Realism in nanosensing:
hard-won insights from the trenches

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Abstract:

Nanosensors have the unprecedented capability to interact with absolute numbers of analytes down to the single molecular scale. The susceptibility of nanosensors to external perturbation, given their size, is unprecedented -- and this essential physics offers exceptional new opportunities. Indeed, we are here to explore, harness, and even celebrate these attributes!

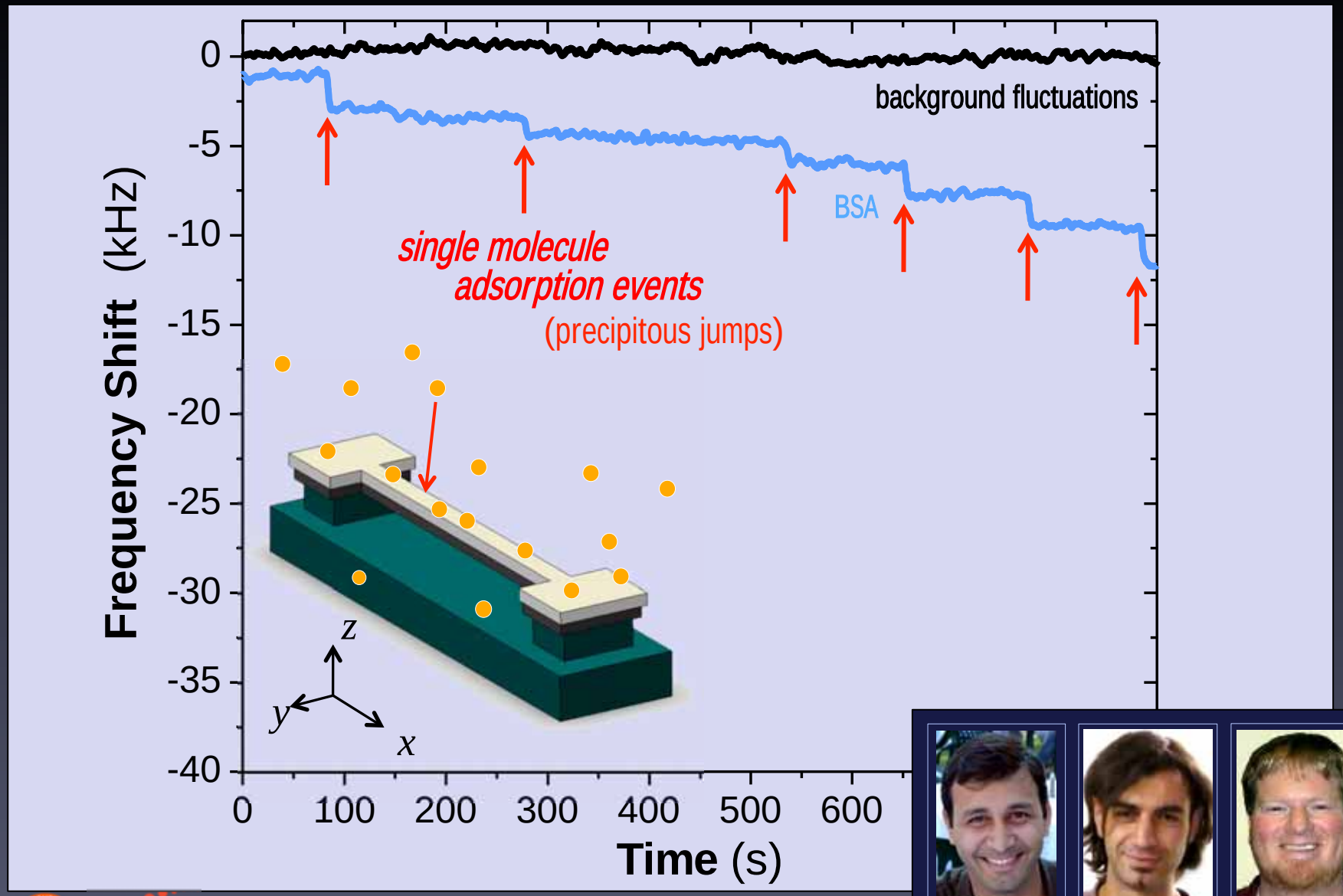
As a archetypal case study of nanosensor physics, I will focus upon resonant NEMS sensors. I will describe the *immense* increase in responsivity obtained with device size reduction that yields, for example, atomic mass resolution. As an archetypal case study of nanosensor physics, we'll focus upon resonant NEMS sensors. I will describe the immense increase in responsivity obtained with device size reduction that yields, for example, atomic mass resolution. We will explore several noise mechanisms and backaction effects imposing ultimate physical limits to the sensitivity, and how matching considerations make it extremely challenging to embed these devices in practical measurement systems.

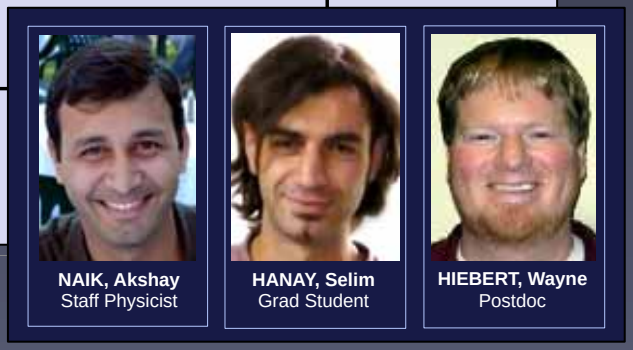
The unique properties of nanodevices, however, are not a panacea that absolves us from the need to contend with long-standing, overarching challenges posed by real-world sensing applications. From about a decade and a half's work focused on metamorphosing nanosensors into nano**systems** through large-scale integration, nature has taught us some hard lessons. In my talk I will share several of these, using examples from NEMS and other sensor systems. Among them are: (a) any stand-alone sensor is unlikely to be up to the full dynamic range of challenges posed in the real world; (b) complex combinations of real-world analytes are unlikely to be resolved by any "one-stop" generic approach; (c) arrays of sensors can often give enhanced performance over individual devices, but achieving such gains may require exceptionally careful attention to device variances; (d) careful choices of platform materials are essential to insure a rapid transitioning into large-scale integration and production *en masse*.

Although these sobering considerations may potentially force an initial downselection from amongst the panoply of exciting possibilities of emerging nanosensors; learning from the past, and considering real-world (not academic laboratory) conditions, will accelerate realization of practical nanosensor systems.

single-molecule NEMS-MS

AK Naik, MS Hanay, WK Hiebert, XL Feng, and ML Roukes,
Nature Nanotechnology **4**, 445-449 (2009)

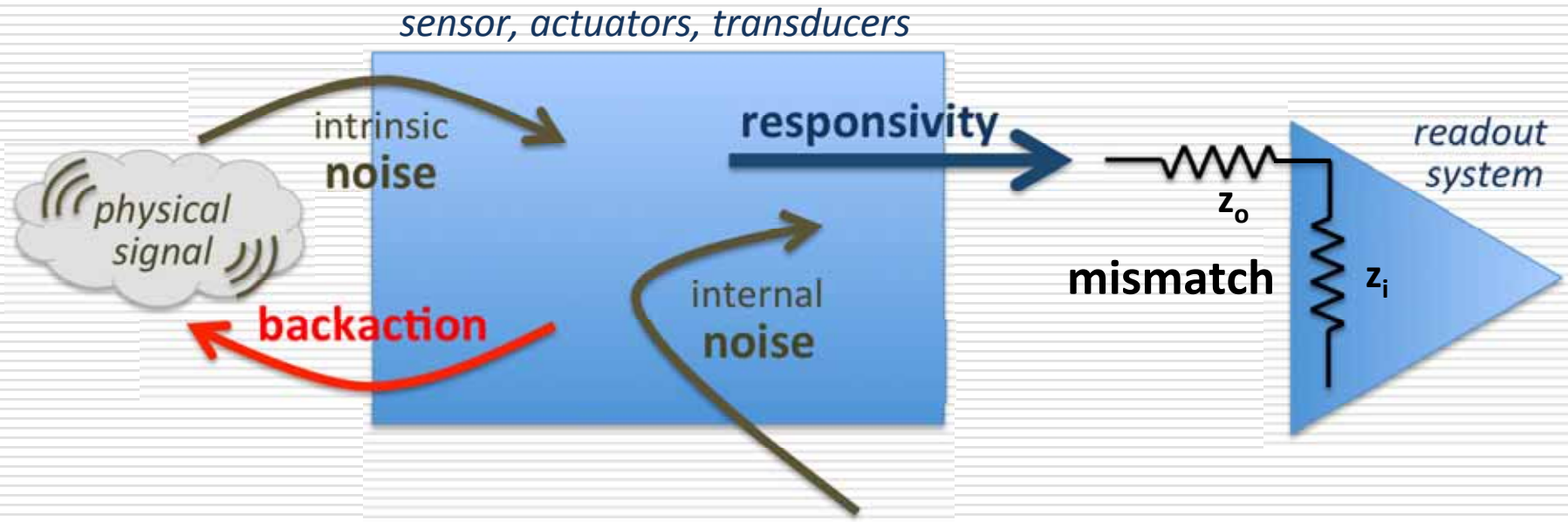




the promise

- Nanosensors have the unprecedented capability to interact with absolute numbers of analytes down to the single molecular scale. The susceptibility of nanosensors to external perturbation, given their size, is unprecedented -- and this essential physics offers exceptional new opportunities. Indeed, we are here to explore, harness, and even celebrate these attributes!

responsivity, noise, backaction, mismatch



… these are the four critical physical considerations.

physics:
responsivity, noise, backaction, mismatch

- As an archetypal case study of nanosensor physics, we'll focus upon resonant NEMS sensors. I will describe the immense increase in responsivity obtained with device size reduction that yields, for example, atomic mass resolution. We will explore several noise mechanisms and backaction effects imposing ultimate physical limits to the sensitivity, and how matching considerations make it extremely challenging to embed these devices in practical measurement systems.

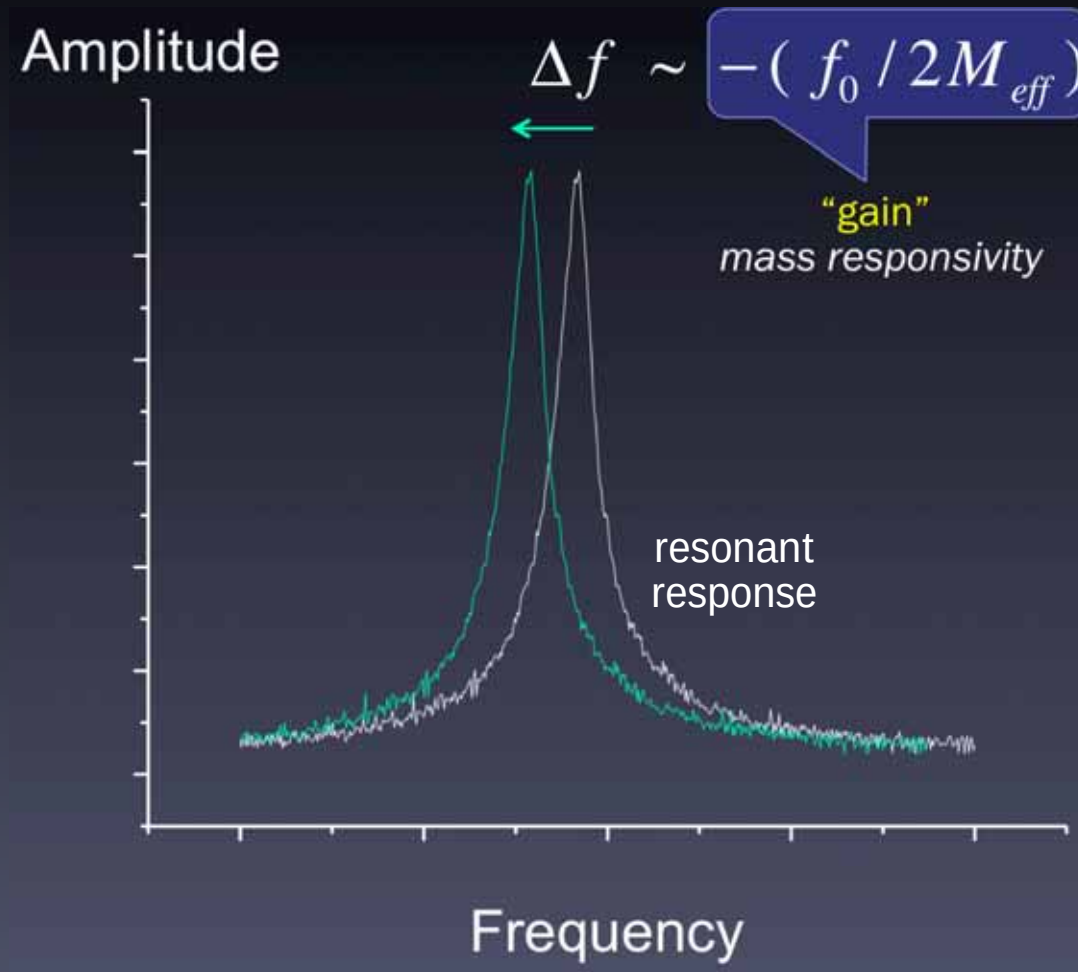
frequency-shift based mass sensing

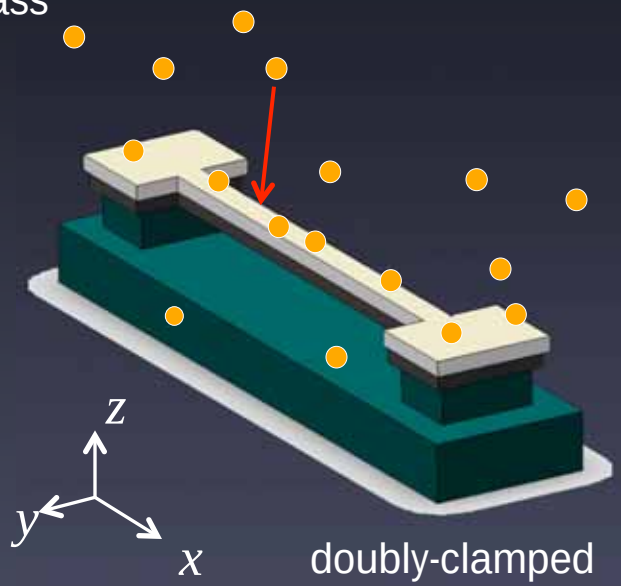
frequency shift

$$\Delta f \sim -(f_0 / 2M_{eff}) \cdot \delta m$$

"gain"
mass responsivity

added mass





doubly-clamped beam resonator

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minimum resolvable mass is determined by "gain" and noise

$$\delta M \approx \frac{\partial M_{eff}}{\partial \omega_0} \delta\omega_0 \sim \mathbf{R^{-1}} \sigma_A(\tau)$$

mass resolution

Mass Responsivity

Allan Deviation

a measure of frequency-fluctuation noise

© Caltech/CEA-LETI 2011

Maximizing mass responsivity leads to minimizing the resolvable mass

$$\delta M \approx \frac{\partial M_{eff}}{\partial \omega_0}\,\delta\omega_0 \sim \boldsymbol{R}^{-1}\,\sigma_A(\tau)$$

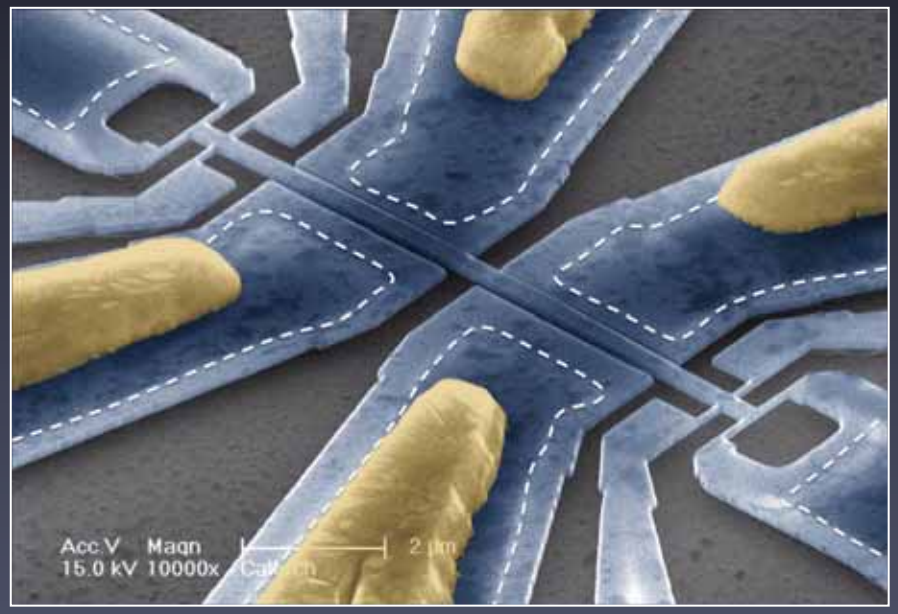
mass resolution

Mass Responsivity

Allan Deviation

a measure of frequency-fluctuation noise

large mass responsivity



For any complex mechanical mode, modeled as a damped simple harmonic oscillator:

$$\boldsymbol{R} \approx -\frac{\omega_0}{2M_{eff}} \propto \frac{1}{\ell^4}$$

→ huge benefit in scaling downward !

