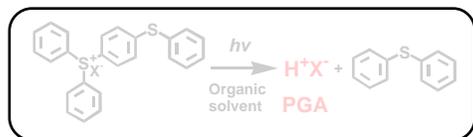
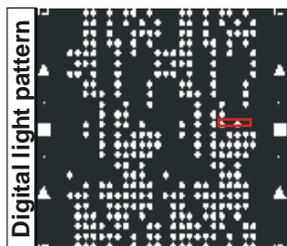
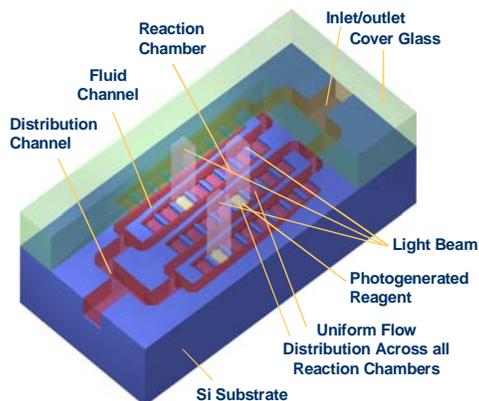
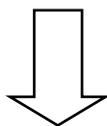


# ▶ $\mu$ ParaFlo™ Synthesis Technology

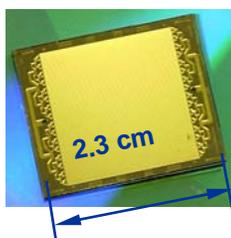
## PicoArray Reactor



A novel and proprietary solution photochemistry



## $\mu$ ParaFlo™ microfluidic chip



## $\mu$ ParaFlo™ Technology Makes it Possible

The scientists and engineers at our technology partner, Atactic Technologies, have developed platform technologies that encompass a new class of microfluidic  $\mu$ ParaFlo™ reaction devices, an advanced digital light synthesizer apparatus, and picoliter scale biochemical processes. The functionalized  $\mu$ ParaFlo™ chips are particularly suited for applications where small sample consumption, contamination-free, and performance-reproducibility are primary concerns.

This technology enables the massively parallel synthesis of high quality DNA and RNA oligonucleotides as well as peptides and peptidomimetics in picoliter-scale reaction chambers at high yield without the need for the expensive, inconvenient microfabricated photomasks previously used.

### PicoArray Reactor

The microfluidic PicoArray reactor is made from silicon using standard microelectronic fabrication procedures. The reactor contains three topographical features: pico-reaction chambers, fluid microchannels, and inlet/outlet through holes. The chip contains 128 x 31 (total 3698) individual reaction chambers, each with an internal volume of 270  $\mu$ l. The fluid microchannels are of a tapered shape that was derived from a fluid mechanical model to produce a uniform flow rate across all reaction chambers. This technology enables a high density of uniform spots.

### Digital Photolithographic Optical Device

A significant improvement in making photolithography a practical method for combinatorial chemical synthesis is the introduction of the digital optical device for light patterning projection onto a reaction surface. This technology allows parallel synthesis of a large number of different molecules on the same reaction surface without the need for expensive, inconvenient microfabricated photomasks.

Instead, a computer generates the digital mask and a Digital Light Projector (DLP) projects the light beam very accurately into the micro reaction chambers where a photogenerated reagent is produced. This method provides greater flexibility since microarrays containing any desirable sequences can be obtained in a much shorter time and at a much lower cost.

### Photo Generated Acid (PGA) Deprotection

A PGA precursor is fed into the microfluidic chamber prior to the light irradiation step to create the acid which removes the acid labile DMT protecting group. This process is simple in that it does not require an electrochemical surface or specialty monomers with photolabile protecting groups (PLPG).

Electrochemical deprotection methods require a complex circuitry of electrodes that can withstand contact with the strong organic reagents through multiple synthesis cycles. Another limitation of deprotection with electrodes is that side reactions can occur on the electrode surface. The need for specialty PLPG monomers means no flexibility for creating content variations in the sequences. Studies show the reaction efficiency is much lower than standard monomers and they have been known to give rise to randomized misincorporation or insertion errors lowering sequence fidelity.

PGA deprotection allows parallel synthesis with conventional chemicals and supplies, following well established synthesis processes. The quality of the synthesis reaction is greater than 98.8% ASWY and this approach is very flexible because virtually any modified monomer can be used creating a wide array of non-regular oligonucleotides.



