# *Laser Processing for Biological Applications*


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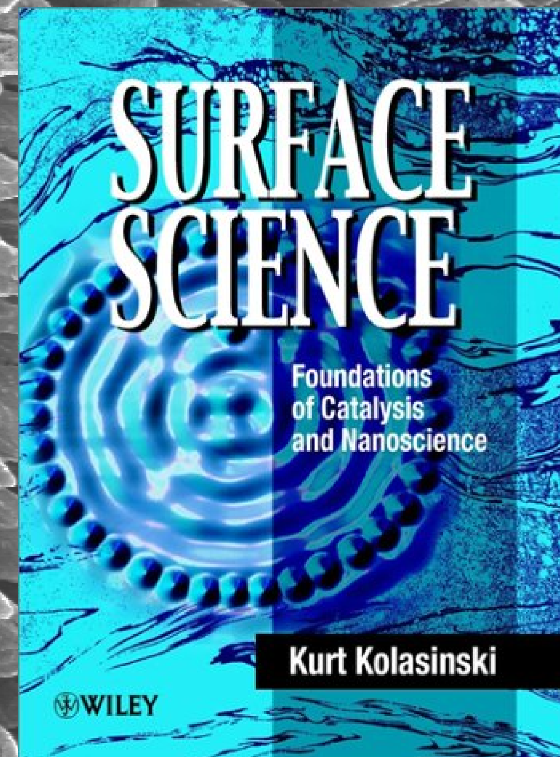


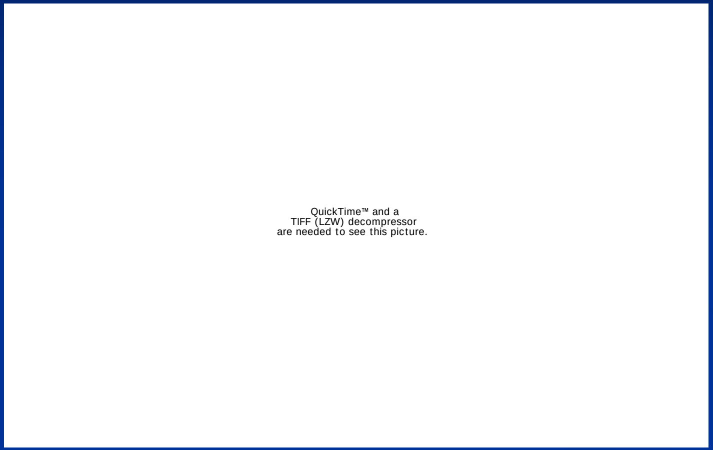

CAMOS
Center for Atomic, Molecular, and Optical Science

# Outline

- Surface Modification (Kolasinski & Harrison)
  - Cell/Surface Interactions
  - Porosity Control
  - Topological Control– Pillar Formation
  - Thin Film Composition Control
- Laser Microfabrication (Helvajian, Karlinsey, Landers)
  - Integrated Devices on a Chip
  - DNA µTotal Analysis
  - High Throughput Analysis

# Motivation

- Black Silicon




- THz
- Microneedles/Drug Delivery
- Biosampling
- Patterning for cell/surface interactions
- Implant coatings
- Separations & Analysis

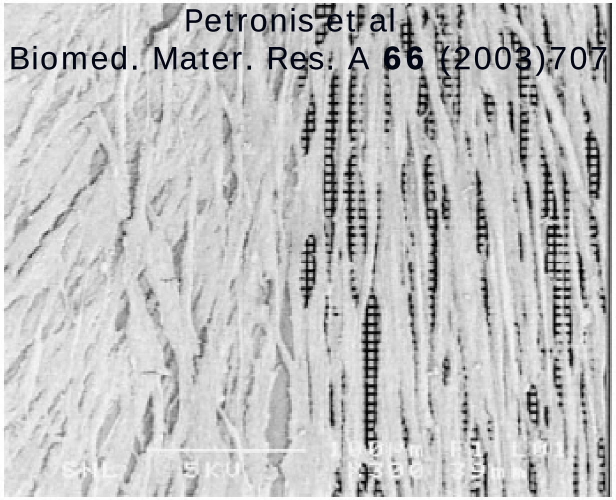
# Cell/Surface Interactions

- Cells respond to several chemical and geometrical variables
- Functional Groups
- Hydrophilicity
- Porosity
- Topography
- Elasticity

Gastner & Ratner, Surf. Sci 500 (2002) 28

Fig. 1. A scanning electron micrograph of a myoblast cell interacting with a synthetic surface. The cell is approximately 10 μm in length.

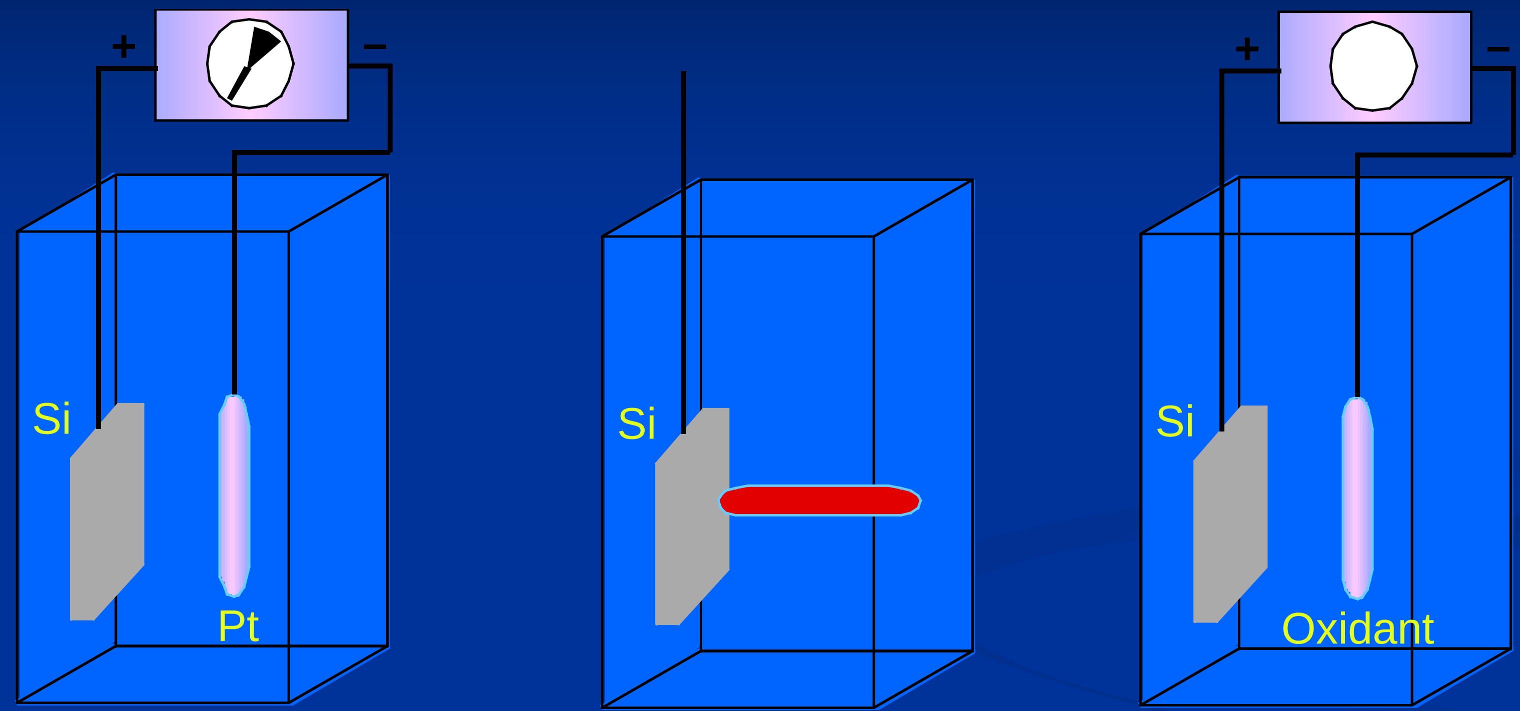
Petronis et al
J. Biomed. Mater. Res. A **66** (2003)707



c)

**Figure 9.** SEM of fibroblast cells cultured for 5 days on 1.8-μm-wide channels. The morphological expression of the cells is typical for a healthy fibroblast culture: (a) cells secrete collagen fibers and (b) are closely packed in an orderly fashion. However, the cells form a denser layer on the flat surface than on the channels (c).

