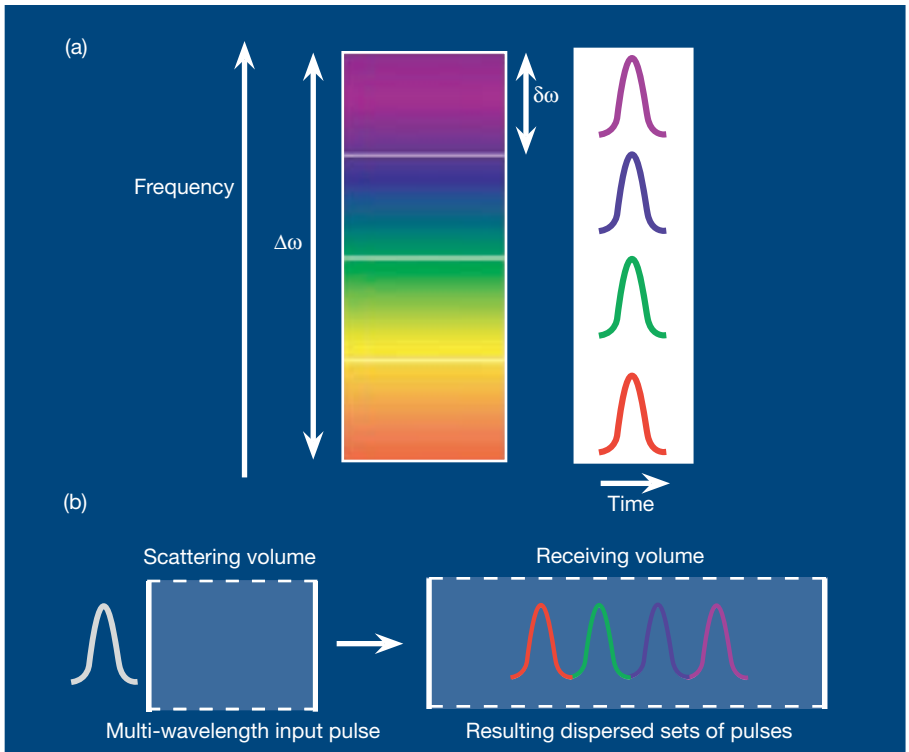
We recently proved a general theorem for such strong multiple scattering,[2] which can be generally stated for linear systems, and can give simple bounding limits for optical components. We also showed explicitly how it can be applied to one-dimensional structures, such as dielectric stacks or single-mode waveguides.

The idea behind the limit is to find a bound to the number of mathematically orthogonal functions that could be generated in a receiving volume as a result of the scattering of an incident wave by a scatterer (i.e., the optical device). Surprisingly, with only minor restrictions, there is quite a specific answer for such a bound.

We can ask, for example, how many distinct colors of pulses can be separated in time (i.e., dispersed) by passing through a one-dimensional structure (see figure). The upper bound to that number is essentially the length of the structure in wavelengths times the magnitude of the largest dielectric constant variation anywhere in the structure, completely independent of the details of the design. An example one-dimensional glass/air structure that would disperse pulses of 32 center wavelengths in the C-band must be at least 41.7 μm thick.

This same result also bounds the performance of fixed linear slow-light structures, including both photonic nanostructures and atomic vapors, where it limits the number of bits of delay with an almost identical product formula.[3]

We expect to be able to extend the use of this broad theorem to 2D and 3D structures to give broad limits to the possible performance of a wide range of optical components, including photonic crystals and other nanophotonic structures. ◭



(a) Pulses of different center frequencies, shown both in frequency and in time. (b) Conceptual structure of a device (the scattering volume) to separate the pulses at the output (the receiving volume).

[David A.B. Miller (dabm@ee.stanford.edu) is with the Ginzton Laboratory, Stanford University, Stanford, Calif.]

References

1. M. Gerken and D.A.B. Miller. "Limits to the performance of dispersive thin-film stacks," Appl. Opt. **44**(18), 3349–57 (2005).
2. D.A.B. Miller. "Fundamental limit for optical components," J. Opt. Soc. Am. B **24**, A1-A18 (2007).
3. D.A.B. Miller. Slow Light and Fast Light Topical Meeting, July 9, 2007, Paper SMB1; "Fundamental Limit to Linear One-Dimensional Slow Light Structures," Phys. Rev. Lett. (to be published) arXiv:0710.3575v1 [physics.optics].