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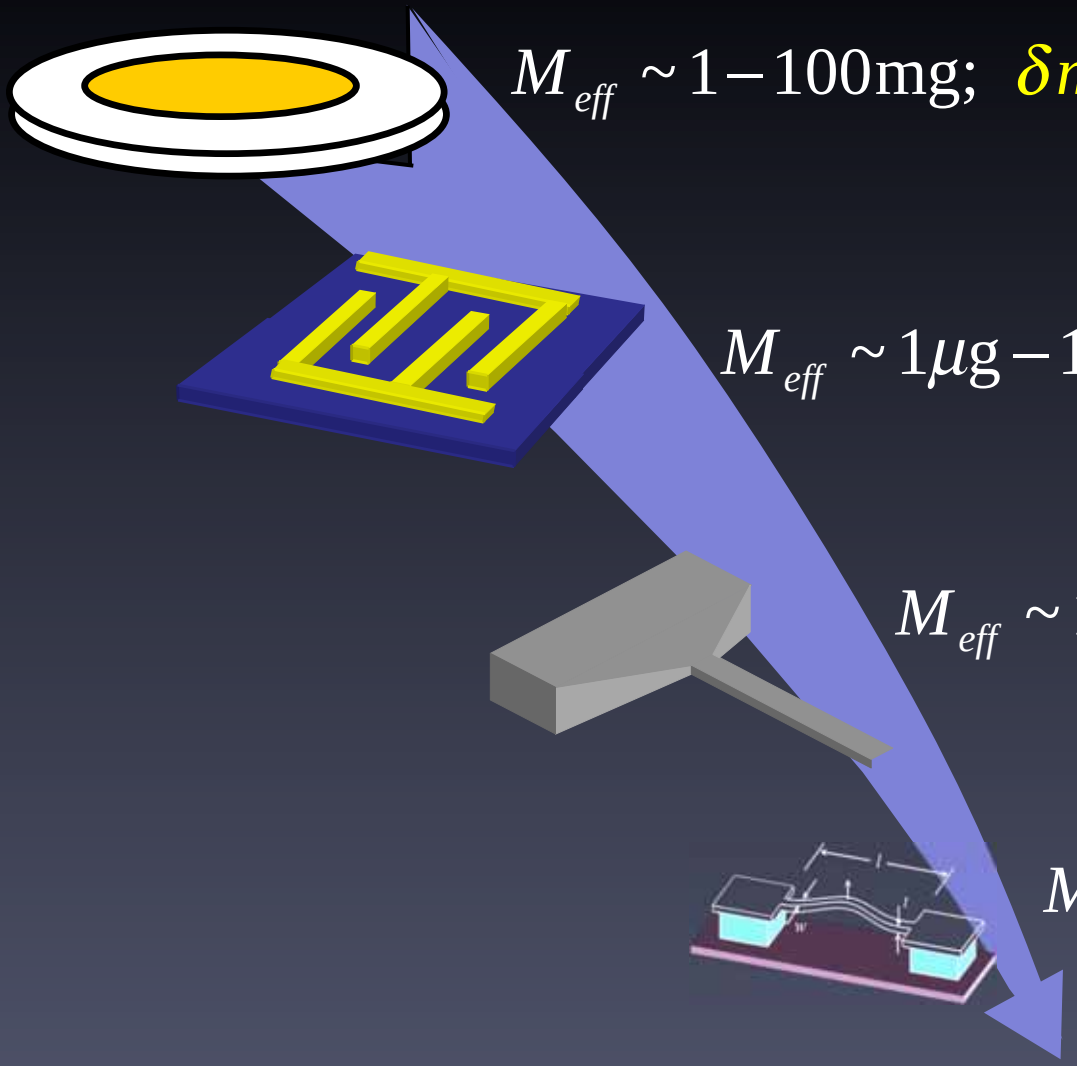
size-scaling the minimum resolvable mass: resonant inertial mass sensors



quartz crystal microbalances

$M_{eff} \sim 1-100\text{mg};\ \ \delta m \sim 1\mu g$

SAW/FPW sensors (MEMS)

$M_{eff} \sim 1\mu g - 1\text{mg};\ \ \delta m \sim 1\text{ng}$

microcantilevers (MEMS)

$M_{eff} \sim 1\text{ng} - 1\mu g;\ \ \delta m \sim 1\text{fg}$

NEMS

$M_{eff} \sim 1\text{fg} - 1\text{pg};\ \ \delta m \leq 1\text{zg}$

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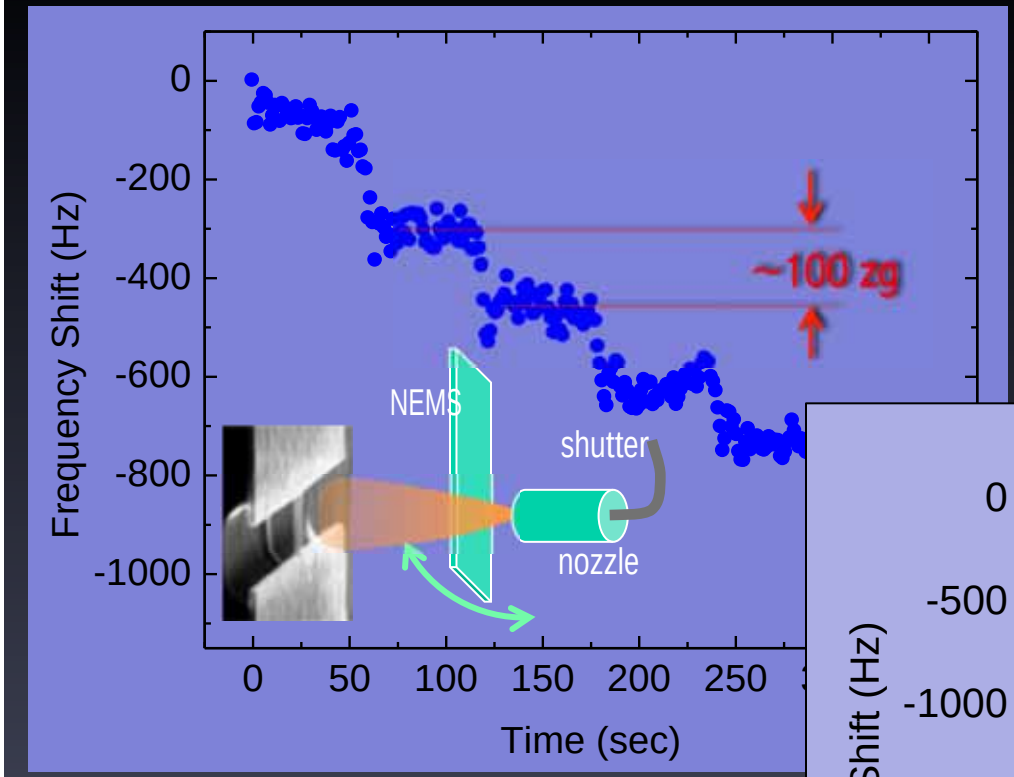
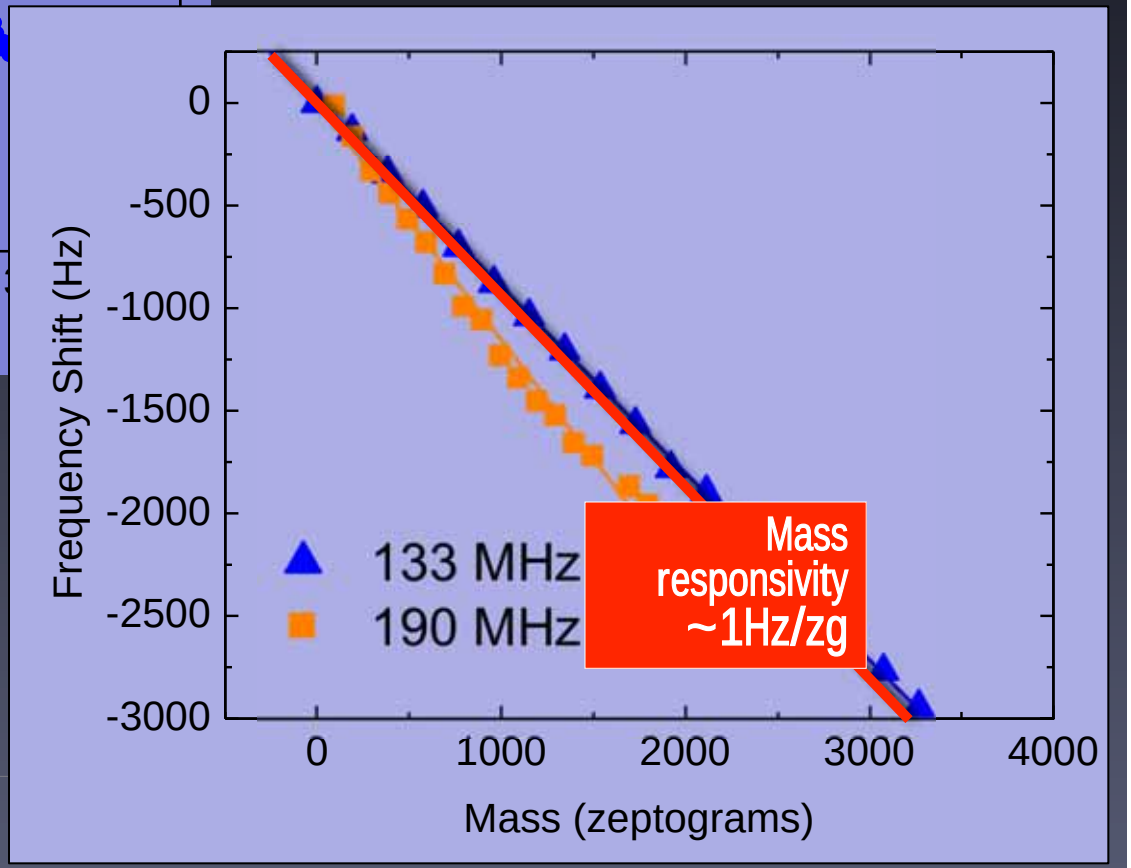
Massive increase in responsivity: zeptogram mass sensitivity *(1zg = 10^{-21}g)*



SiC doubly clamped beam NEMS
UHF bridge configuration
(f_0 ~ 133 and 190 MHz)
Ultralow noise PLL readout

Nano Lett. 6, *583* (2006)



Ya-Tang Yang, Carlo Callegari,
Xiaoli Feng, Kamil Ekinci, MLR

BUT... minimizing frequency-fluctuation noise is also critical !!!

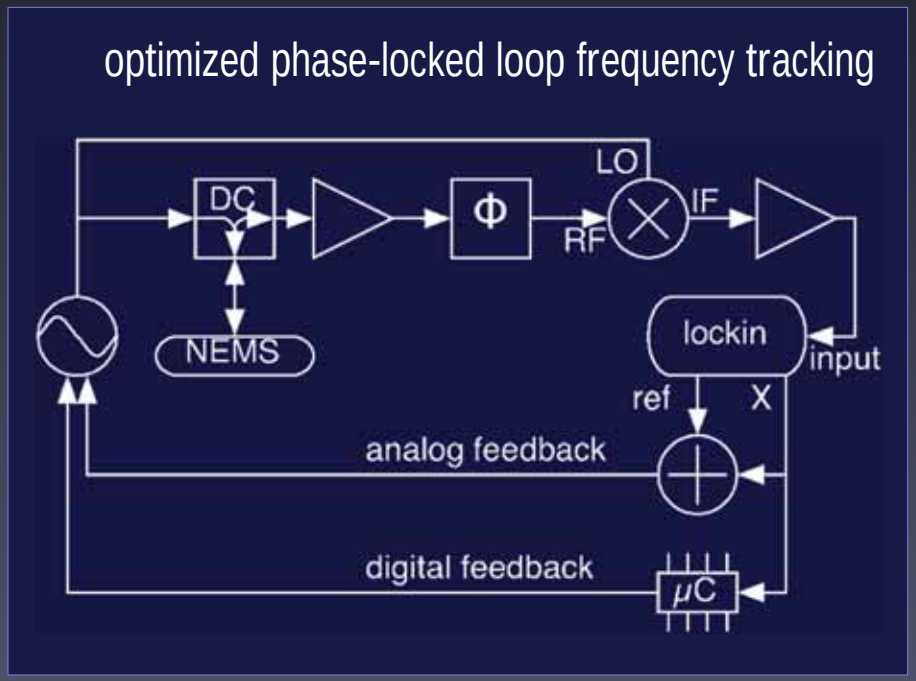
$$\delta M \approx \frac{\partial M_{eff}}{\partial \omega_0} \delta\omega_0 \sim \boldsymbol{R}^{-1}$$