# Porous Si Formation



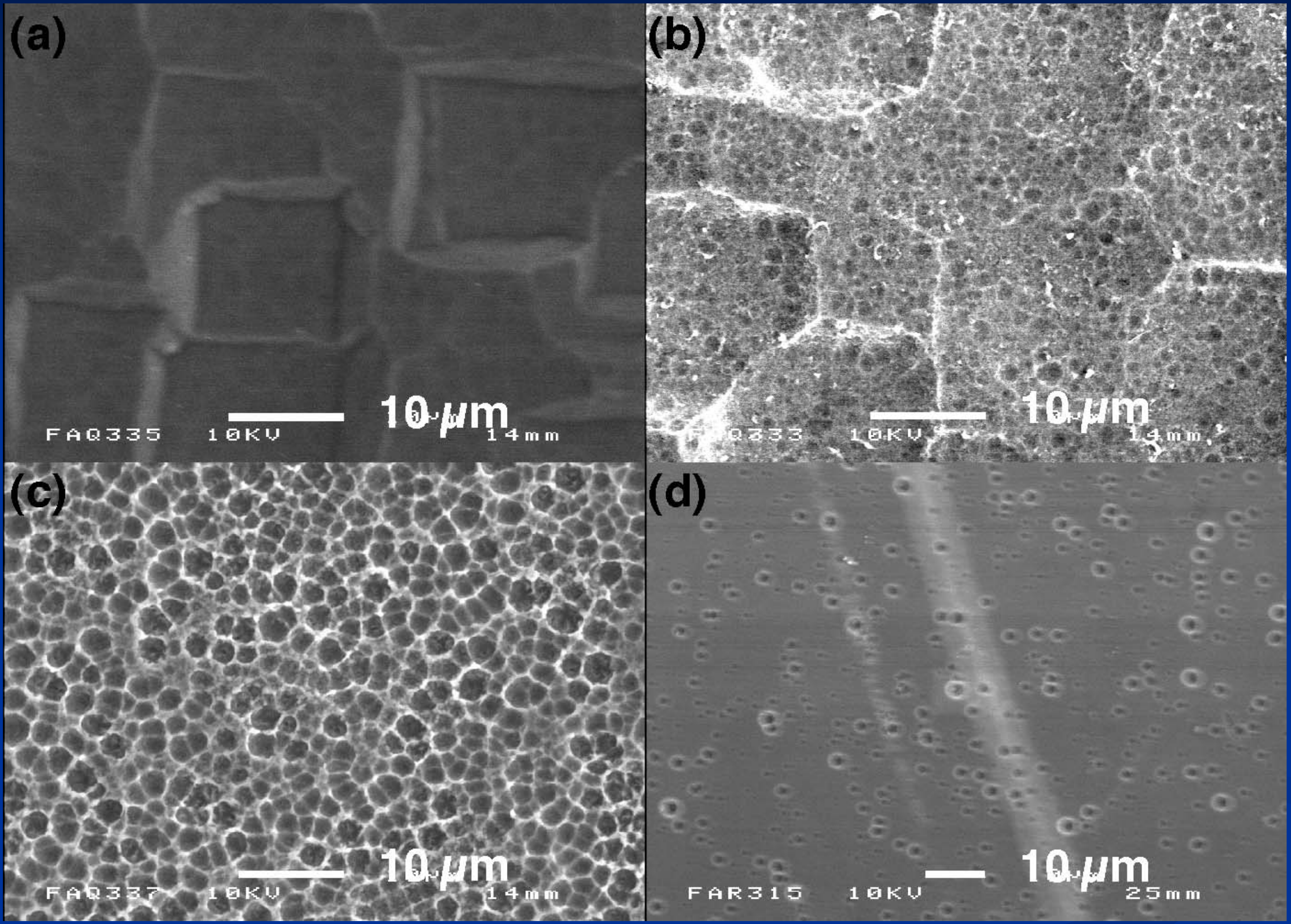

HF + $H_2O$ + ethanol

HF + $H_2O$ + laser

HF + $H_2O$ + $Fe^{3+}$/$Mn^{7+}$/$HNO_3$

- Requires acidified fluoride solution (HF, $NH_4HF_2$, etc)
- + source of valence band holes

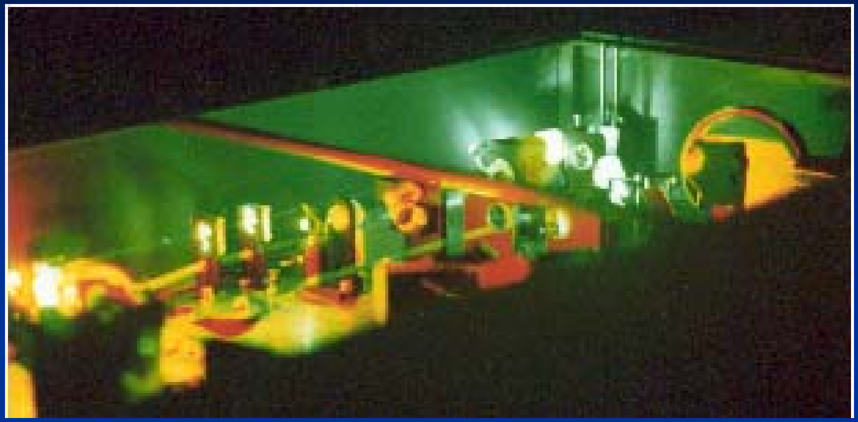
# Pore Structure Control

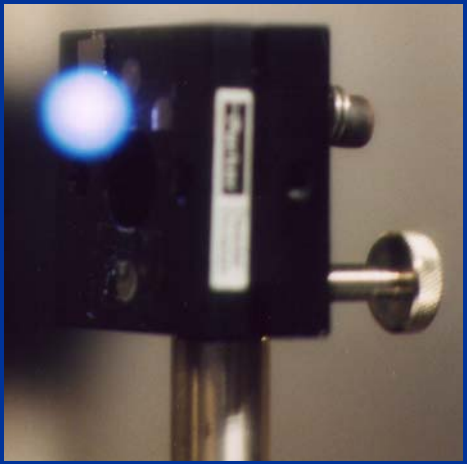



Solution composition & etching parameter can be used to control porosity & pore size distribution

Nahidi & Kolasinski, J Electrochem Soc (submitted)

# Chemically Assisted Laser Ablation





- Ti:Sapphire (Femto Pillars)
  - 50 Hz – 1 kHz rep rate
  - ≤3 mJ per pulse
  - 120 fs pulse duration
  - ~1 J $cm^{-2}$
  - ~$10^{13}$ W $cm^{-2}$
  - 780 or 390 nm
- XeCl Excimer (ns Pillars)
  - 1 – 50 Hz rep rate
  - ≤150 mJ per pulse
  - 20 ns pulse duration
  - ~3 J $cm^{-2}$
  - ~$10^{8}$ W $cm^{-2}$
  - 308 nm

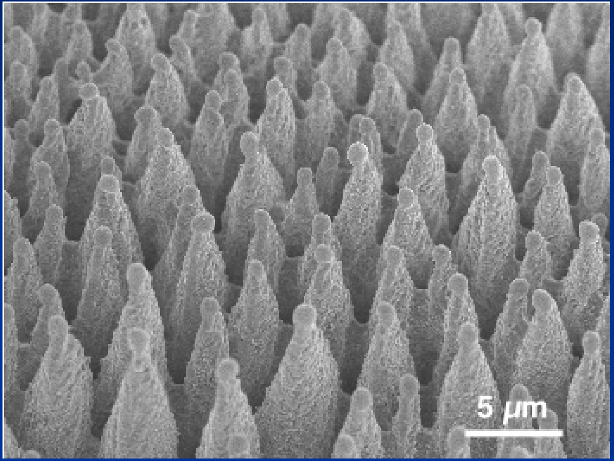
500-1000 Shots

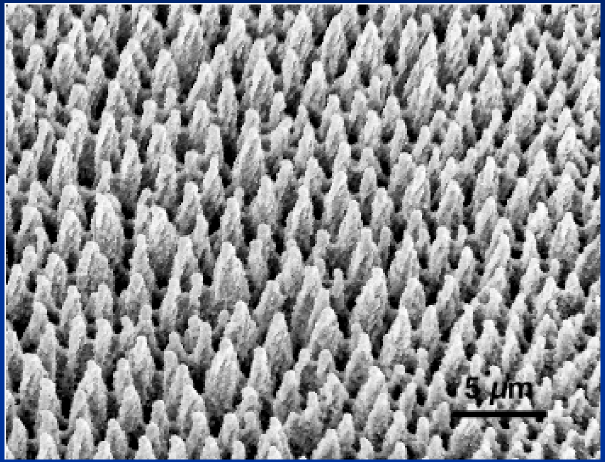
# Femto vs ns Pillars

780 nm fs

390 nm fs

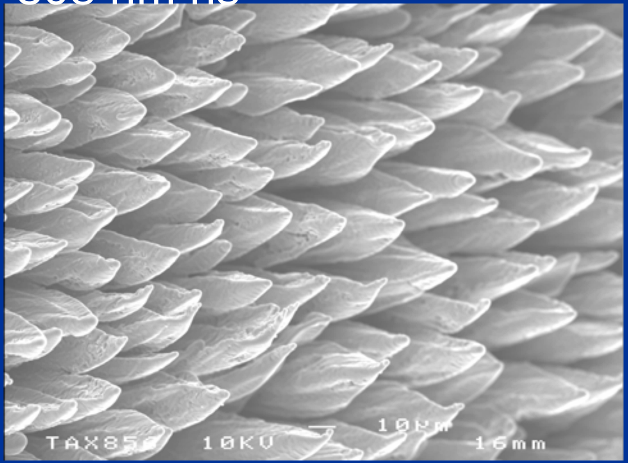
Riedel, Hernández-Pozos, Kolasinski & Palmer, Appl. Phys. A **78** (2004) 381