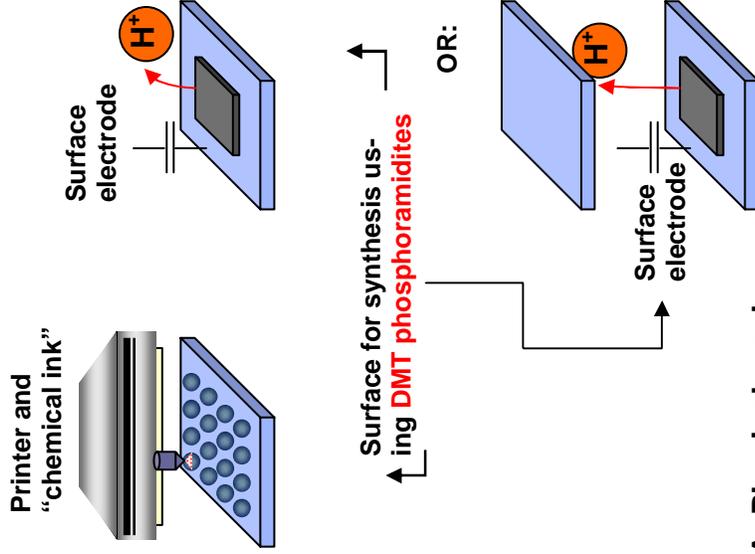
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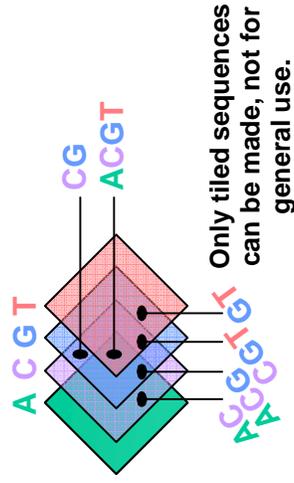
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# Progression of *in situ* Synthesis of Oligonucleotide Microarrays

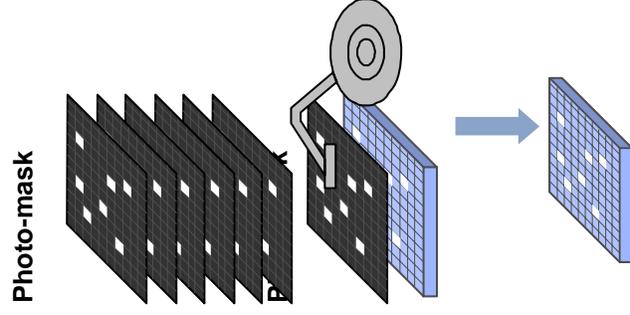
## C. Electrochemical deprotection based synthesis



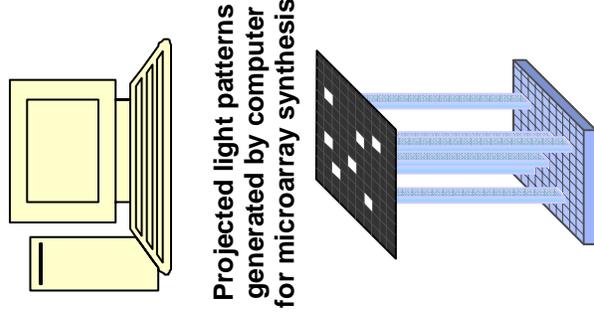
## A. Physical masks



## D. Photolabile deprotection and mask based synthesis

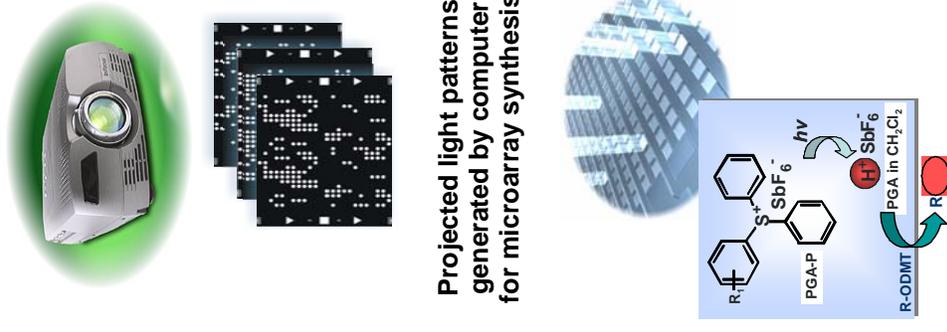


## E. Photolabile deprotection and digital lithography based synthesis



Surface for synthesis using **photolabile group protected phosphoramidites**  
Not suitable for anything else but DNA chips

## F. PGA deprotection and digital lithography based synthesis



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