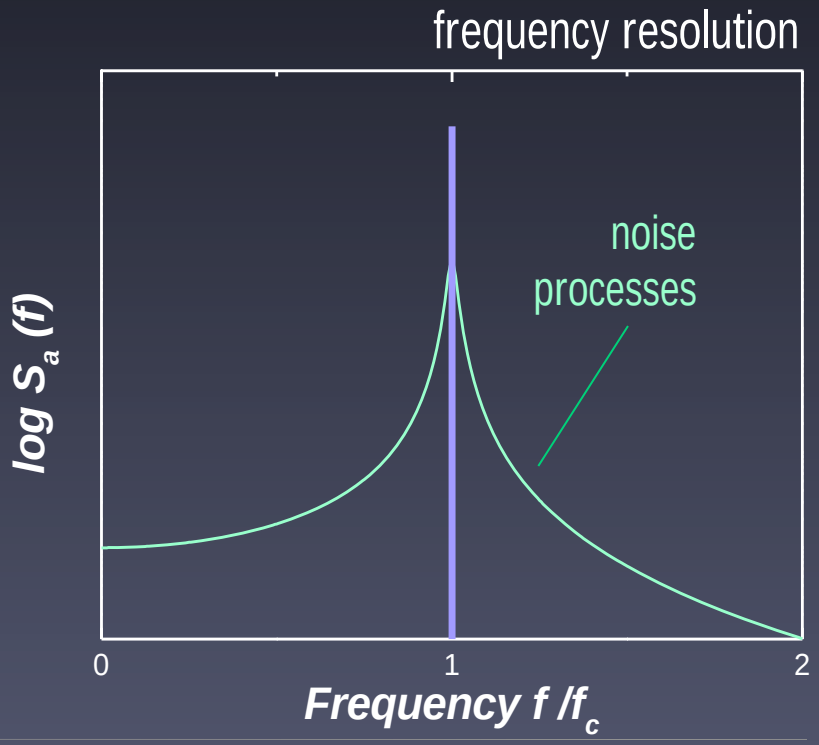
mass resolution

Mass Responsivity

$\sigma_A(\tau)$ *Allan Deviation*

a measure of frequency-fluctuation noise





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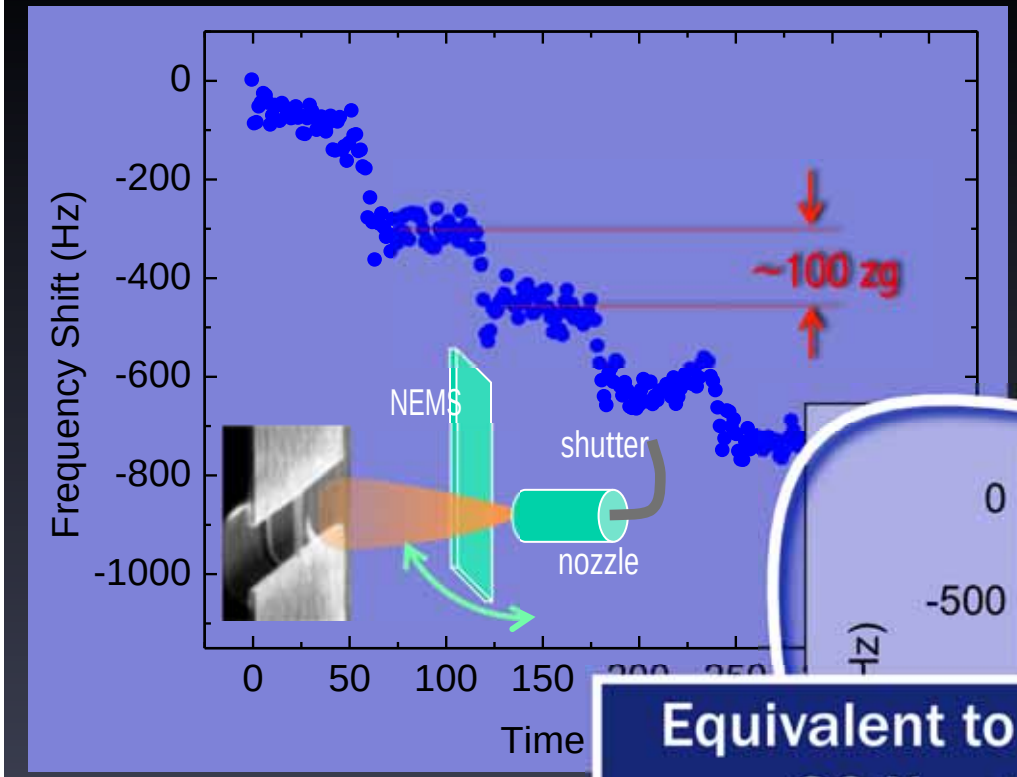
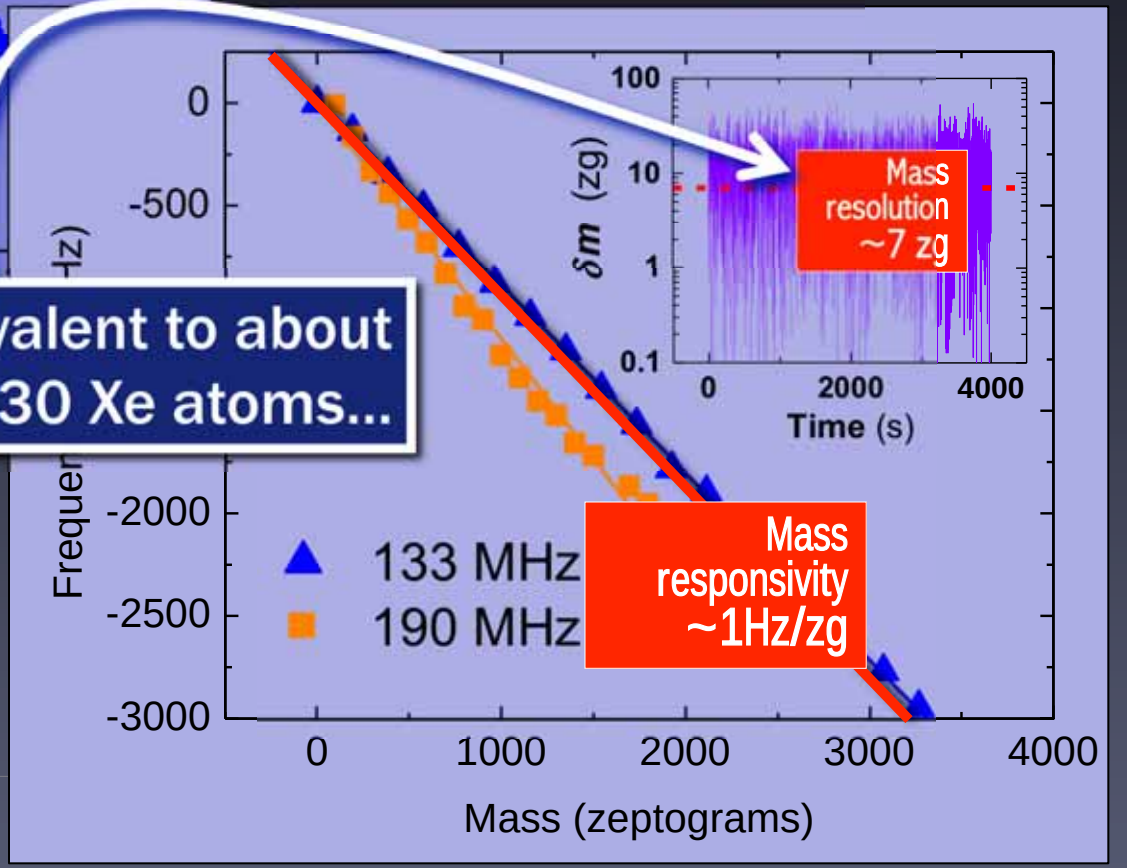
Real-time zeptogram mass sensitivity

(1zg = 10^{-21}g)



SiC doubly clamped beam NEMS
UHF bridge configuration
(f_0 ~ 133 and 190 MHz)
Ultralow noise PLL readout

Nano Lett. 6, *583* (2006)



Equivalent to about 30 Xe atoms...

Ya-Tang Yang, Carlo Callegari, Xiaoli Feng, Kamil Ekinci, MLR

physics:
responsivity, noise, backaction, mismatch

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sources of frequency-fluctuation noise

JOURNAL OF APPLIED PHYSICS VOLUME 92, NUMBER 5 1 SEPTEMBER 2002

Noise processes in nanomechanical resonators

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California 93106

M. L. Roukes
Department of Physics, California Ins

(Received 15 February 2002; acce

Nanomechanical resonators can
approaching 1 GHz, with quality f
as highly selective rf filters and
nonfundamental noise processes w
include thermomechanical noise, N
important noise sources include th
In this article, we develop a self-c
estimate the impact that these noise
consisting of a doubly clamped be

NANO LETTERS Nano Lett. 2011, 11, 1753–1759 LETTER
pubs.acs.org/NanoLett

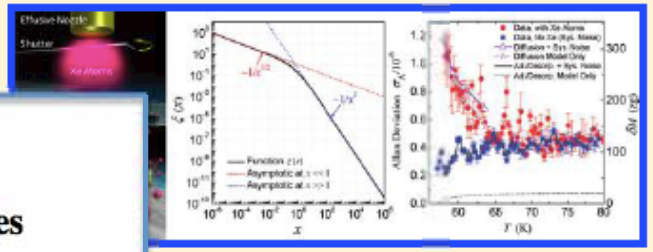
Surface Adsorbate Fluctuations and Noise in Nanoelectromechanical Systems

Y. T. Yang,[†,‡] C. Callegari,[†,§] X. L. Feng,[†,∥] and M. L. Roukes*

Kavli Nanoscience Institute, Mail Code 114-36, California Institute of Technology, Pasadena, California 91125, United States

Supporting Information

ABSTRACT: Physisorption on solid surfaces is important in both fundamental studies and technology. Adsorbates can also be critical for the performance of miniature electromechanical



luctuations of physisorbed xenon (Xe) atoms on a
ctrum and frequency noise, combined with analytic
hat diffusion dominates the observed excess noise.
which could be important in other low-dimensional

sorption−desorption, diffusion, resonator, noise

(VHF) NEMS resonator to investigate the behavior of
d xenon (Xe) atoms, by performing precise measure-

PHYSICAL REVIEW B **84,** 144301 (2011)

Detecting and characterizing frequency fluctuations of vibrational modes

Z. A. Maizelis,[1] M. L. Roukes,[2] and M. I. Dykman[1]
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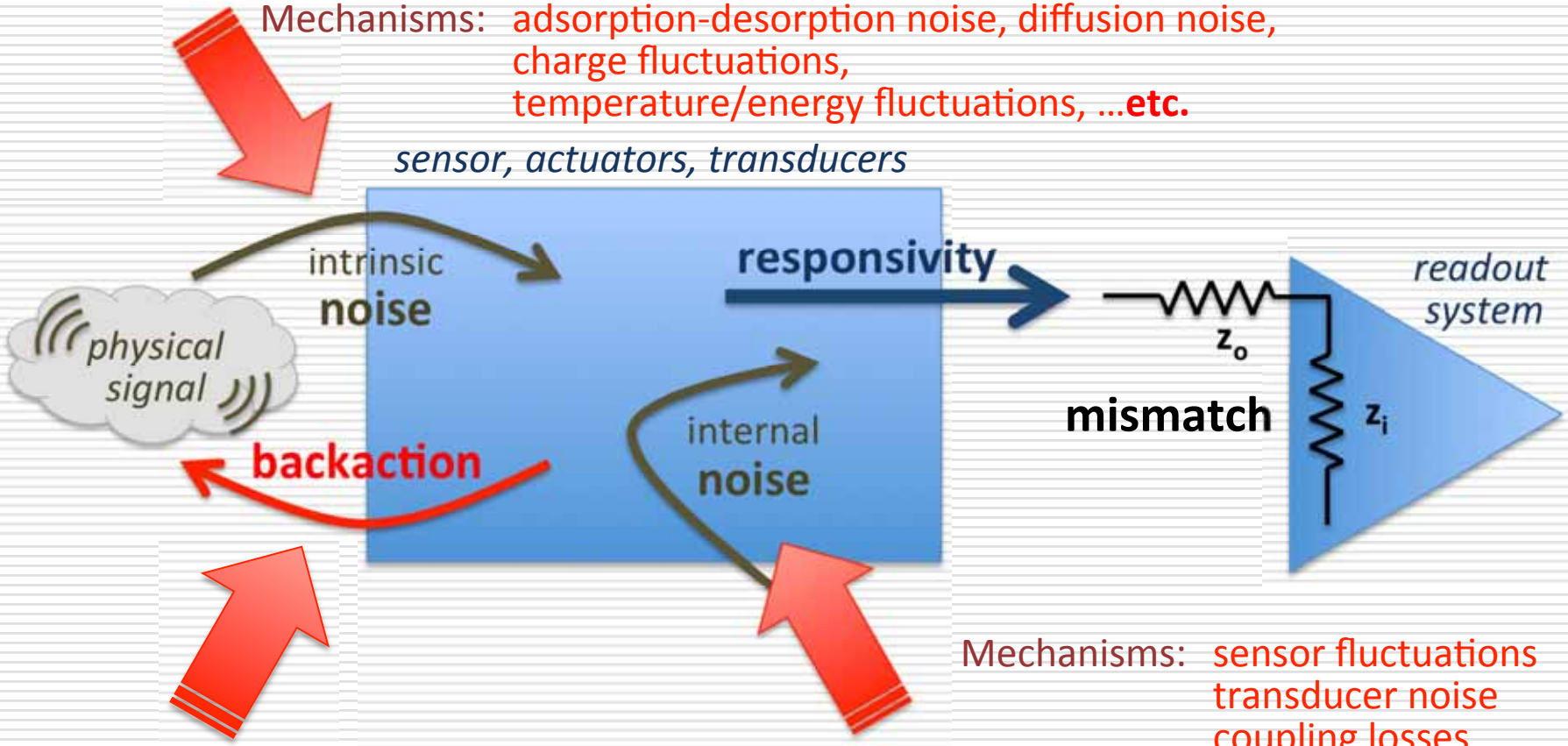
(Received 15 July 2011; published 3 October 2011)

We show how frequency fluctuations of a vibrational mode can be separated from other sources of phase noise. The method is based on the analysis of the time dependence of the complex amplitude of forced vibrations. The moments of the complex amplitude sensitively depend on the frequency noise statistics and its power spectrum.
which require extensive separate circuitry at

responsivity, noise, backaction, mismatch

Mechanisms: adsorption-desorption noise, diffusion noise,
charge fluctuations,
temperature/energy fluctuations, …**etc.**



Mechanisms: sensor fluctuations
transducer noise
coupling losses

Mechanisms: bias currents, voltages
S_{12} / reverse transfer
=> leakage, heating,
activated processes, noise

… these are the four critical physical considerations.

physics:
responsivity, noise, backaction, mismatch

- As an archetypal case study of nanosensor physics, we'll focus upon resonant NEMS sensors. I will describe the immense increase in responsivity obtained with device size reduction that yields, for example, atomic mass resolution. We will explore several noise mechanisms and backaction effects imposing ultimate physical limits to the sensitivity, and how matching considerations make it extremely challenging to embed these devices in practical measurement systems.

Cantilever tales: "Can a gauge factor ever be "too big"?

APPLIED PHYSICS LETTERS VOLUME 75, NUMBER 2 12 JULY 1999

High-sensitivity piezoresistive cantilevers under 1000 Å thick

J. A. Harley[a)] and T. W. Kenny
Department of Mechanical Engineering, Stanford University, Stanford, California 94305-4021

(Received 1 March 1999; accepted for publication 17 May 1999)

Ultrathin, high-sensitivity piezoresistive cantilevers were constructed using vapor-phase epitaxy to grow the conducting layer. A fourfold reduction in thickness was achieved over the thinnest implanted piezoresistive cantilevers, allowing improved force or displacement sensitivity and increased bandwidth. In cantilevers 890 Å thick, the dopant is well confined to the surface, and the sensitivity is 70% of the theoretical maximum. A cantilever fabricated for high force resolution has a minimum detectable force of 8.6 fN/$\sqrt{\text{Hz}}$ in air. Additionally, the $1/f$ noise is shown to follow the relation proposed by Hooge [Phys. Lett A **29**, 139 (1969)], increasing in inverse proportion to the number of carriers. © *1999 American Institute of Physics.* [S0003-6951(99)01728-3]

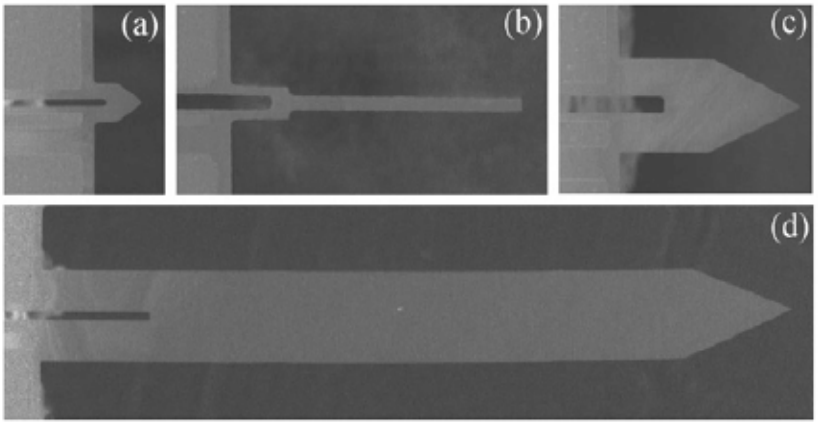


FIG. 1. SEMs of 0.087–0.090-μm-thick piezoresistive cantilevers. (a) 10 μm×8 μm. (b) 60 μm×4 μm. (c) 40 μm×20 μm. (d) 350 μm×44 μm. Note that image (d) is at 0.45% scale from the others.