⇓ **7× scale change** ⇑

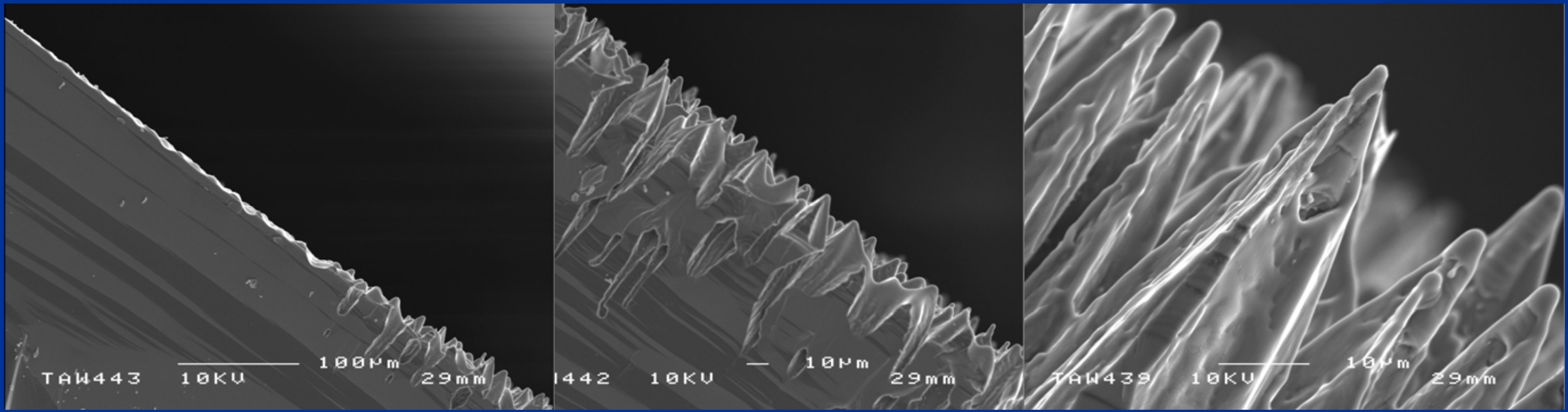
308 nm ns



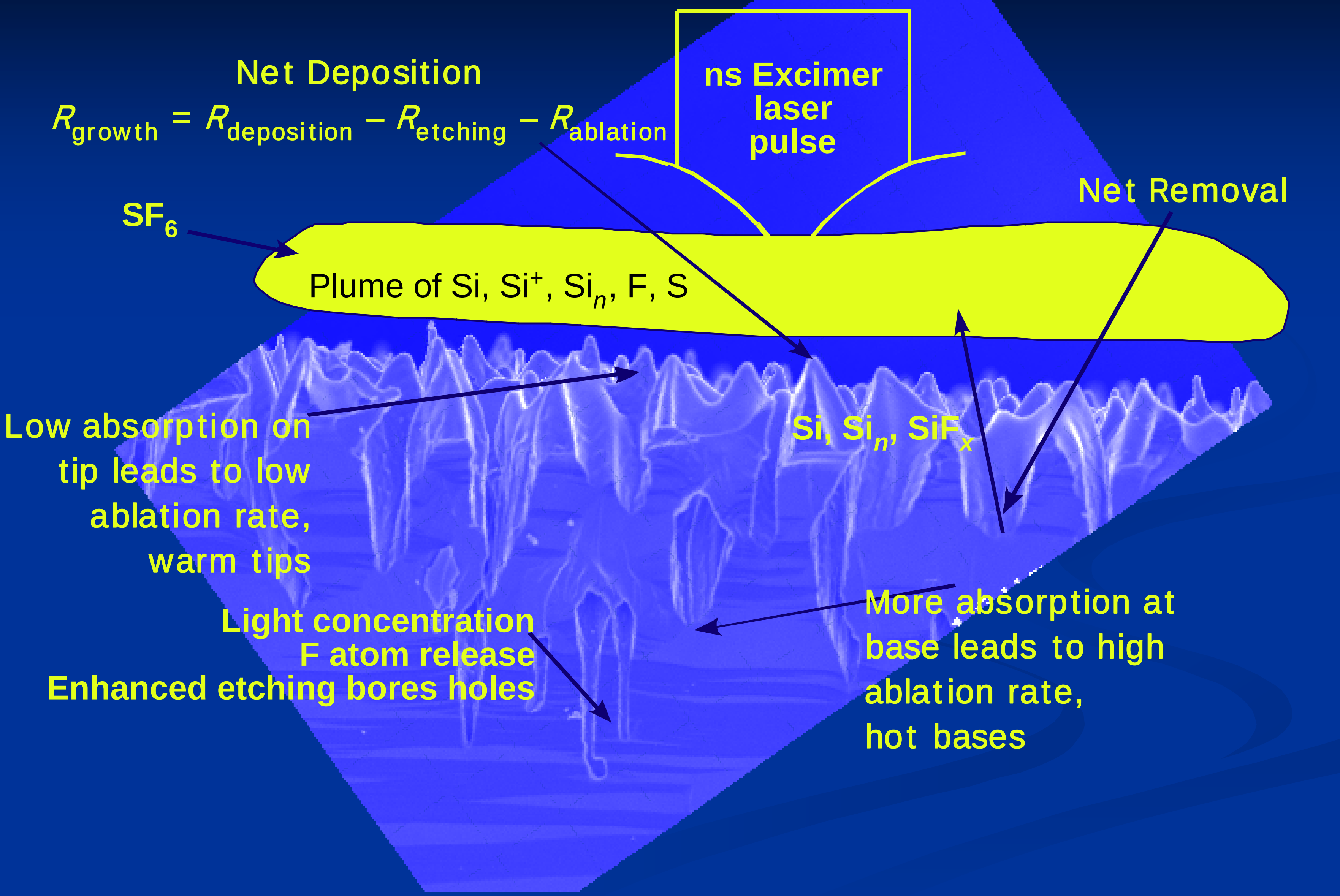

- Femto pillars are much smaller
- Characteristic ball on top for fs
- Response of pillar size to wavelength much different (fs proportional, ns no dependence)
- Length scale of initial surface modulation is different fs vs ns

# ns Pillar Development

- Modulations
- Precursor Holes
- Pillars

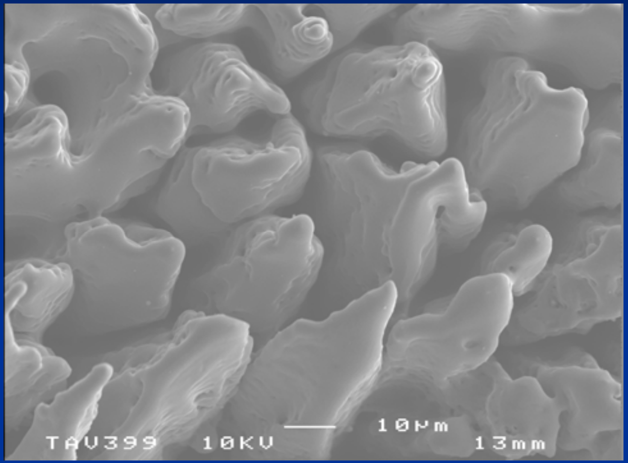


# Pillar Formation Processes

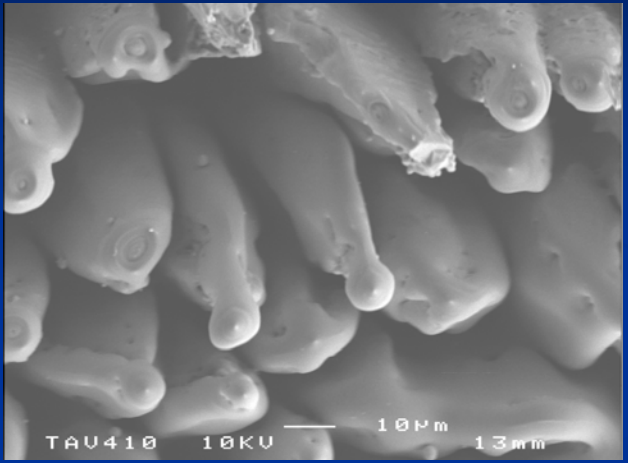


# ns Irradiation
# Gas composition strongly effects pillars

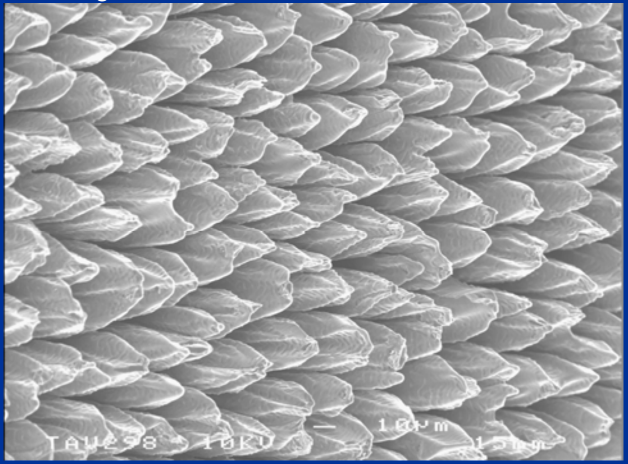
$NF_3$




5% HCl/He

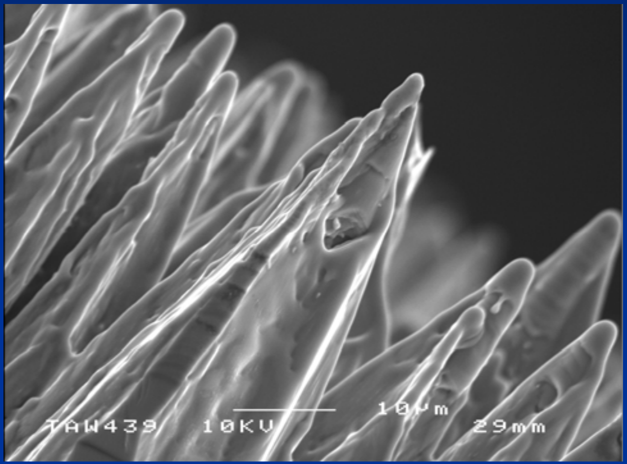


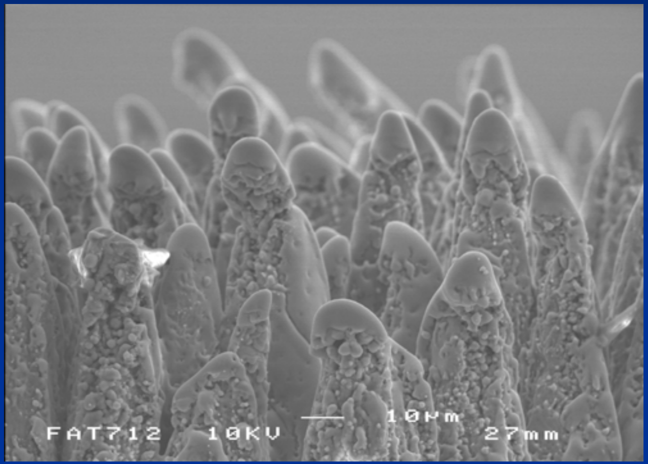

$SF_6$



- No pillars formed in $NH_3$, $CF_3I$, $CF_3CH_3$
- Most regular, densely packed pillars form in $SF_6$
  - Tens of µm long
  - ~5 µm at apex
  - ~1400 pillars $mm^{-2}$

