**Adding the chemical dimension to lithography at all scales:   
Enabling cellular therapies & other adventures in biology and medicine**

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**Chemical Patterning and Lithography**

By controlling the exposed chemical functionality of materials from the submolecular through the centimeter scales, we have enabled new capabilities in biology, medicine, and other areas.1 I will discuss current and upcoming advances and will pose the challenges that lie ahead in creating, developing, and applying new tools using this capability.

**Sensing Signaling Molecules and Biomarkers**

These advances include using biomolecular recognition in sensor arrays to probe dynamic chemistry in the brain and microbiome systems.2-4 We have developed and are applying highly sensitive and specific field-effect transistor-based sensors that are functionalized with aptamers as are artificial receptors for signalling molecules and biomarkers. By design, these sensors can operate *in vivo* as well as in biological fluids without dilution. 2

**Cellular Therapies**

We introduce biomolecular payloads into cells for gene editing at high throughput for off-the-shelf solutions targeting hemoglobinopathies, immune diseases, and cancers. We circumvent the need for viral transfection and electroporation, both of which have significant disadvantages in safety, throughput, cell viability, and cost. Mechanical deformation can make cell membranes transiently porous and enable gene-editing payloads to enter cells. These methods use specific chemical functionalization and control of surface contact and adhesion in microfluidic channels.

**References**

1. Claridge, S. A., Liao, W.-S., Thomas, J. C., Zhao, Y., Cao, H., Cheunkar, S., Serino, A. C., Andrews, A. M., & Weiss, P. S. (2013). From the bottom up: Dimensional control and characterization in molecular monolayers. Chem. Soc. Rev., 2013, 42, 2725-2745.
2. Nakatsuka, N., Yang, K. A., Abendroth, J. M., Cheung, K., Xu, X., Yang, H., Zhao, C., Zhu, B., Rim, Y. S., Yang Y., Weiss, P. S., Stojanović, M. N., & Andrews, A. M. (2017). Aptamer–field-effect transistors overcome Debye length limitations for small-molecule sensing. Science, 362, 319-324.
3. Alivisatos, A. P. *et al*. (2013). Nanotools for neuroscience and brain activity mapping. ACS Nano, 7, 1850-1866.
4. Biteen, J. S. *et al*. (2016). Tools for the microbiome: Nano and beyond. ACS Nano, 10, 6-37.