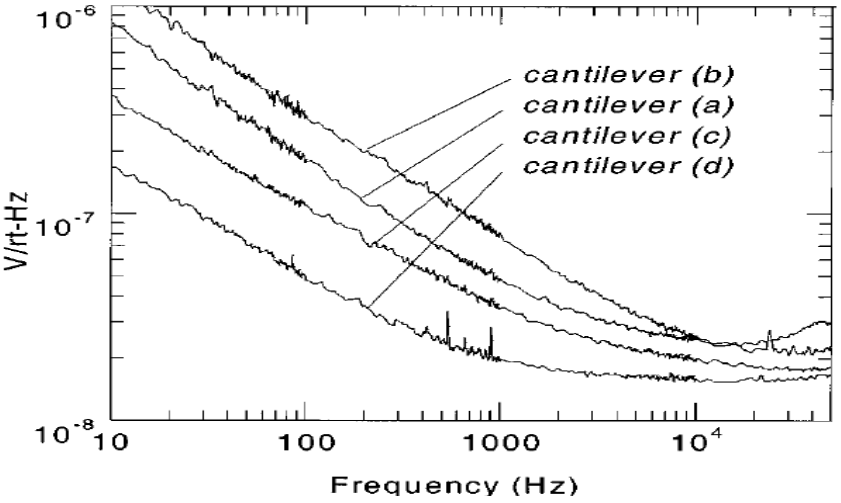
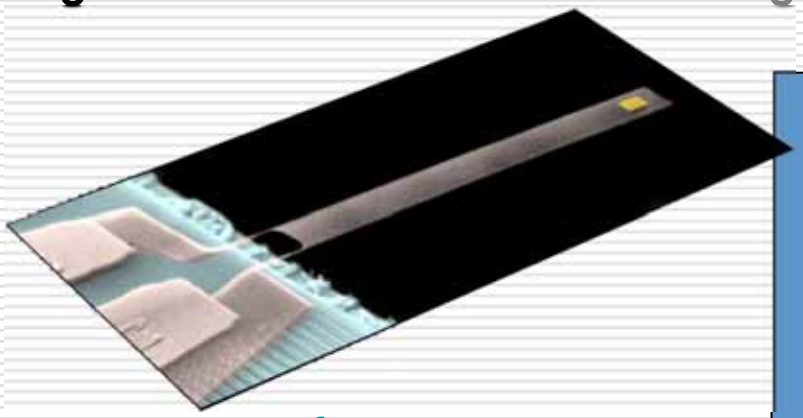


FIG. 4. Noise spectrum of cantilevers shown in Fig. 1 with 5 V bias. Peaks at 60 Hz and harmonics have been removed for clarity.

Scaling down: semiconducting nanopiezoresistor "issues"

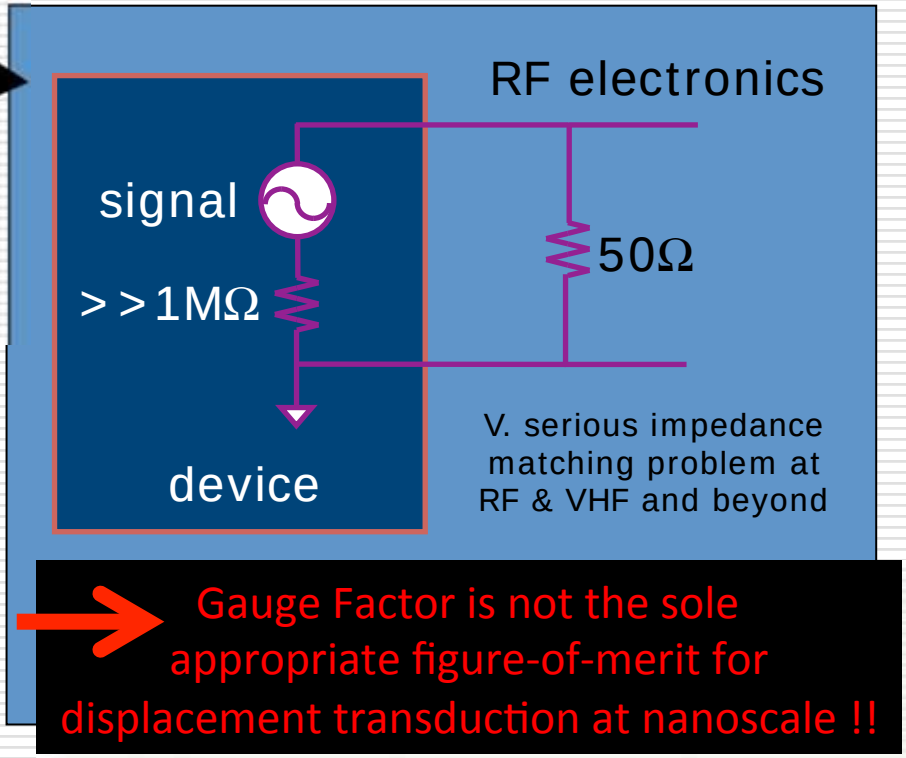


Pros:

1. A large gauge factor

Cons:

1. V. high resistance
2. Scaling exacerbates "issues"
3. Noisy (Johnson + 1/f)
4. Large temp. coefficients
5. Difficult to fabricate (epi Si)
6. Expensive to produce



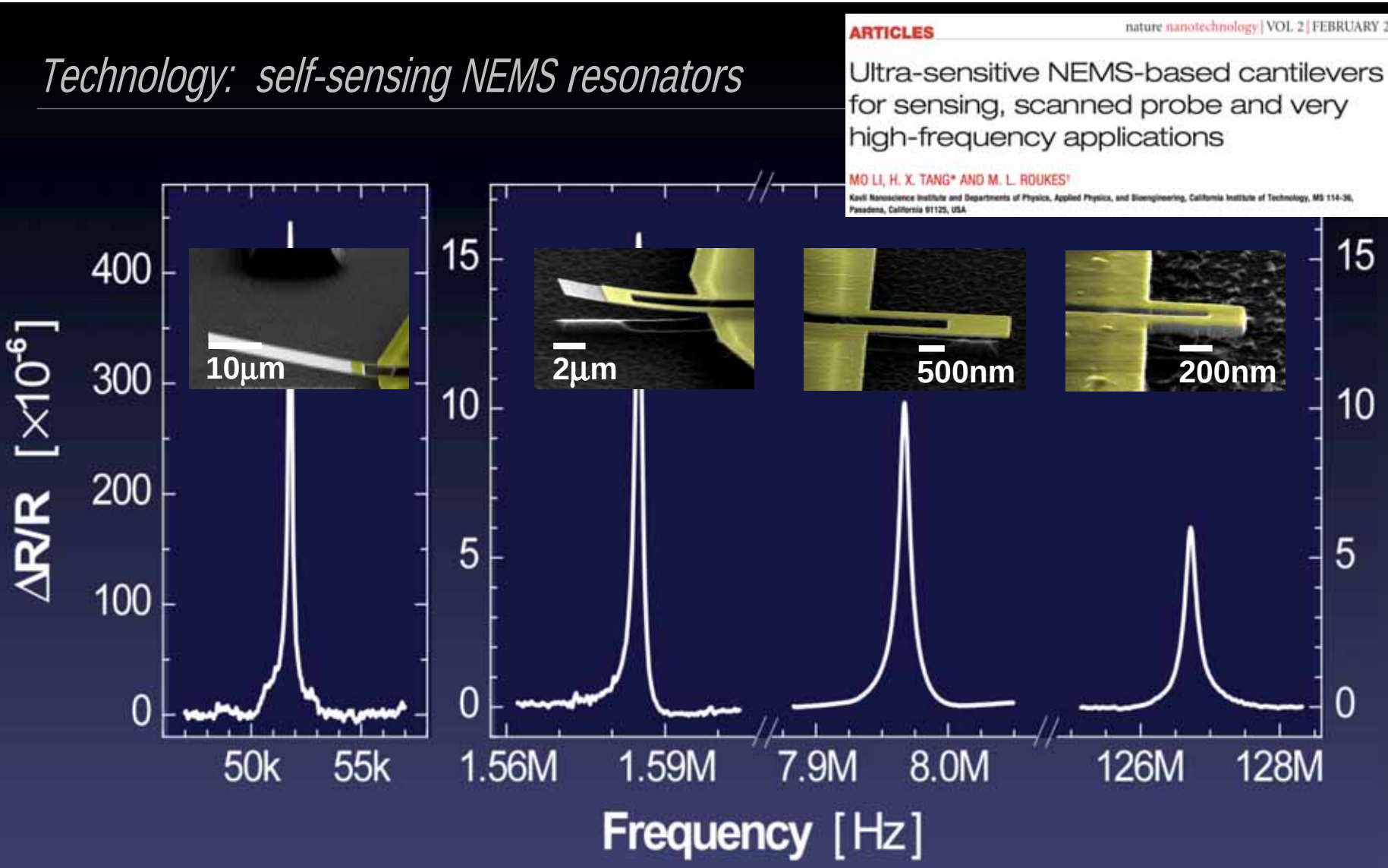
NANO LETTERS
2006
Vol. 6, No. 5
1000−1006

Self-Sensing Micro- and Nanocantilevers with Attonewton-Scale Force Resolution

J. L. Arlett, J. R. Maloney, B. Gudlewski, M. Muluneh, and M. L. Roukes*

Kavli Nanoscience Institute and Departments of Physics, Applied Physics, and Bioengineering, California Institute of Technology, 114-36,

Technology: self-sensing NEMS resonators



Piezoresistively-detected resonant response from a family of SiC nanocantilevers to a 1nN AC drive signal vs. frequency using metallic piezoresistors, at room temperature in vacuo.

Mo Li, HX Tang, ML Roukes,
Nature Nanotechnology **2**, 114 (2007)

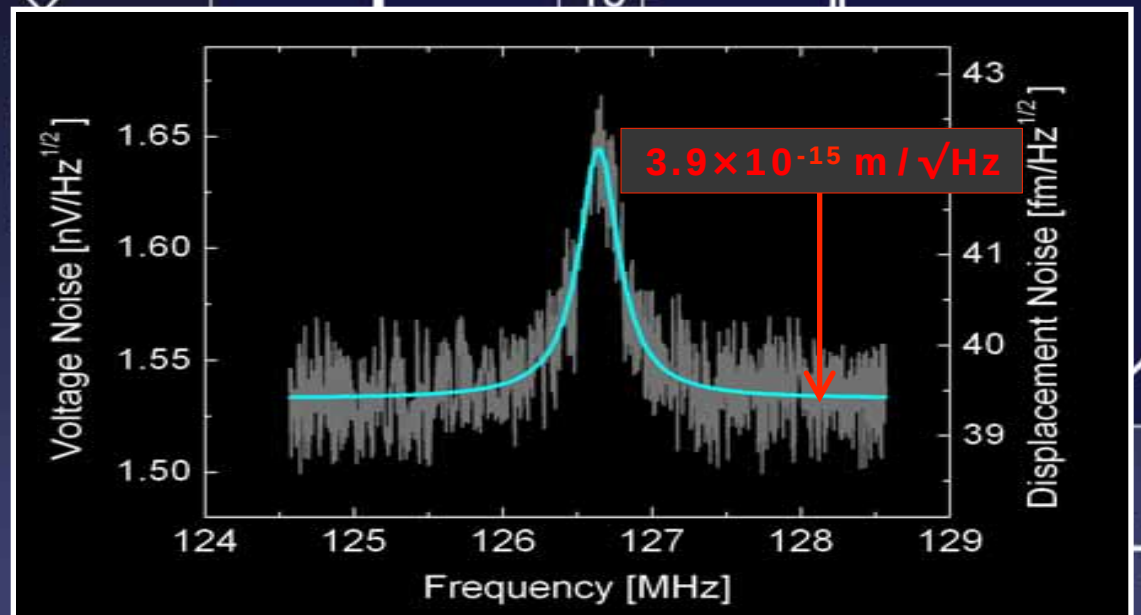
Technology: self-sensing NEMS resonators

ARTICLES nature nanotechnology | VOL 2 | FEBRUARY 2007

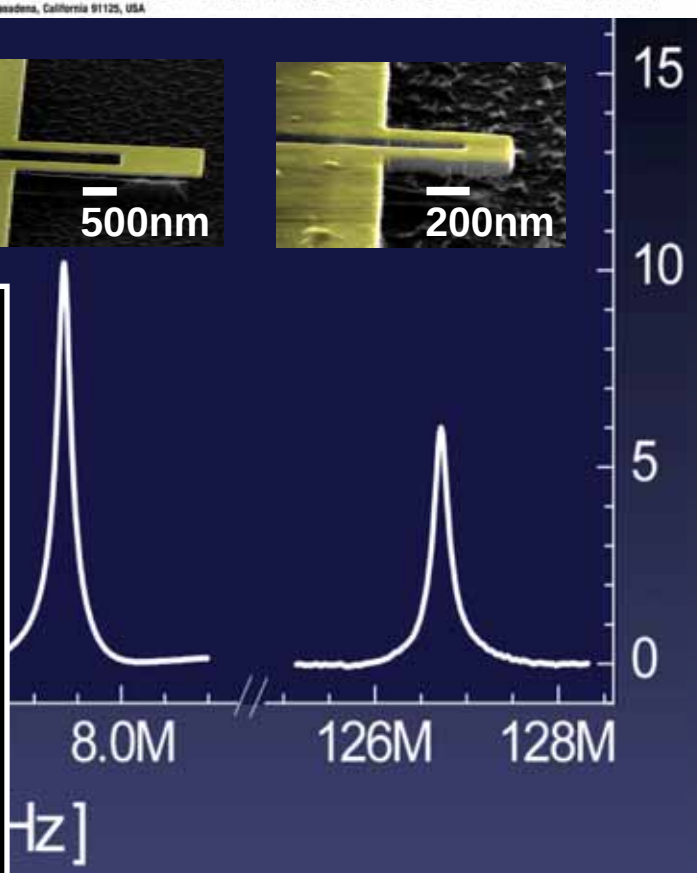
Ultra-sensitive NEMS-based cantilevers for sensing, scanned probe and very high-frequency applications

MO LI, H. X. TANG* AND M. L. ROUKES†

Kavli Nanoscience Institute and Departments of Physics, Applied Physics, and Bioengineering, California Institute of Technology, MS 114-36, Pasadena, California 91125, USA



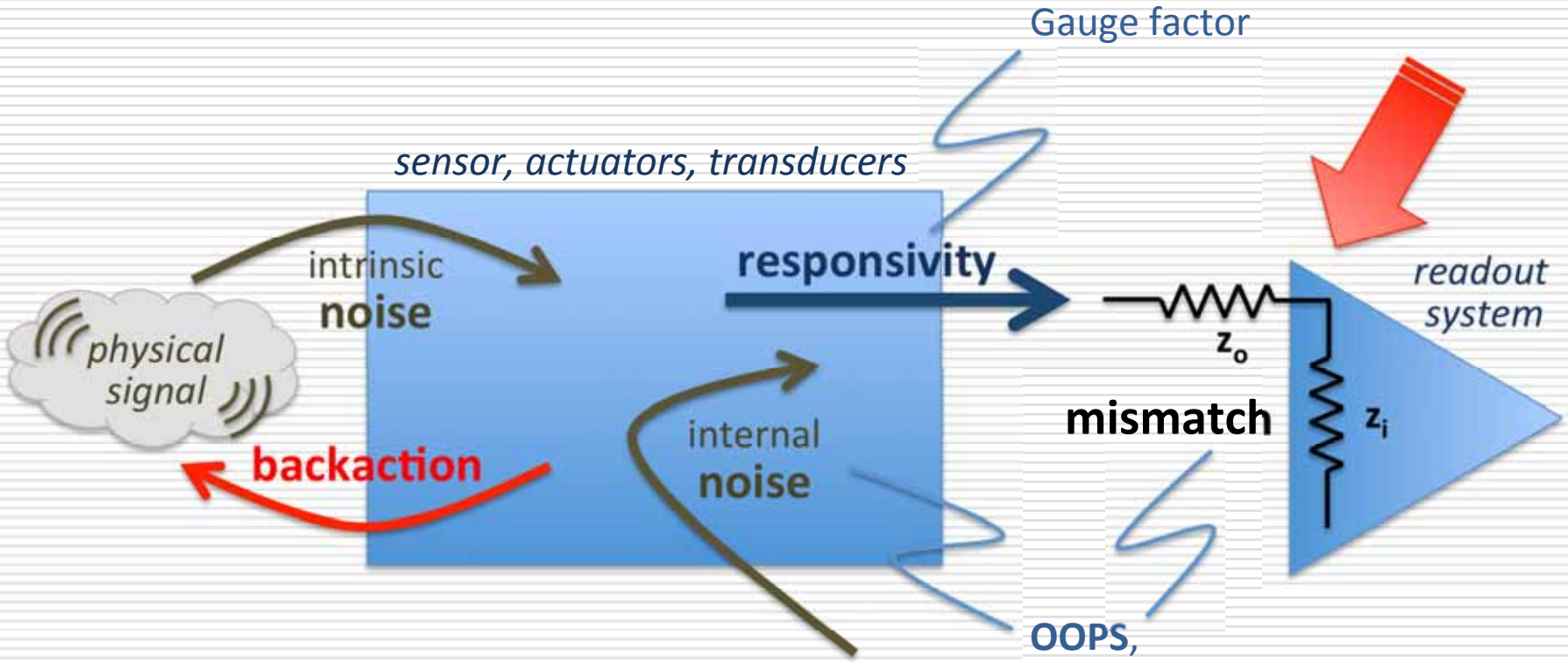
Thermomechanical noise spectrum and Lorentzian fit (red trace) for a 123 MHz nanocantilever measured at room temperature and atmospheric pressure.



y of SiC nanocantilevers to a 1nN
s, at room temperature in vacuo.