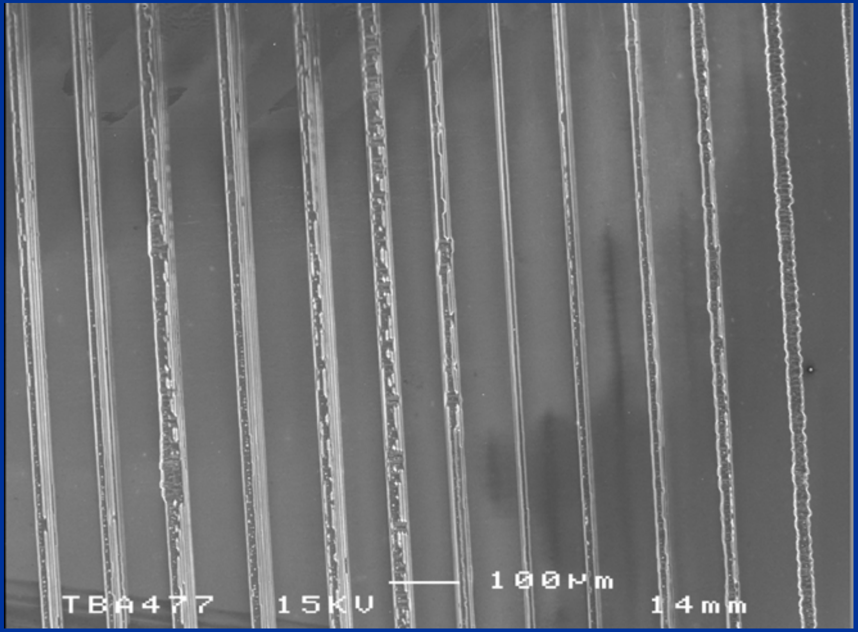
# $SiF_6$ vs HCl



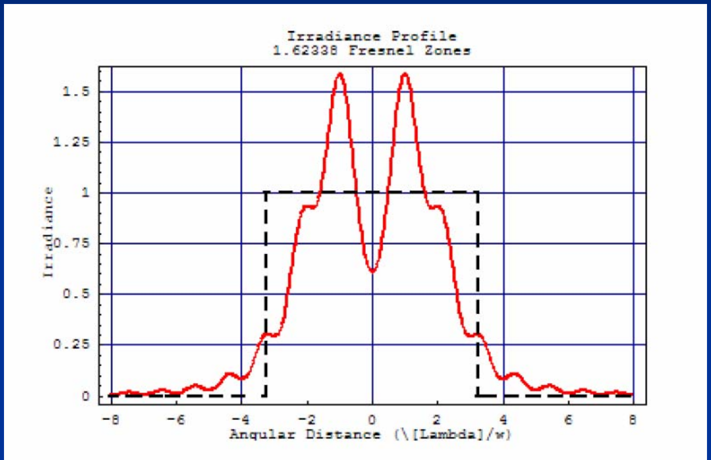

- $SiF_6$
  Smooth, regular, conical, straight, more etching
- HCl
  Spackled, blunt, drooping, big, more clusters

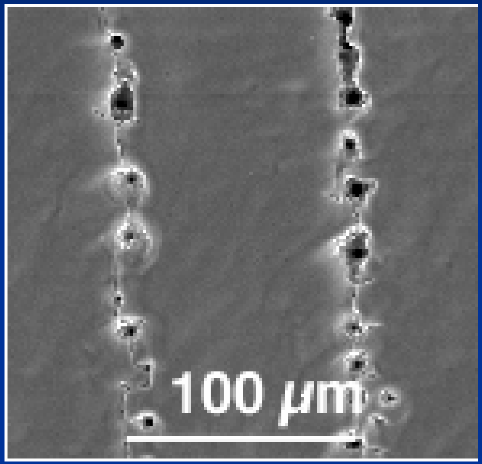
# Etch Grating Prior to Irradiation

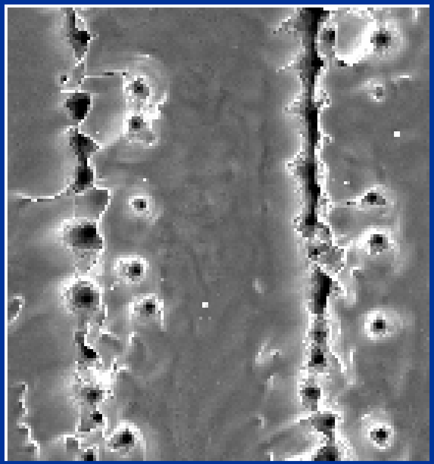


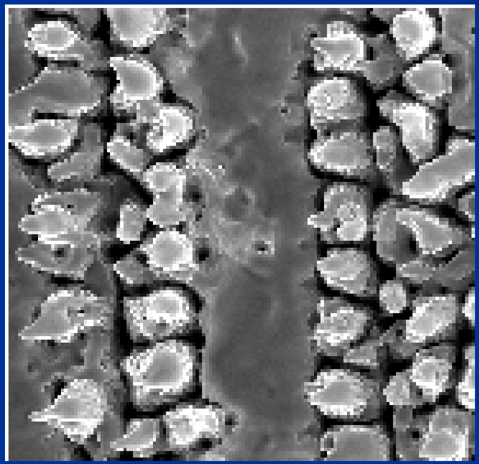

- Mechanically scribe rules
- Straighten & sharpen edges with KOH etching
- Width, depth, pitch all critical
- Rule used to align precursor holes

# Pre-Treatment for Ordering

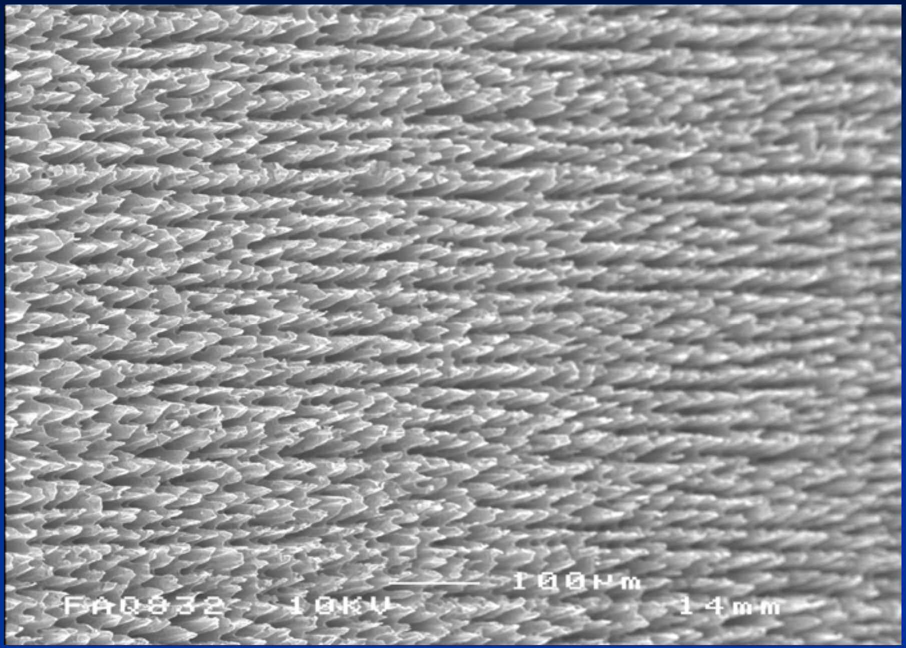




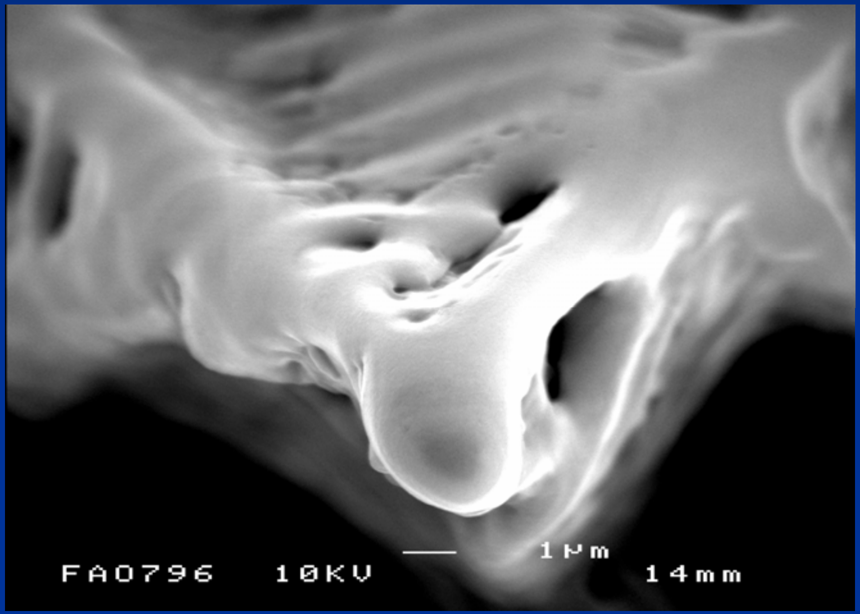
# Ordered Arrays of Pillars




Mills & Kolasinski, *J Phys D 38* (2005) 632

- Arbitrarily large areas can be patterned & covered
- Grating rules enhance intensity guide initial hole formation
- Adjacent row of holes aligned parallel
- Coupling due to lattice strain
- Growth faster in unpolished areas
- Best ordering when grating on polished side

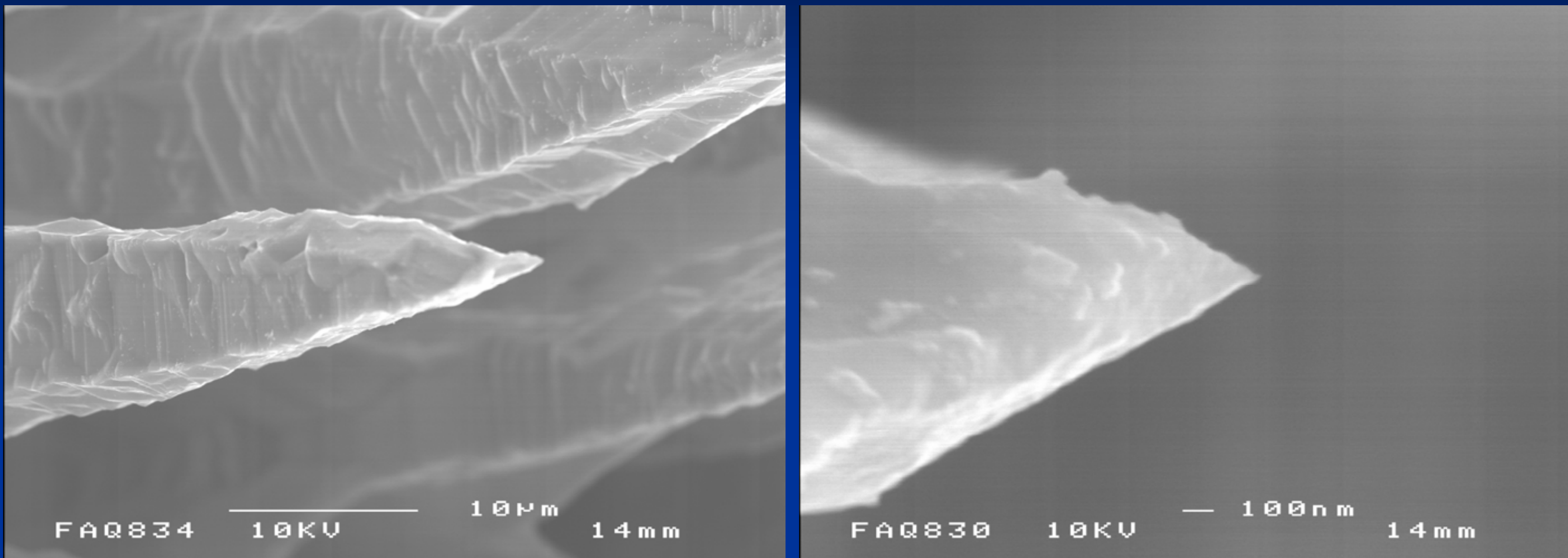
# Post-Treatment Porous Pillars




- Pillars porosified by stain etching
  HF + $HNO_3$ or $Fe^{3+}$ or $MnO_4^-$
- μporous layer on solid core
- Gross structure of pillar not changed

Mills & Kolasinski, *J Vac Sci Technol A* 22 (2004) 1647

# Thinning Pillars in KOH

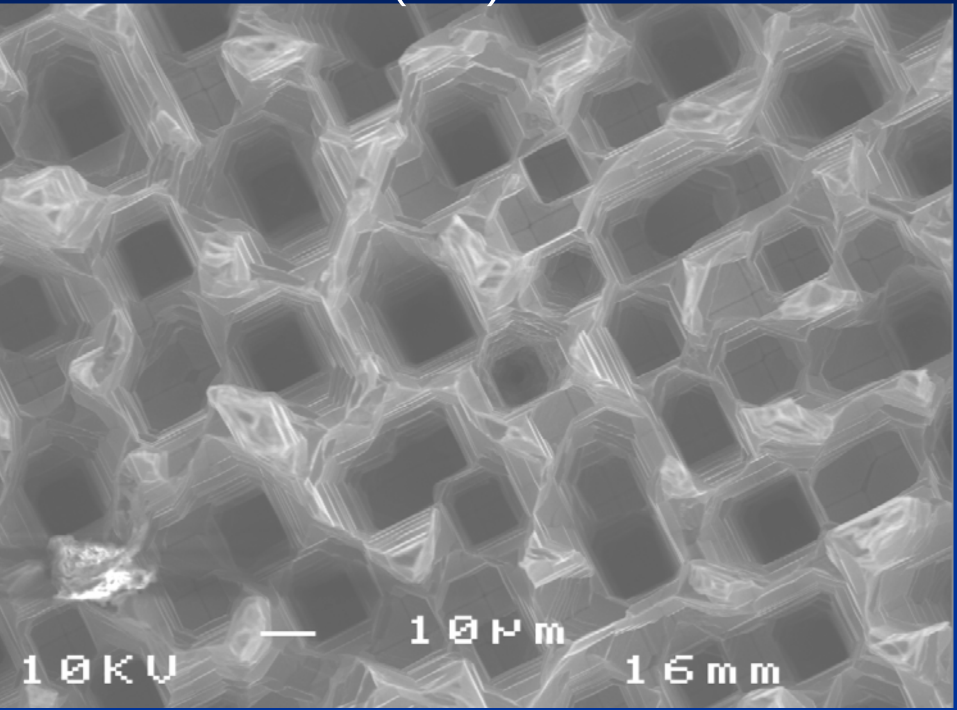



- Height >50 µm, tip ~10 nm
- Aspect ratio $>10^3$

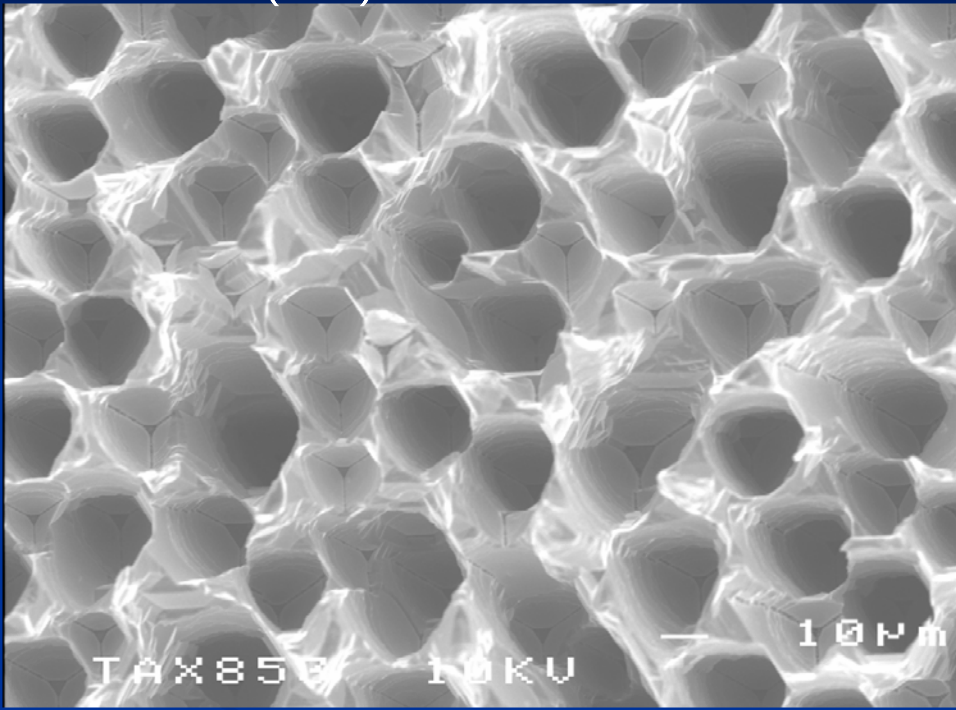
Mills & Kolasinski, *J Phys D 38* (2005) 632

# A New Route to Macroporous Si

Si(100) KOH Etched




Si(111) KOH Etched




Pillars are surrounded by holes that can be removed by KOH. KOH etches anisotropically and enforces a pore shape determined by crystallography