Mo Li, HX Tang, ML Roukes,
Nature Nanotechnology **2**, 114 (2007)

responsivity, noise, backaction, mismatch



OOPS,
Gauge factor figures here also!
(In the sense that impedance and noise depend on some of the same parameters.)

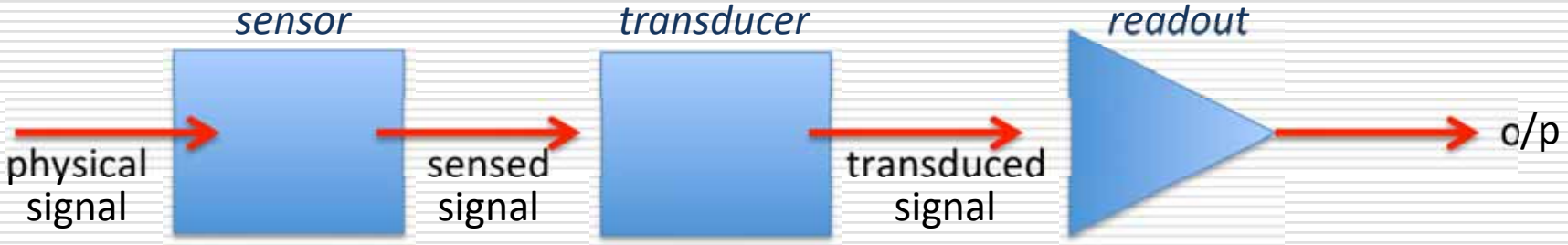
moral:

OPTIMIZE THE **SYSTEM,** ***in toto***

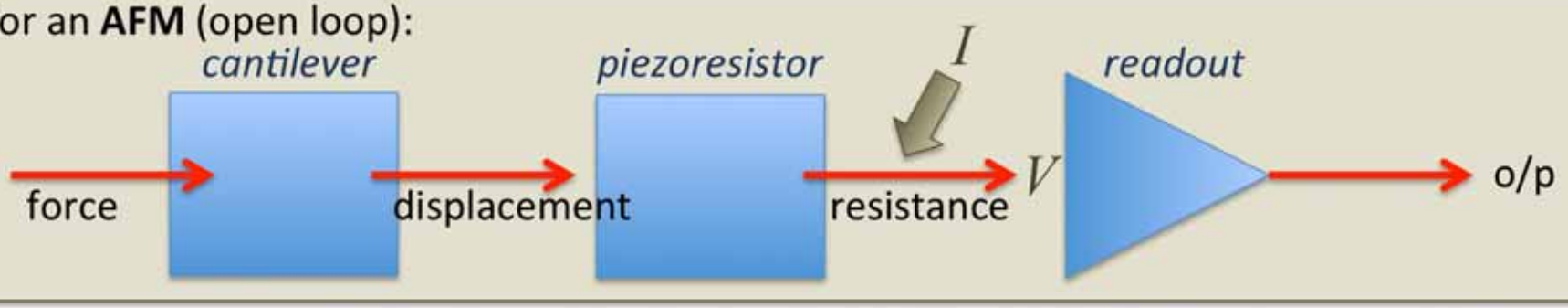
… these are the four critical physical considerations.

Systems: ingredients

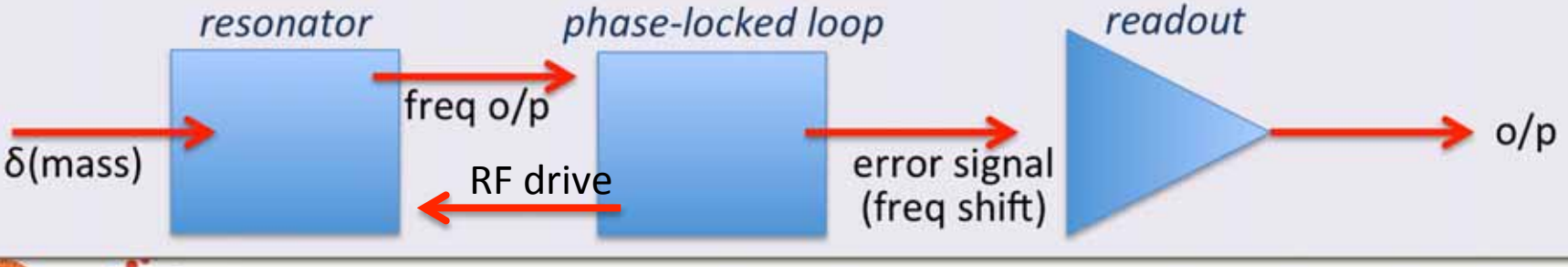
I now want to move toward addressing the organizer's question as to whether we can think of there being a **universal sensor platform**. Let's define nomenclature:



For an **AFM** (open loop):



A resonant **mass sensing system** is somewhat more complex:



Resonant Systems: Generic Platforms

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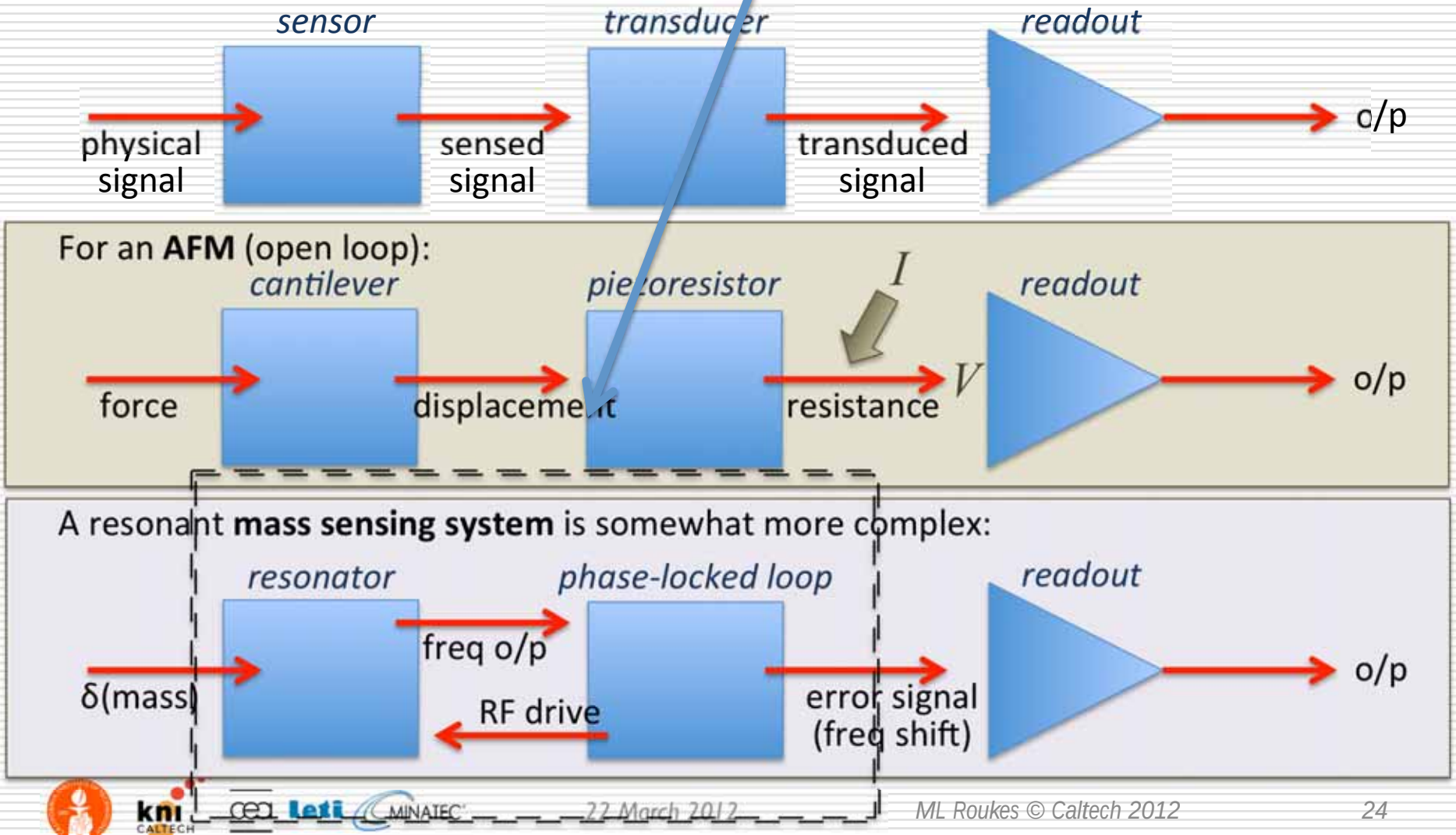
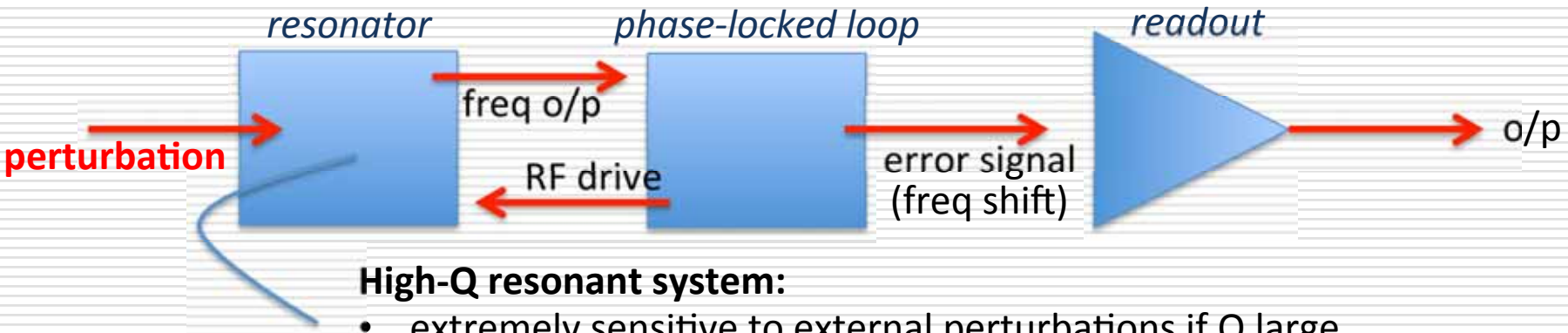


Resonant Systems: Generic Platforms

A generic **resonant sensing system** architecture :



High-Q resonant system:

- extremely sensitive to external perturbations if Q large
- Maintained in steady-state operations by control system (by PLL or low-noise oscillator circuitry)
- Low-phase-noise oscillator technology is well-validated/mature: large drive make feasible observations of *exceptionally* small changes
- However if Q is large, time response (~Q/ω_0) can be slow unless ω_0 is high. So use UHF/microwave NEMS, *or* integrated photonic resonators.

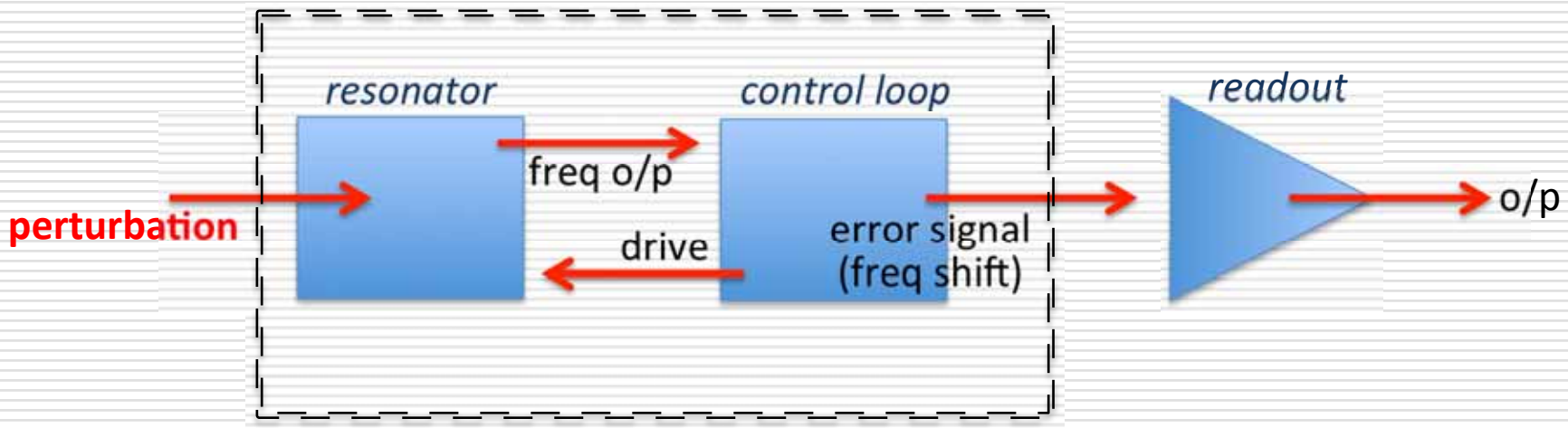
perturbations: (NEMS sensors)

mass, force *(frequency shift in a nonlinear potential, i.e. position bias)*, **acceleration, displacement, temperature** *(conducted through* **phonons***)*, microwave/IR/optical **photons** *(radiated energy)*, **chem/bio sensing** *(chemical binding force detection via entropic and steric effects; calorimetric detection via enthalpic or absorption spectroscopy)*; …etc.

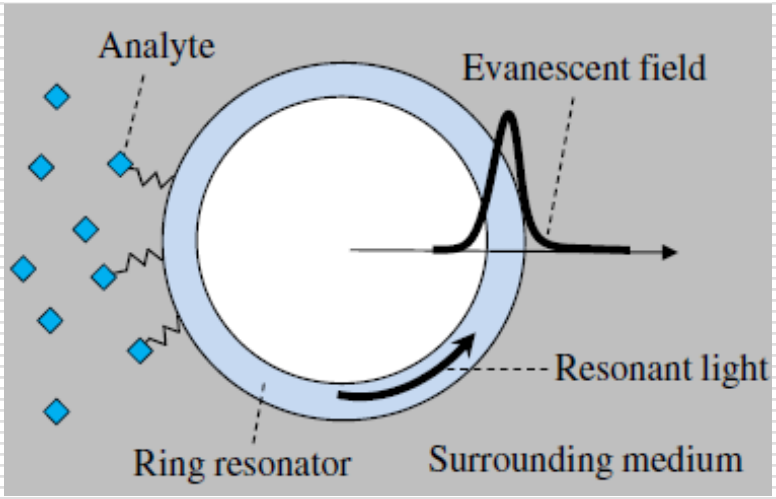
generalization

- I will attempt to generalize the discussion (a little) by considering other state-of-the-art sensors such as resonant photonic devices.