Mills & Kolasinski, *J Phys D 38* (2005) 632

# Hydroxyapatite

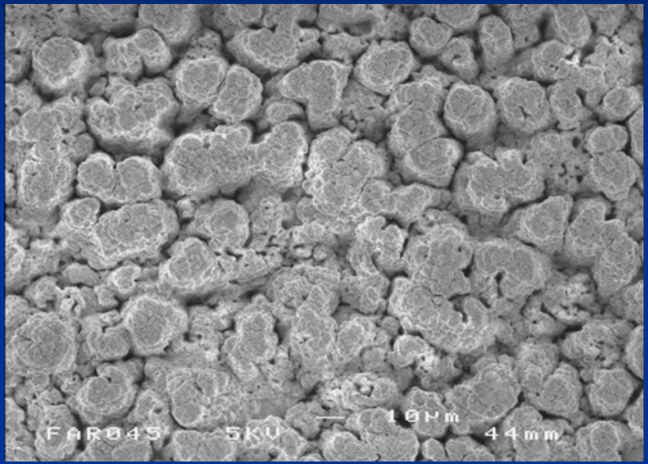
- Stability vs bioactivity
- Regrowth vs dissolution
- Coating of implants
- Drug delivery

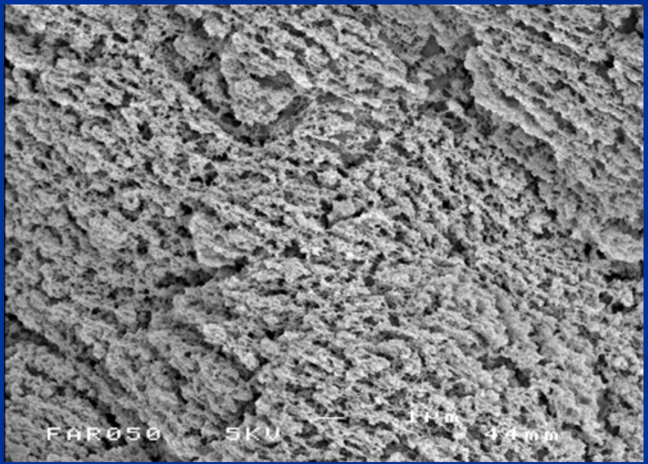
Queen Mary
University of London

Norton
Rehman
Elliott
Vadgama

# Laser Restructuring of HA

- Can we exercise similar control over the structure of HA surfaces?
- What are  the effects of laser irradiation not only on structure but on composition?
- IR microscopy



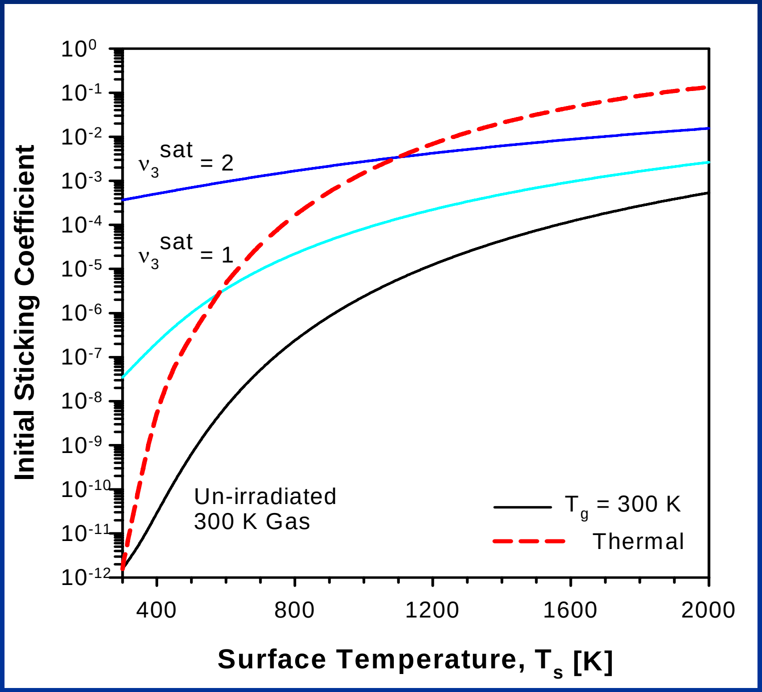
# IR Laser Assisted Catalysis

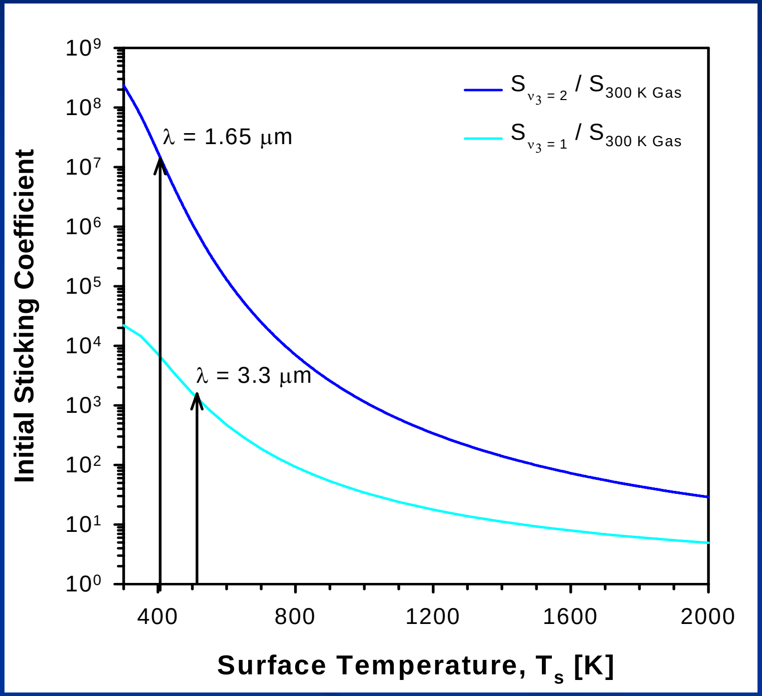
## Harrison & Abbott

- Photons are used to excite a particular vibrational mode of the reactants, increasing dissociation and deposition rates
- This technique is used in conjunction with CVD
- Potential to
  - Grow nanostructured films under low $T_s$ conditions where thermal diffusion can be minimized
  - Utilize mode specific chemistry to deposit a particular gas from a mixture
  - Increase dissociative sticking probabilities by several orders of magnitude
    - e.g., pumping the $\nu_3$ vibration of $CH_4$ at 300 K can give enhancements in sticking of $10^8$

# Laser Pumping vs. Thermal Activation

CH$_4$ Dissociation on Ni(100)



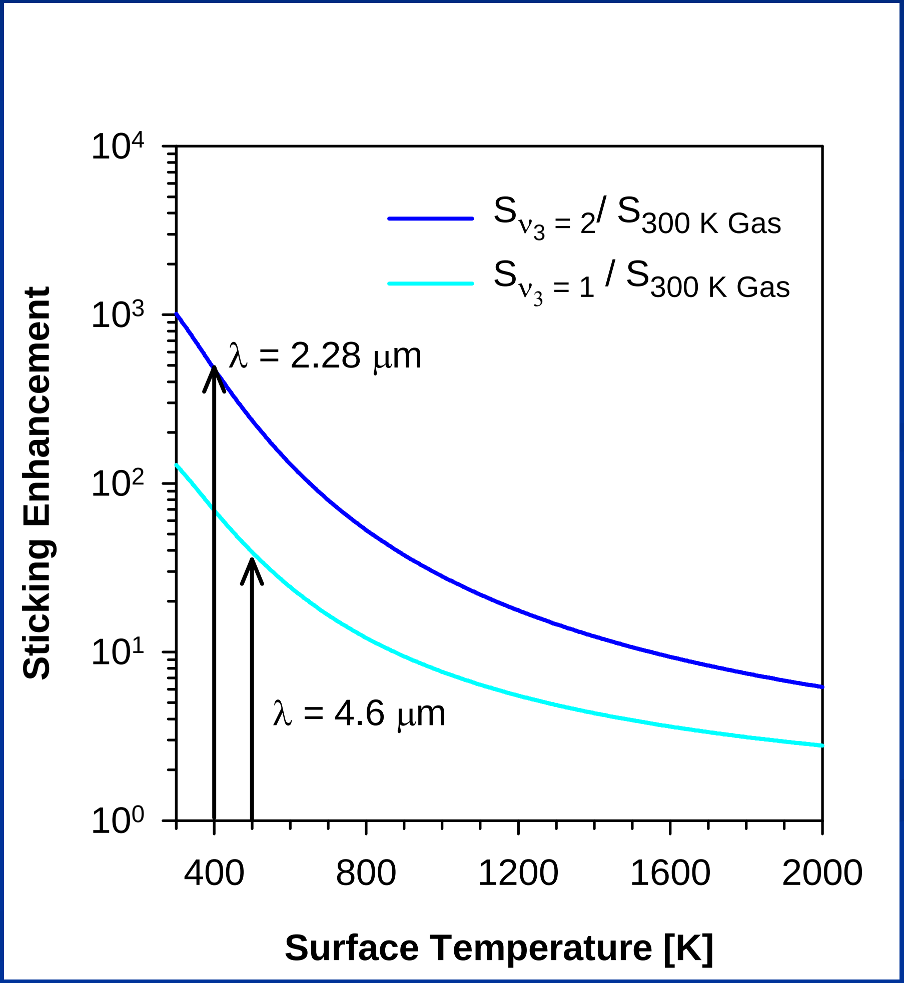




- Laser pumping a 300 K thermal CH$_4$/Ni(100) system leads to reactivity levels appropriate to surface temperatures of $T_s$ = 675 K and $T_s$ = 1875 K for 1$\nu_3$ and 2$\nu_3$ respectively.
- Sticking enhancements for a 300 K ambient CH$_4$ gas pumped to saturation over a 500 K Ni(100) surface would be ~10$^3$ and ~10$^6$ for 1$\nu_3$ and 2$\nu_3$ respectively.

# Laser Pumping vs. Thermal Activation

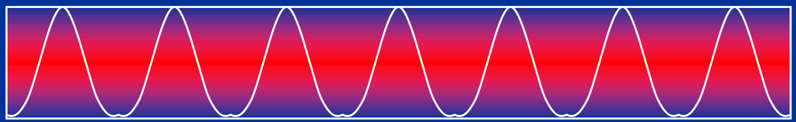
- Typically, experiments are performed with $T_s$ > 1000 K to avoid H passivation of the surface.
- The threshold energy for dissociation is low ($E_0$ = 19 kJ mol$^{-1}$) on Si(100), but on the H-passivated surface the threshold energy may be significantly higher ($E_0$ ~ 100 kJ mol$^{-1}$).
- Possibly large enhancement of sticking at low $T_s$ (i.e., $10^8$ – $10^{12}$) on the passivated surfaces.

$SiH_4$ Dissociation on Si(100)

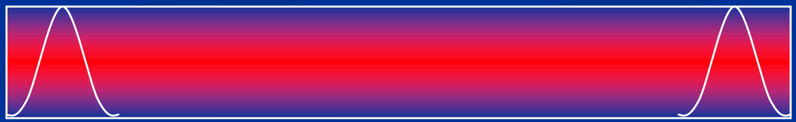


# Comparison of Lasers

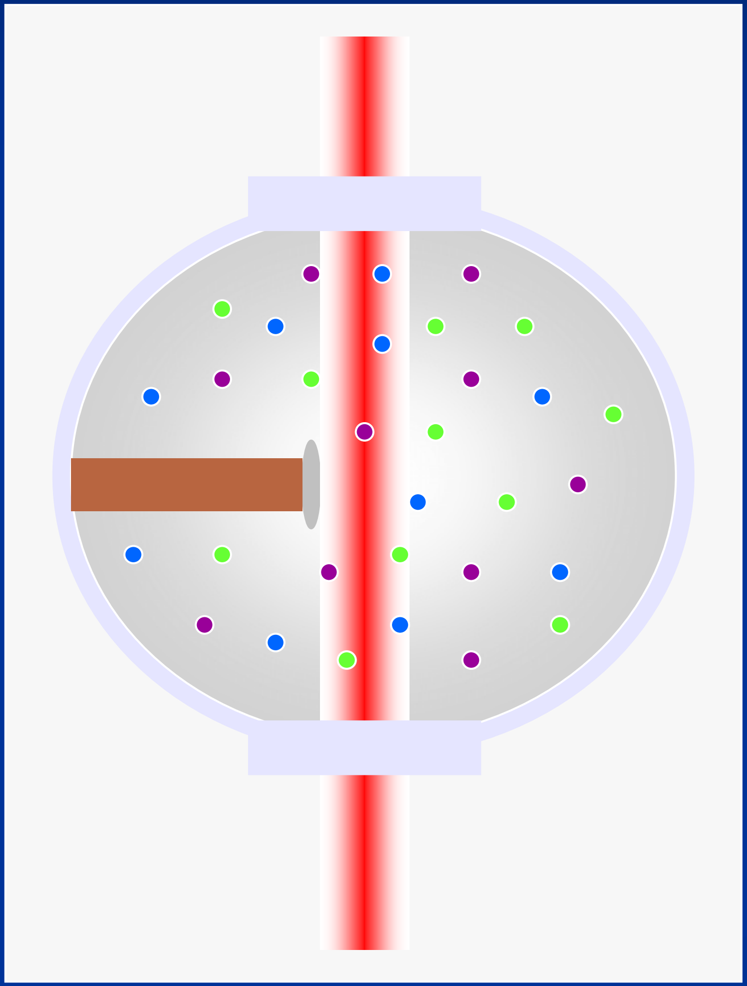
- Jefferson Lab Free Electron Laser
  - A tunable IR laser with 10 kW (133 μJ/pulse)
  - Individual pulses are 800 fs in duration and 20 $cm^{-1}$ in bandwidth
  - Repetition rate of 75 MHz



- Amplified Ti:Sapphire/OPA System at UVA
  - A tunable IR laser with 300 mW (300 μJ/pulse)
  - Individual pulses are 100 fs in duration and 150 $cm^{-1}$ in bandwidth
  - Repetition rate of 1 kHz

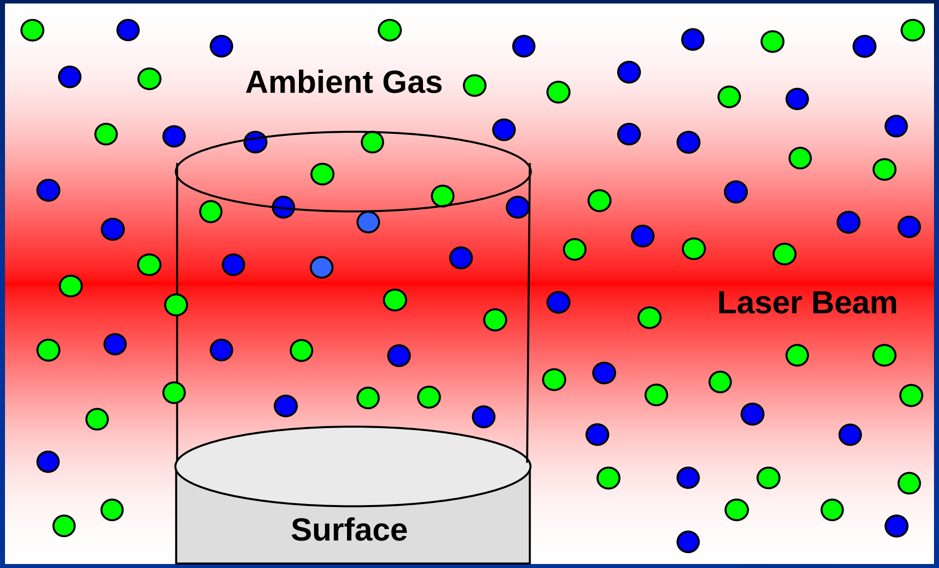


# Potential Experiment at JLAB-FEL



- Backfill a chamber with $CH_4$, $SiH_4$, and $GeH_4$ ambient gases above a low $T_s$ growth surface.
- Change the laser wavelength to excite 2 quanta of the $\nu_3$ asymmetric stretching vibration and selectively enhance the deposition of:
  - C ($\lambda_{2\nu 3}$ = 1.656 μm)
  - Si ($\lambda_{2\nu 3}$ = 2.282 μm)
  - Ge ($\lambda_{2\nu 3}$ = 2.365 μm)