A generic **resonant sensing system** architecture :



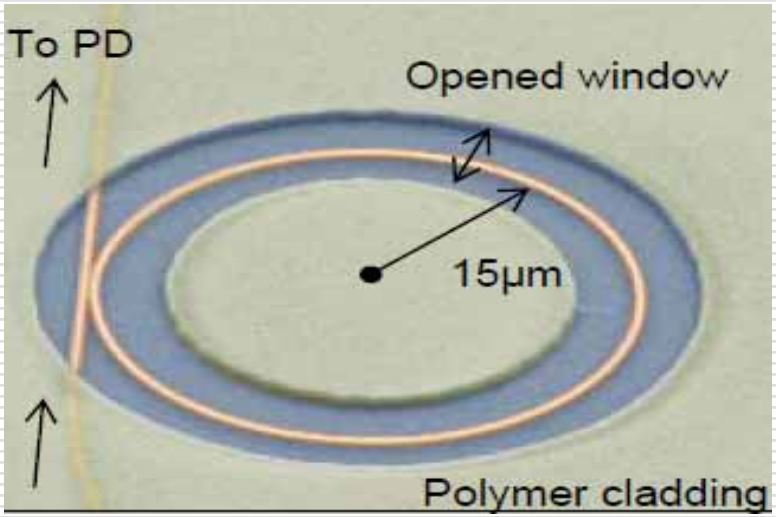
Photonic micro-ring resonators



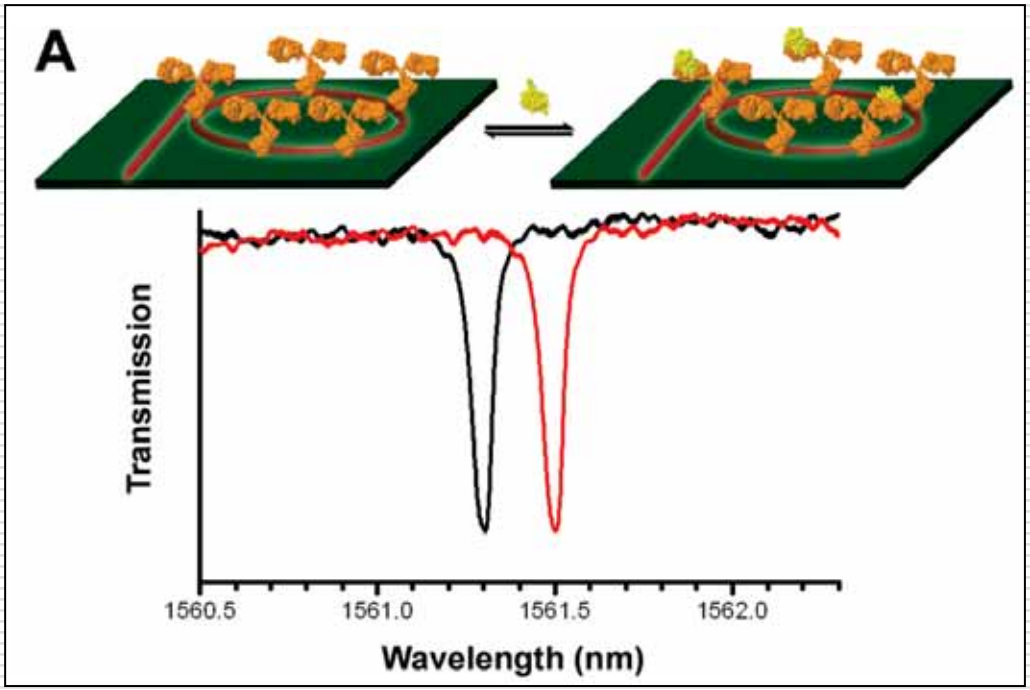
Y. Sun & X. Fan, Anal. Bioanal. Chem (2011)

integer Radius Refractive index

$$m\lambda = 2\pi r n_{eff}$$



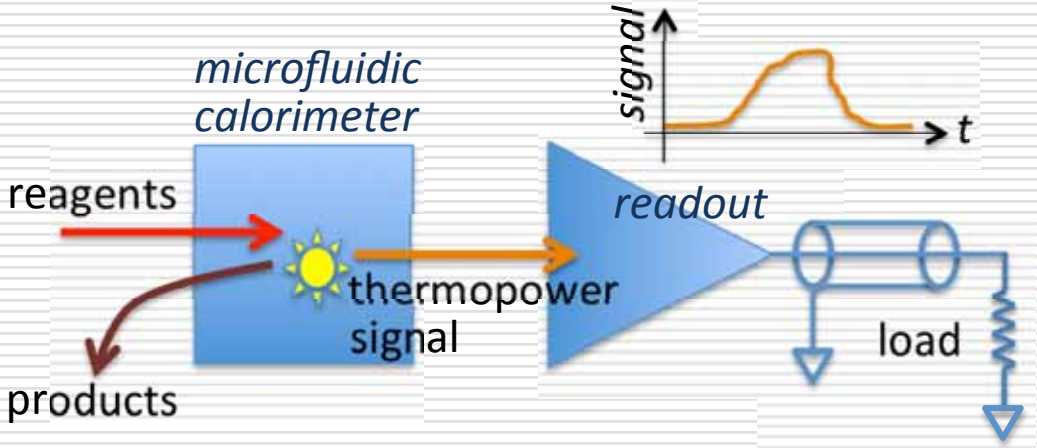
C. Gunn, Genalyte (2010)



Washburn *et al.*, Anal Chem. (2009)

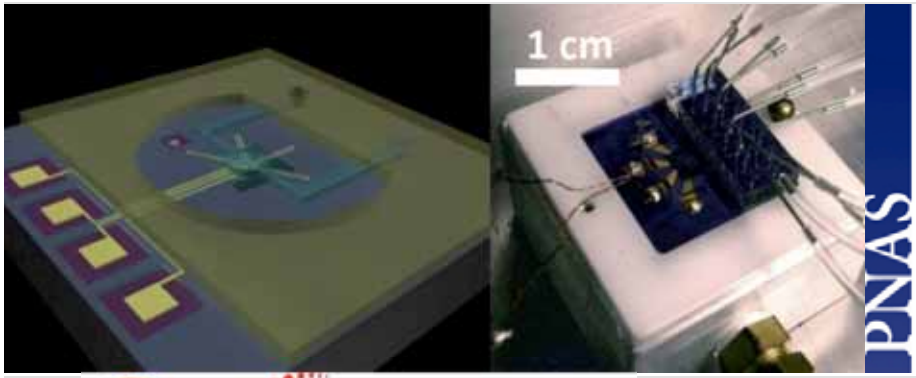
Zero-power sensors: a promising idea?

- One last organizers' thought to address: is there a way, *power-wise*, to get your data for nothing (and your chips for free?) Let's take the archetypal case of thermoelectric μfluidic calorimeters.



Signal may be generated with zero power, but:
- Always have transmission lines to drive
- If wireless, transmitters have power budget
- ***It COSTS to transmit information***

Furthermore:
- Signal may be embedded in 1/f band
- Costs to use active electronics to move to finite frequency (chopper/lock-in amps)
- ***It COSTS to perform signal conditioning***



PNAS | September 8, 2009 | vol. 106 | no. 36 | 15225–15230

High-sensitivity microfluidic calorimeters for biological and chemical applications

Wonhee Lee, Warren Fon, Blake W. Axelrod, and Michael L. Roukes[1]

Kavli Nanoscience Institute, California Institute of Technology, Pasadena, CA 91125

Edited by George M. Whitesides, Harvard University, Cambridge, MA, and approved July 22, 2009 (received for review F

High-sensitivity microfluidic calorimeters raise the prospect of achieving high-throughput biochemical measurements with minimal sample consumption. However, it has been challenging to

arising from evaporation and aw
These can readily lead to erroneo
hand, closed-chamber chip calor

(hard) lessons learned

- The unique properties of nanodevices, however, are not a panacea that absolves us from the need to contend with long-standing, overarching challenges posed by real-world sensing applications. From about a decade and a half's work focused on metamorphosing nanosensors into nanosystems through large-scale integration, nature has taught us some hard lessons.

(hard) lessons learned

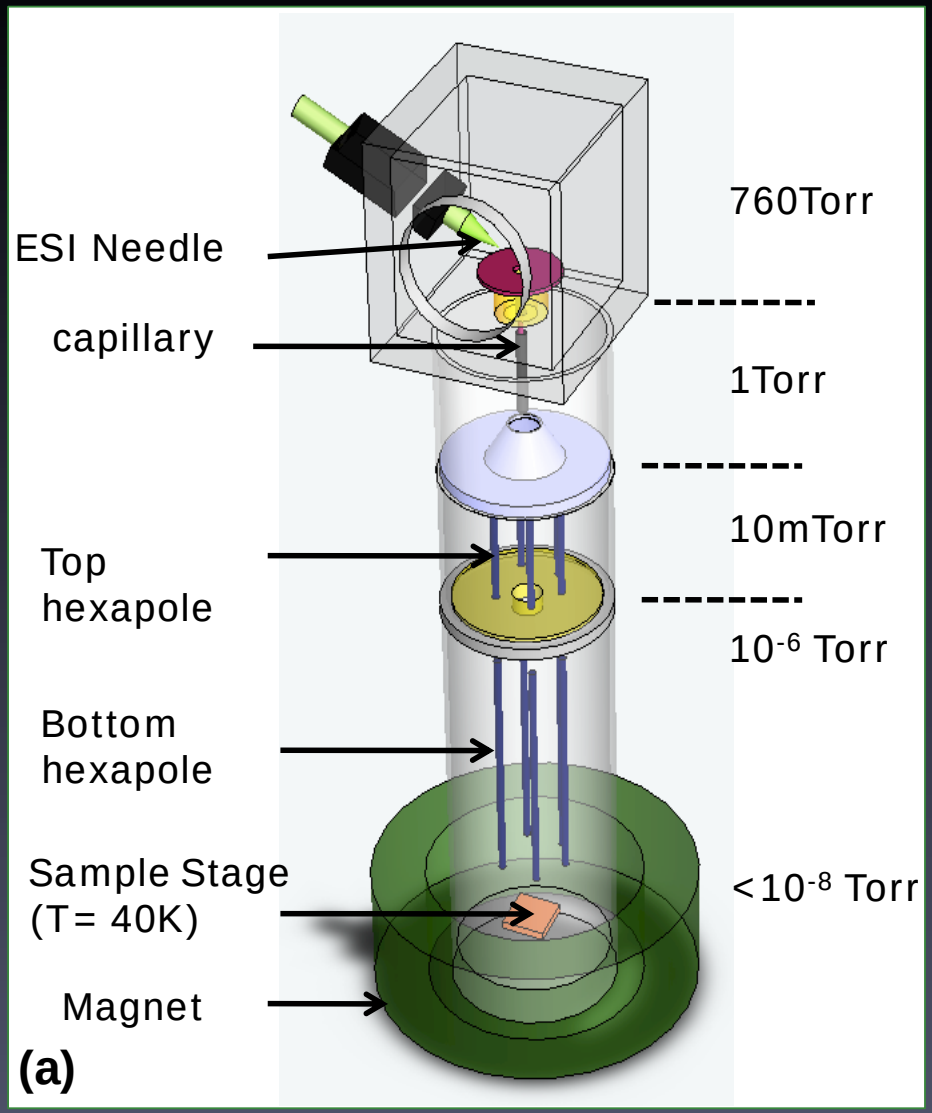
- Among them are: (a) much, if not most of the work in applying nanosensors must be invested in embedding them into functional *systems*;

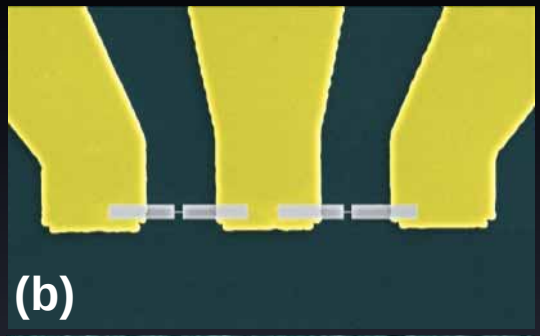
The following whirlwind tour of NEMS-MS work spanning 2000-2012 is presented, just for fun, as an example…

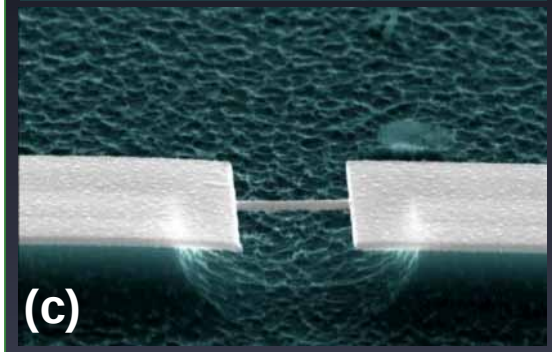
From proteins in solution to vacuum-based adsorption

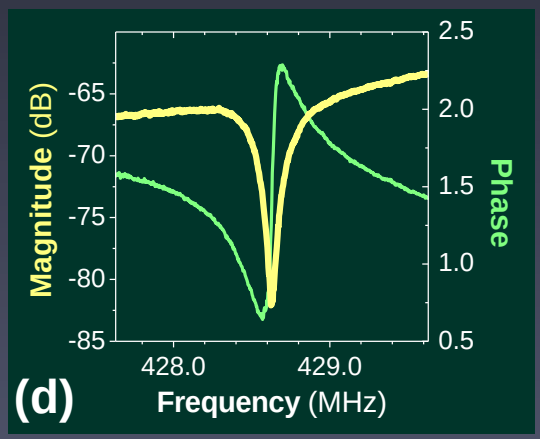
- electrospray **Injection**
- dual differential **pumping**
- dual hexapole **ion gudes**
- faraday cup
- phase-locked UHF NEMS **mass sensor** *(~428 MHz)*

Wayne Hiebert
Selim Hanay
Akshay Naik
Philip Feng
Steve Stryker
(2004-08)









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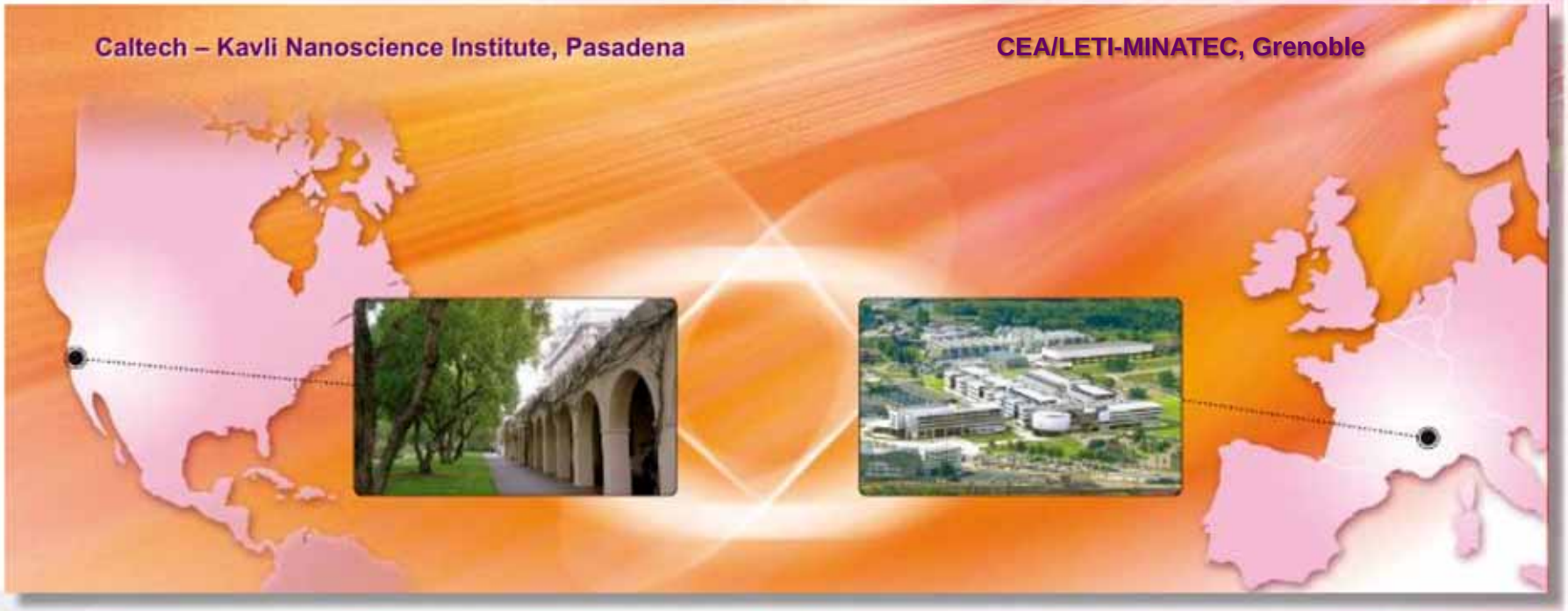
(hard) lessons learned

- (b) careful choices of platform materials are essential to insure a rapid transition into large-scale integration and production *en-masse*.