# Prediction: $CH_4$ / Ni(100)

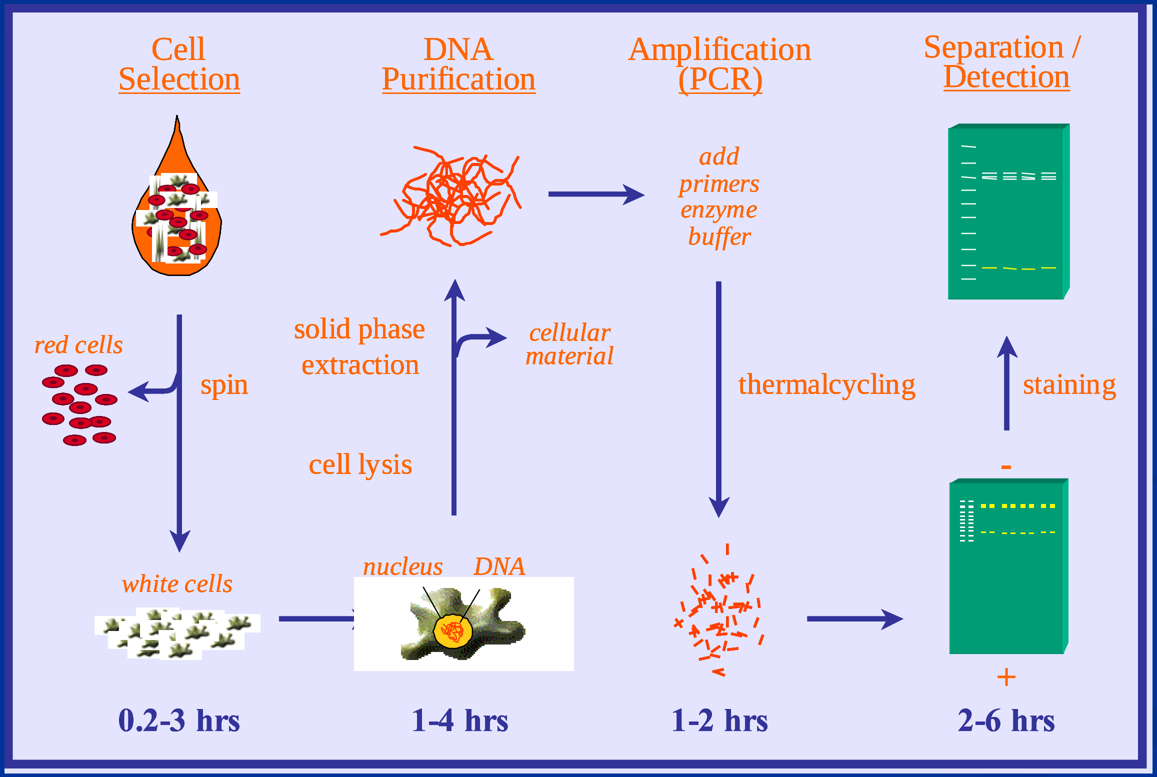



**Percentage of Molecules Excited and Time to Deposit 1 ML of C for the 0 → 2 Transition of $CH_4$ on Ni(100)**

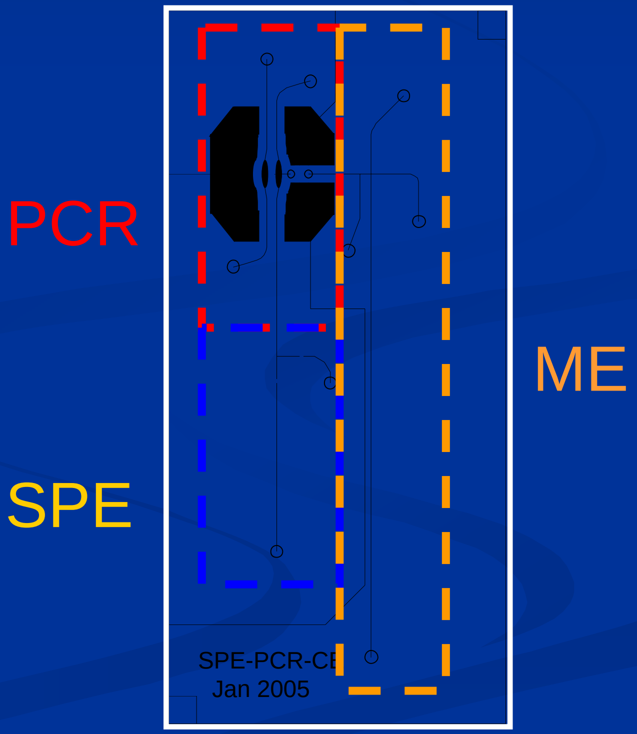
| Laser | Percent Excited (%*s$^{-1}$) | Experimental Time |
|---|---|---|
| JLAB FEL | saturation | 11 minutes |
| Ti:Sapphire OPA | 0.5 % | 1.05 years |

# The Application of Laser Microfabrication of Photostructurable Glass Devices for DNA Micro Total Analysis Systems (µTAS)

**Karlinsey, Landers & Helvajian**




Conventional Methodology




µTAS

# Photostructurable Glass Processing

The ability to fabricate true 3D microstructures in photostructurable glass with pulsed UV laser exposure was first developed by Helvajian's group at Aerospace Corporation.

Fuqua, et al. *SPIE Proc. Laser App. in Microelec. and Optoelec. Manufacturing* 3618 (1999) 213

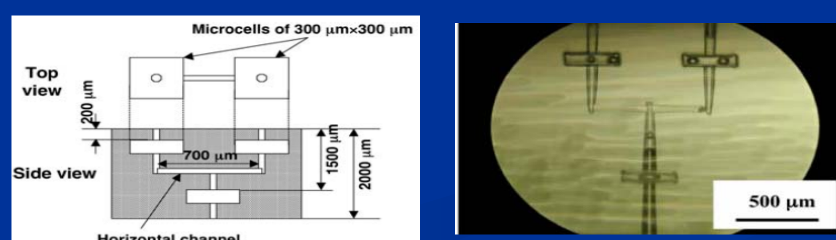

| | Borofloat | Foturan™ |
|---|---|---|
| Glass Composition (major components) | 60% $SiO_2$<br>5% $B_2O_3$ | 75-85% $SiO_2$<br>7-11% $Li_2O$<br>0.05-0.15% $Ag_2O$ |
| Pattern Transfer | Photomask | CAD |
| Exposure | UV lamp | Pulsed UV laser |
| Pre-etch Bake | 110° C | 605° C |
| Material Removal | Isotropic HF | Preferential HF etch |
| Variable Etch Depths | Multiple Steps | Single Step |
| Access Holes | Drilled | Included in pattern |
| Bonding | 540° C | Not necessary |

# Photostructurable Glass Processing

The Aerospace group has made significant strides in the direct-write processing of the photosensitive glass/ceramic material. They have demonstrated variable feature heights as well as embedded and stacked embedded structures (eg. tunnels).


Livingston and Helvajian, *SPIE Proc. Laser Adv. Mater. Proc.* 4830 (2002) 189

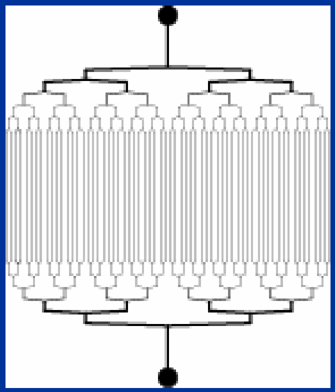
Microchannels and microcells have also been patterned in photostructurable glass using a commercial fs laser micromachining workstation.



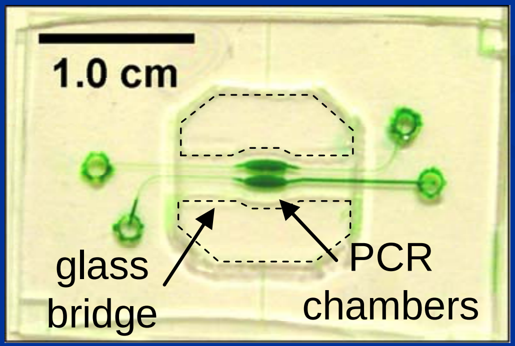

Sugioka, et al. *Applied Physics A* 79 (2004) 815

# Proposed Work

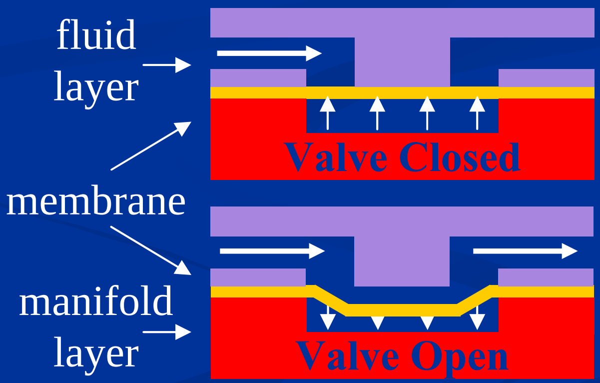
- Possible applications of photostructurable glass for microfluidic-based DNA analyses include:
  - Solid phase extraction (SPE) → Large surface area-to-volume is needed to provide an efficient chromatographic solid phase for DNA extraction.
  - Polymerase chain reaction (PCR) → When thermal cycling, a reduction in surrounding glass greatly increases cycling rates.
  - Microchip electrophoresis (ME) → Reproducible injections could be performed using a pumping technique through variable depth patterning.



**SPE:** A high density array of channels could replace a solid phase (eg. beads).




**PCR:** Using IR-mediated heating, amplification has been performed at 10 seconds per cycle.

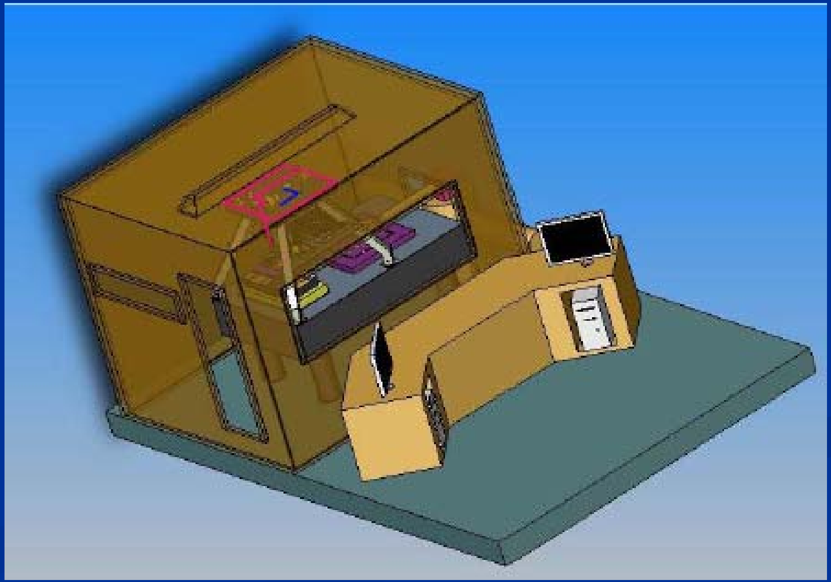



**ME:** Three-dimensional patterning would enable valve fabrication without introducing a bonding step.

# High-Throughput Processing

Benefits of using microchips over conventional gels or capillaries include the small volume requirements and the fast time response. However, the microchip also offers the most promise for integrating multiple reactions (eg. sample preparation steps) and multiple analysis channels or chambers for high-throughput analysis. With the high resolution, fast prototyping, and reproducibility of the direct-write laser processing, the microfluidics field should benefit greatly from this technology.

With the capability of the Laser Microengineering Experimental Station being set up at the Jefferson Laboratory Free Electron Laser Facility, it should be be possible to produce large quantities of disposable integrated analysis devices to be used for clinical and forensic analyses of DNA.



http://www.jlab.org/FEL/LPC/04lpc-helvajian.pdf

# Conclusions

- Laser & Chemical processing can be used to modify surface composition & profile
- Both ordered and random structures
- Pillars & pores of various aspect ratios
- Laser micromachining may be able to create lab-on-a-chip structures