The Alliance for Nanosystems VLSI



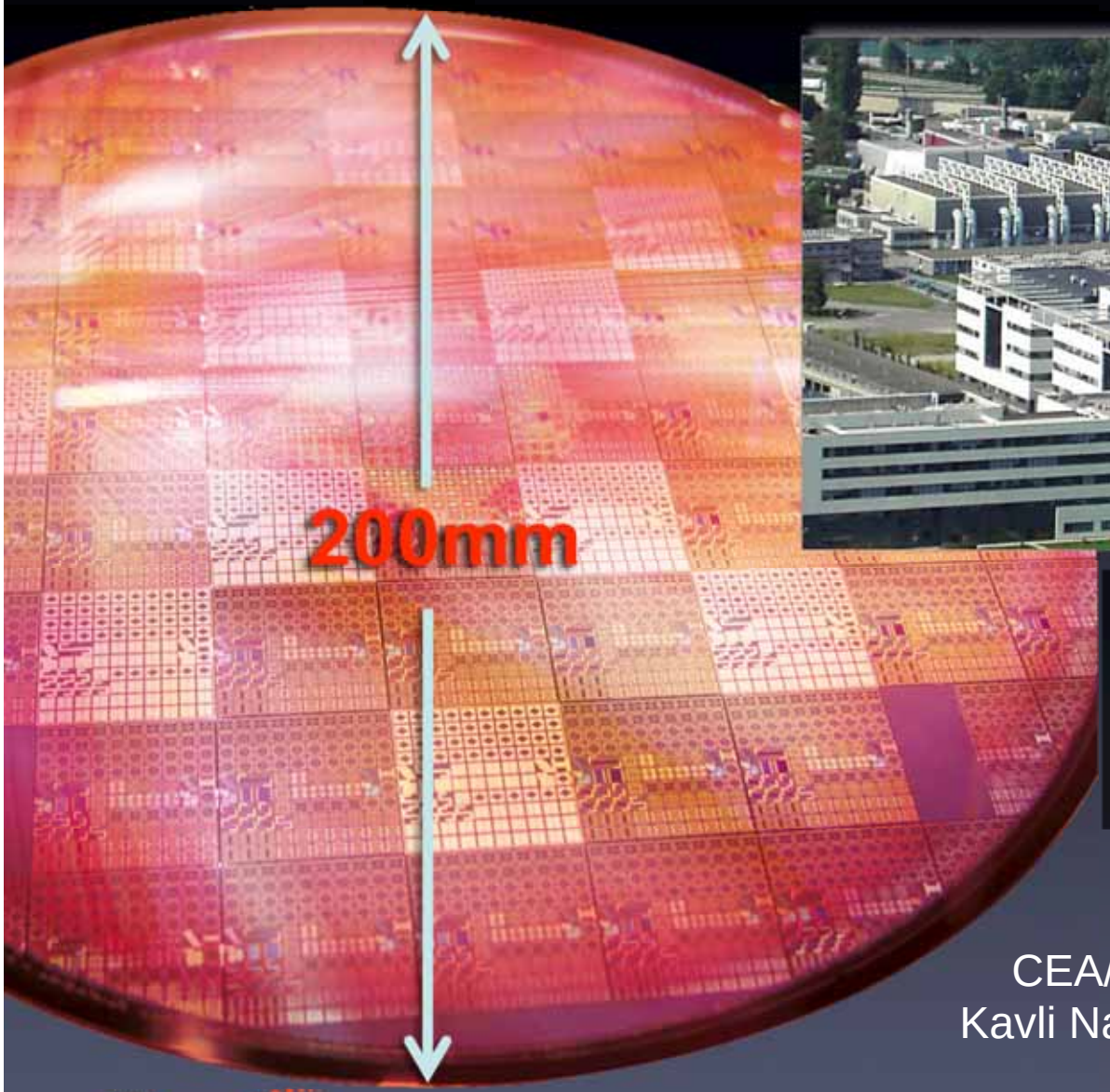
Functional validation of nanosystems

- >20 years in nanosystems and nanosciences
- understanding of underlying physics: ultimate limits
- NEMS (nanoelectromechanical systems)
- Physics, Biophysics, Engineering
- Quick prototyping; Kavli Nanoscience Institute

Very-large-scale Integration

- 200 & 300 mm technological facilities
- Systems architecture and integration (from design to packaging)
- Applied research / applications
- Technology transfer to industry

$B-scale microelectronic foundry required...

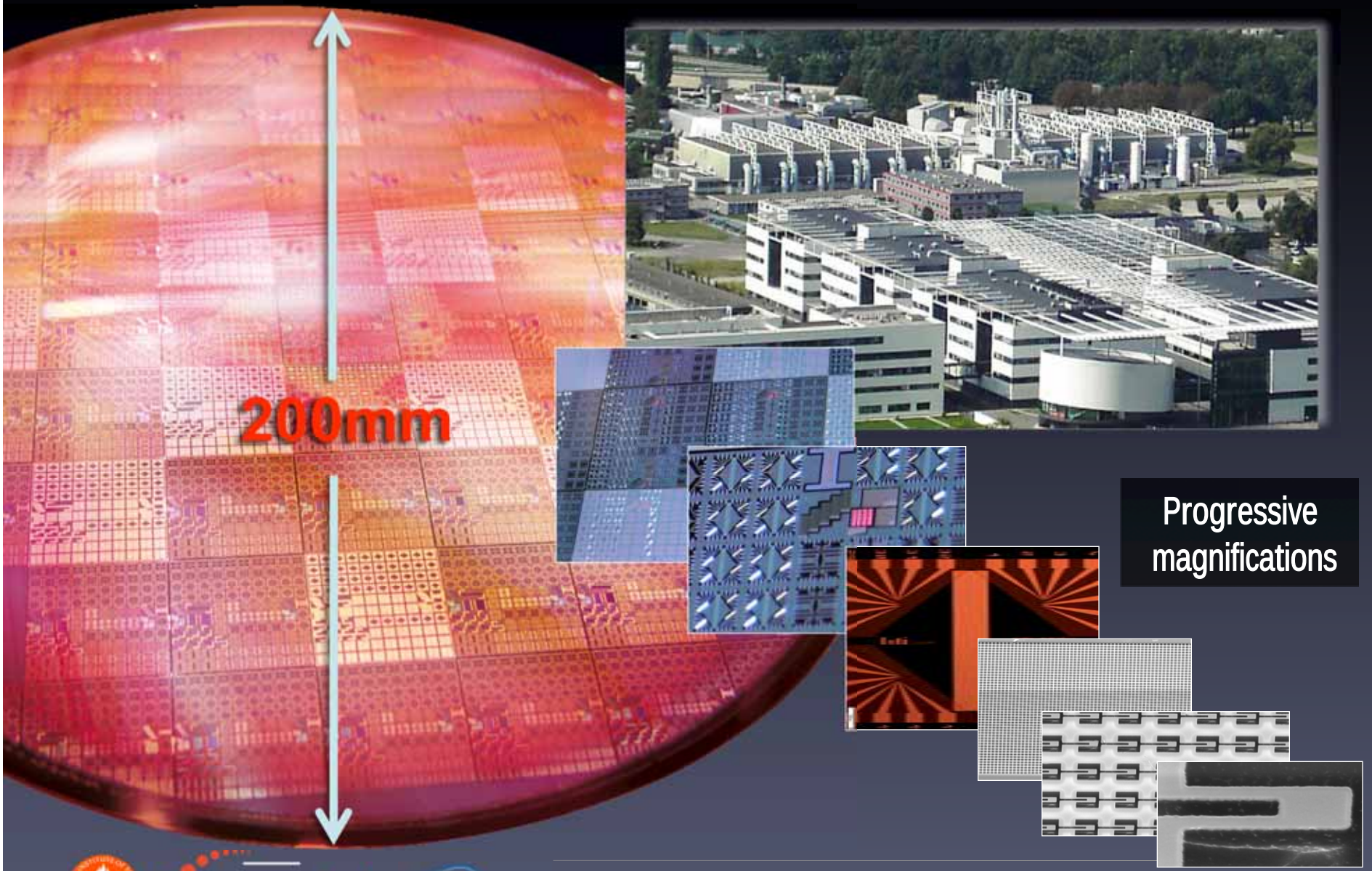


- $B-scale “foundry”
- fabrication of millions of nanodevices via standard 200mm (8”) VLSI processes

CEA/LETI-MINATEC, Grenoble &
Kavli Nanoscience Institute, Caltech

© Caltech/CEA-LETI 2011

$B-scale microelectronic foundry required...



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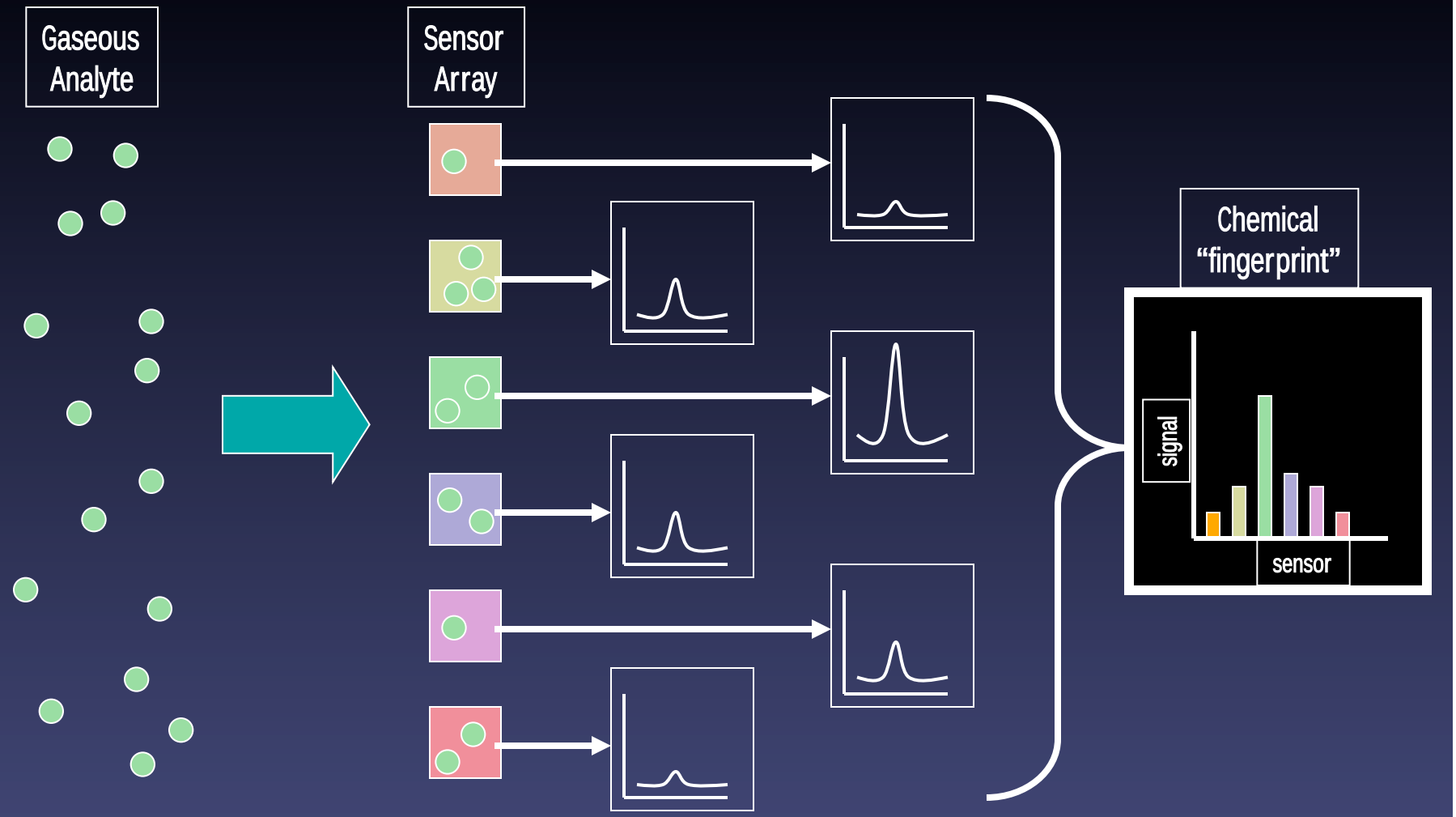
(hard) lessons learned

- (c) any stand-alone sensor is unlikely to be up to the full dynamic range of challenges posed in the real world;

Microsystems for gas phase chemical analysis

The "electronic nose" paradigm: a chemical sensor array



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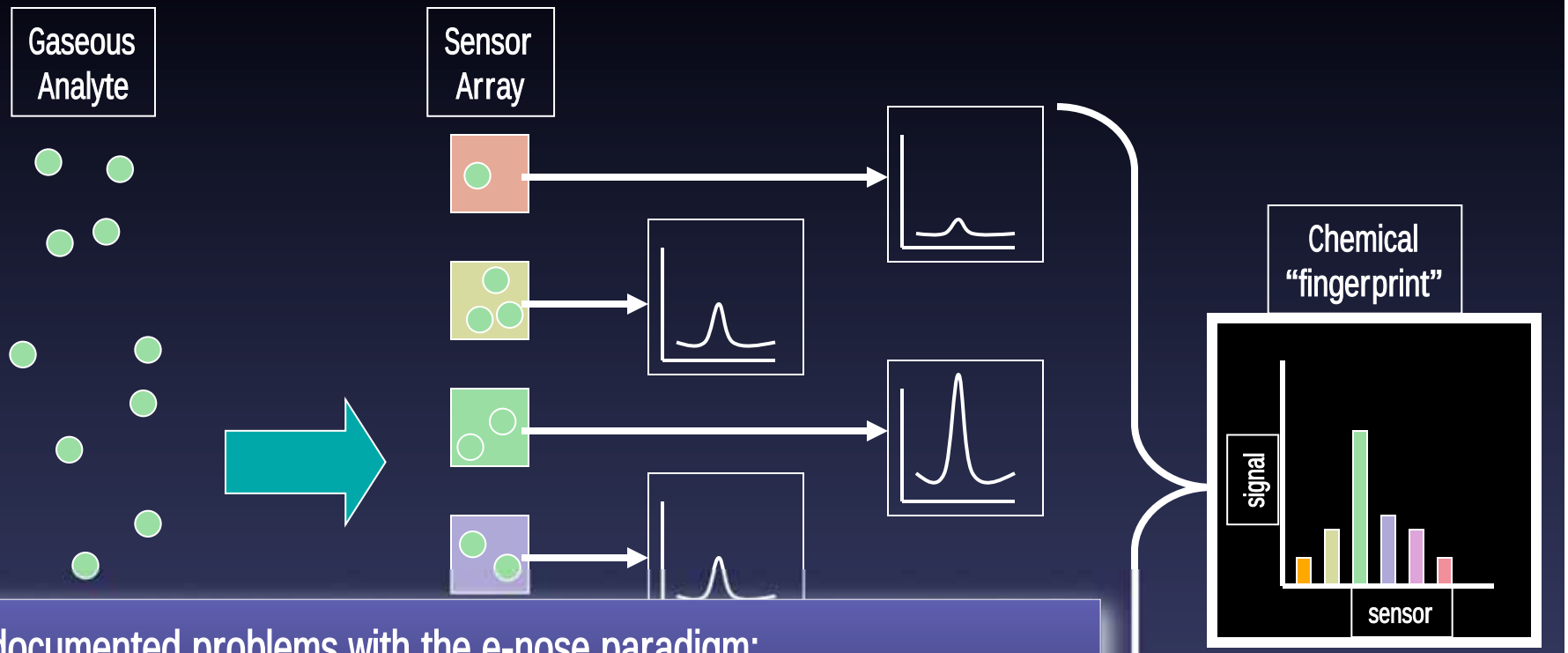
The "electronic nose" paradigm: a chemical sensor array



Well-documented problems with the e-nose paradigm:

- **crosstalk:** "fingerprint" changes with exposure to multiple analytes
- **environmental fluctuations:** *e.g.* temperature, humidity
- **saturation:** hard to look for analytes at few ppt level ("*t*"=*trillion*) in the presence of few percent H_20, 1000ppm smog, *etc.*

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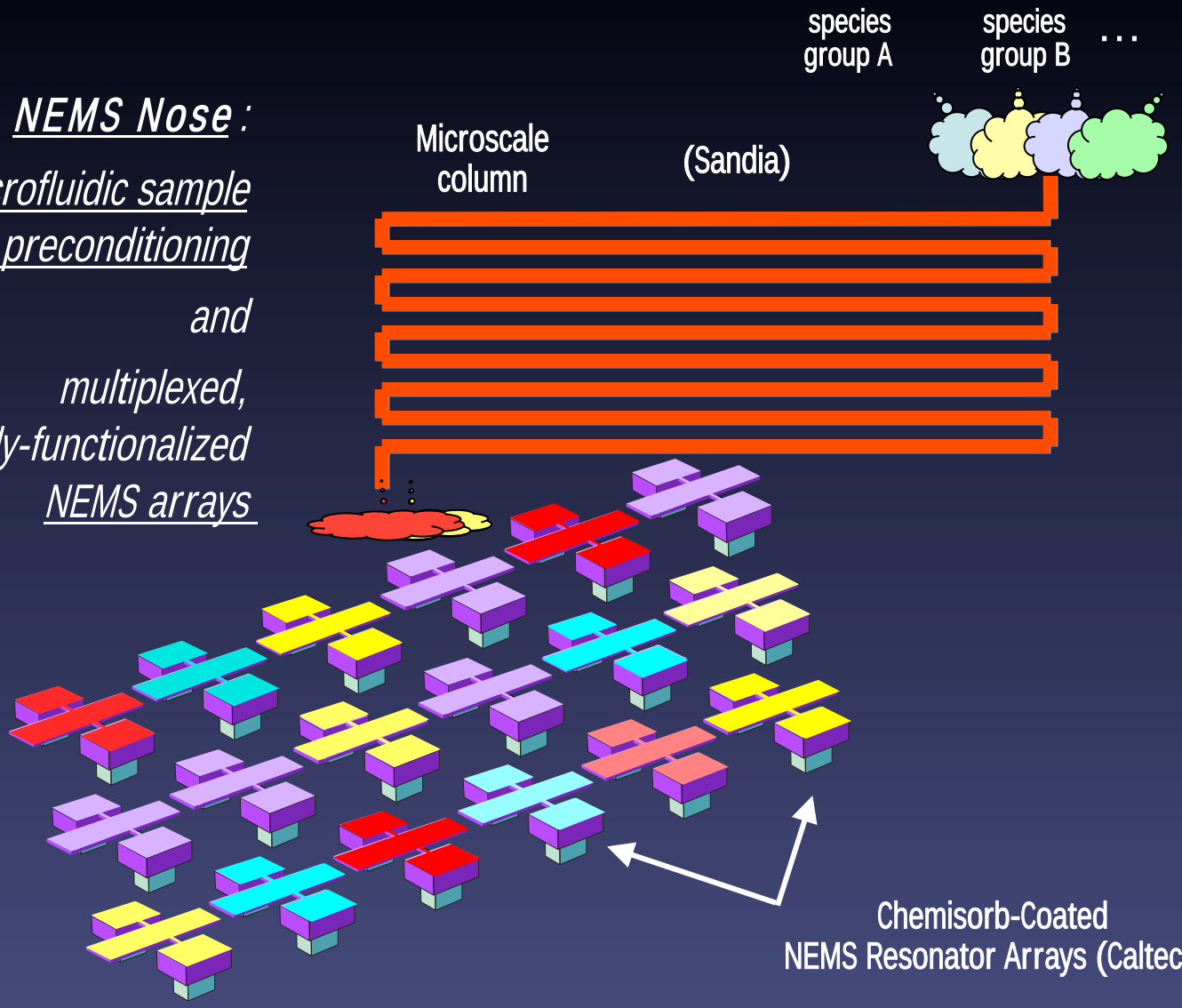
Caltech-Sandia Project: microGC + NEMS sensor array

NEMS Nose *:*

microfluidic sample preconditioning

and

multiplexed, chemically-functionalized NEMS arrays



Sandia National Laboratories

© Caltech 2010-2012

Chemical functionalization preferentially "sorbs" analytes from ambient (1 Atm)

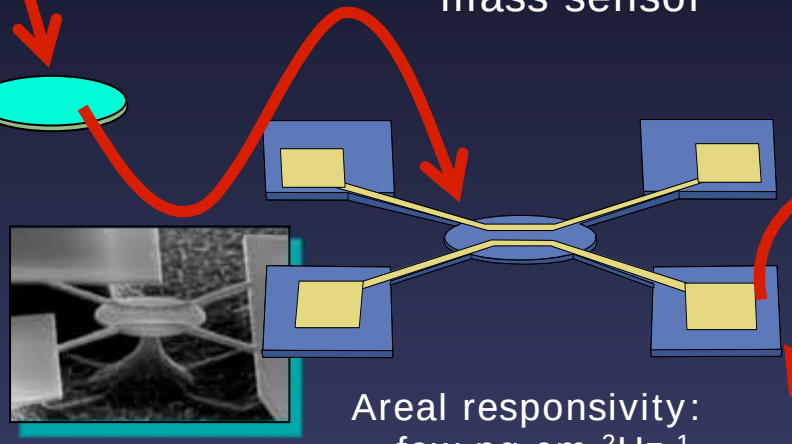
Ingredients: Chemisorptive NEMS Sensor

(a) chemisorptive coating

µGC pulse

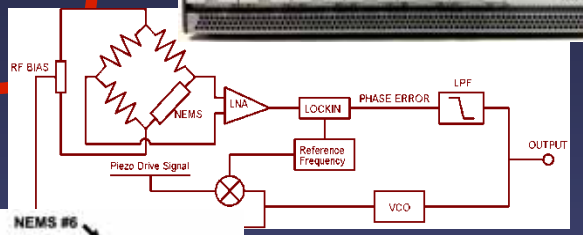
1ppt CWA to MGA yields a pulse from GC that is ~10ppb for 10ms (typ.)

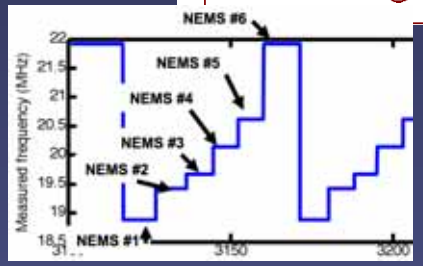
(b) resonant NEMS mass sensor



Areal responsivity:
~ few pg $cm^{-2}Hz^{-1}$

(c) control-loop readout





Frequency Resolution:
~1×10^{-8}

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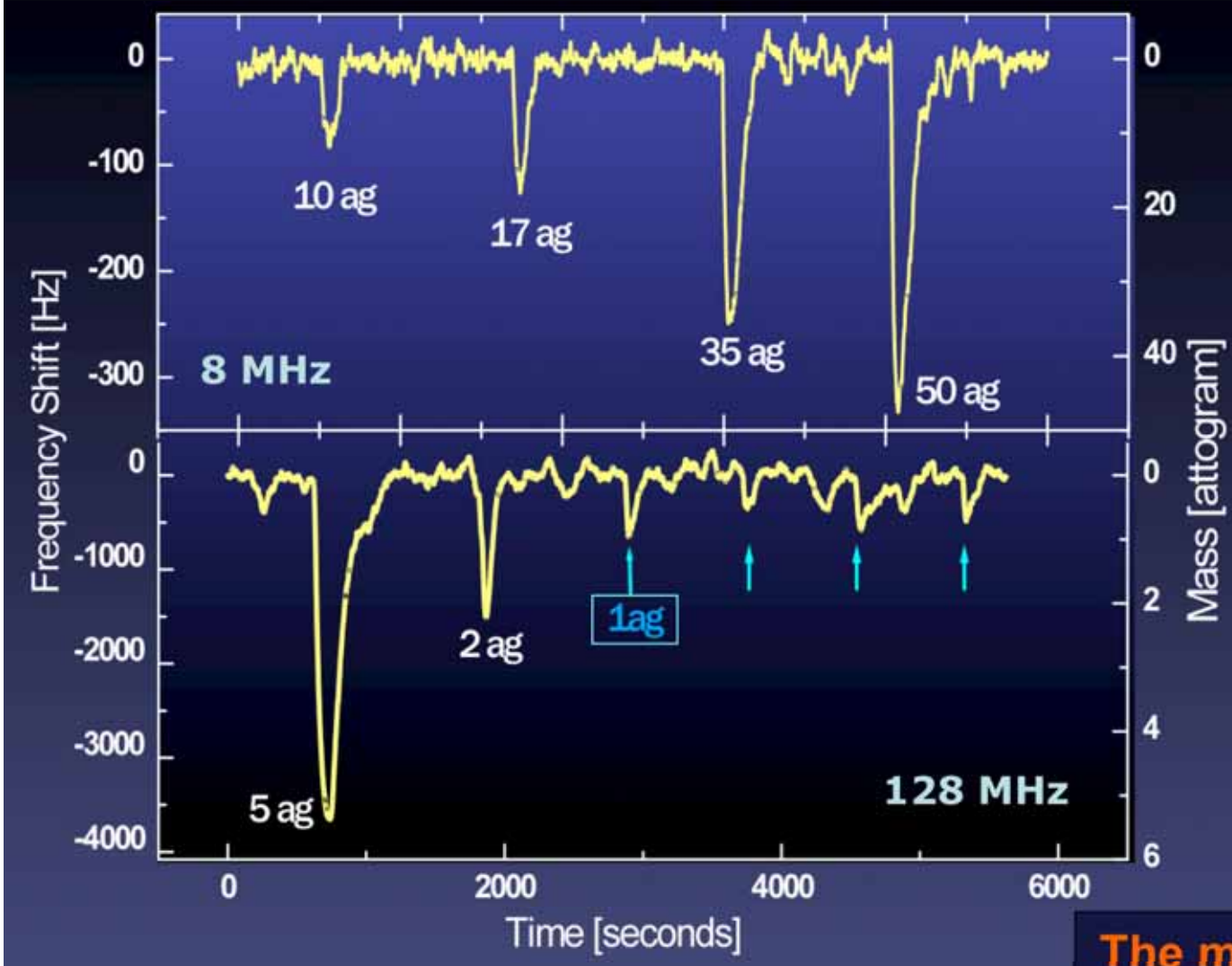
NEMS mass sensing at 1 Atm

Ultra-sensitive NEMS-based cantilevers for sensing, scanned probe and very high-frequency applications
Mo Li, HX Tang, ML Roukes,
Nature Nanotechnology **2**, 114 (2007)



Real time chemisorption measurements with two PMMA-coated NEMS resonators. Displayed are frequency shift steps upon of adsorption of difluoroethane gas molecules onto device surface.

These measurements are carried out at atmospheric pressure & room temperature.

The top and bottom traces are measured with 8 MHz and 128 MHz nanocantilever devices, respectively.

The minimum resolvable mass is ~100 zg.

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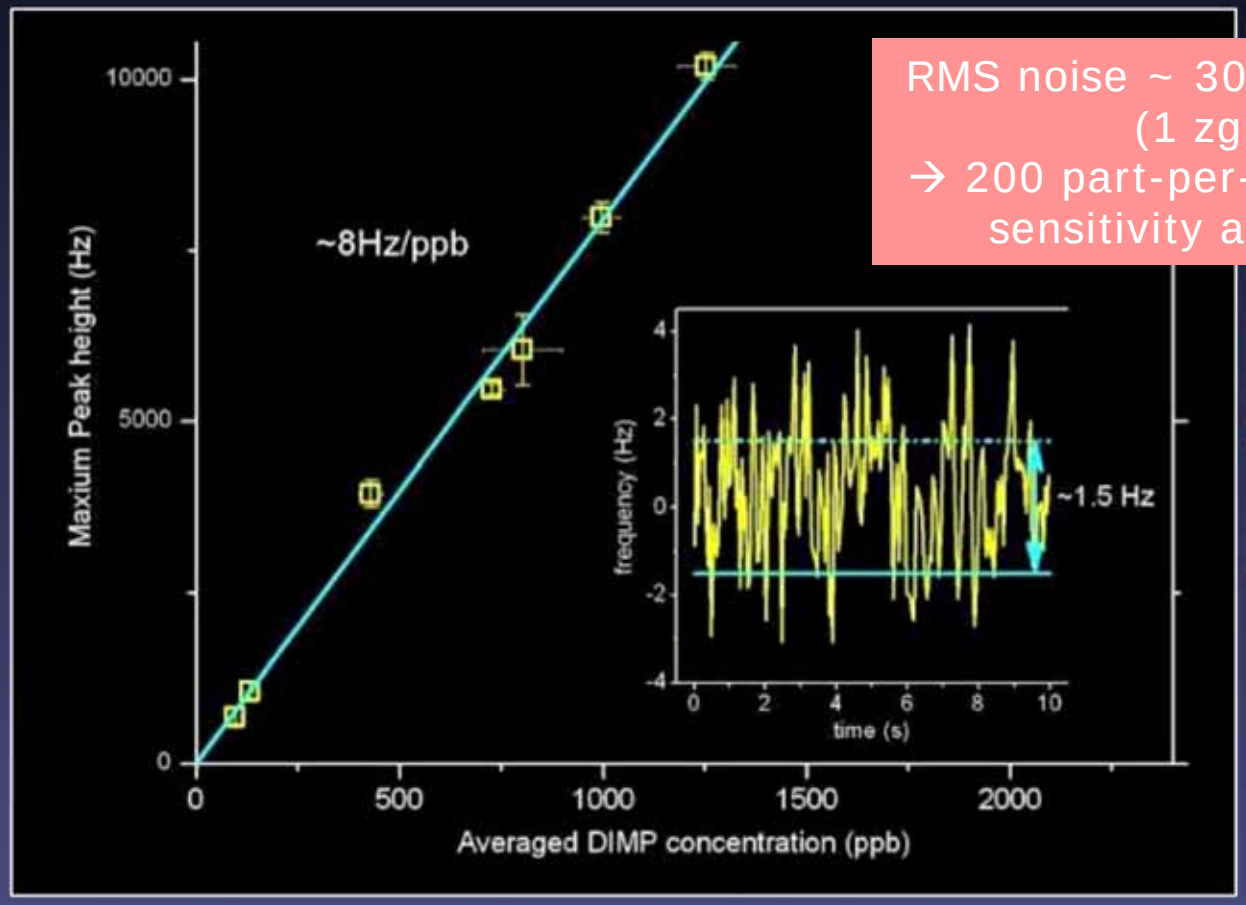
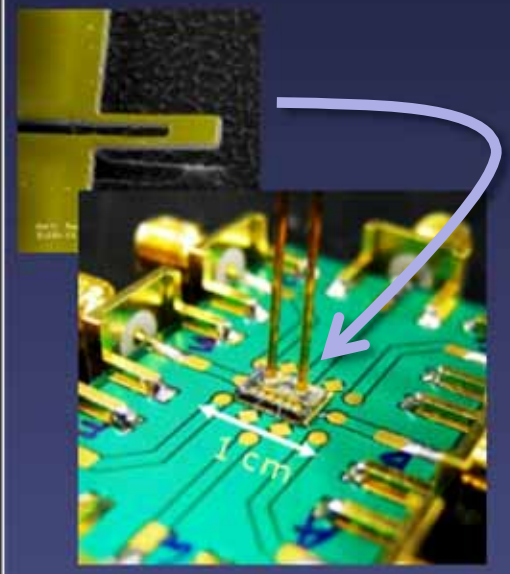
Analytical grade performance achieved, from devices millions of times smaller than anything before

Nanoelectromechanical Resonator Arrays for Ultrafast, Gas-Phase Chromatographic Chemical Analysis
Mo Li, EB Myers, HX Tang, SJ Aldridge, HC McCaig, JJ Whiting, RJ Simonson, NS Lewis, ML Roukes, *Nano Letters* **10**, 3899 (2010)

- Frequency shift response to DIMP (a CWA simulant) is linear from ppm concentrations -> *sub ppb* levels
- Sub-ppb sensitivity is comparable to that attained with state-of-the-art laboratory technologies for ultralight (non-sticky) analytes



RMS noise ~ 300 zg DIMP sensitivity
(1 zg = 10^{-21} g)
→ 200 part-per-trillion concentration sensitivity attained **at 1 Atm**



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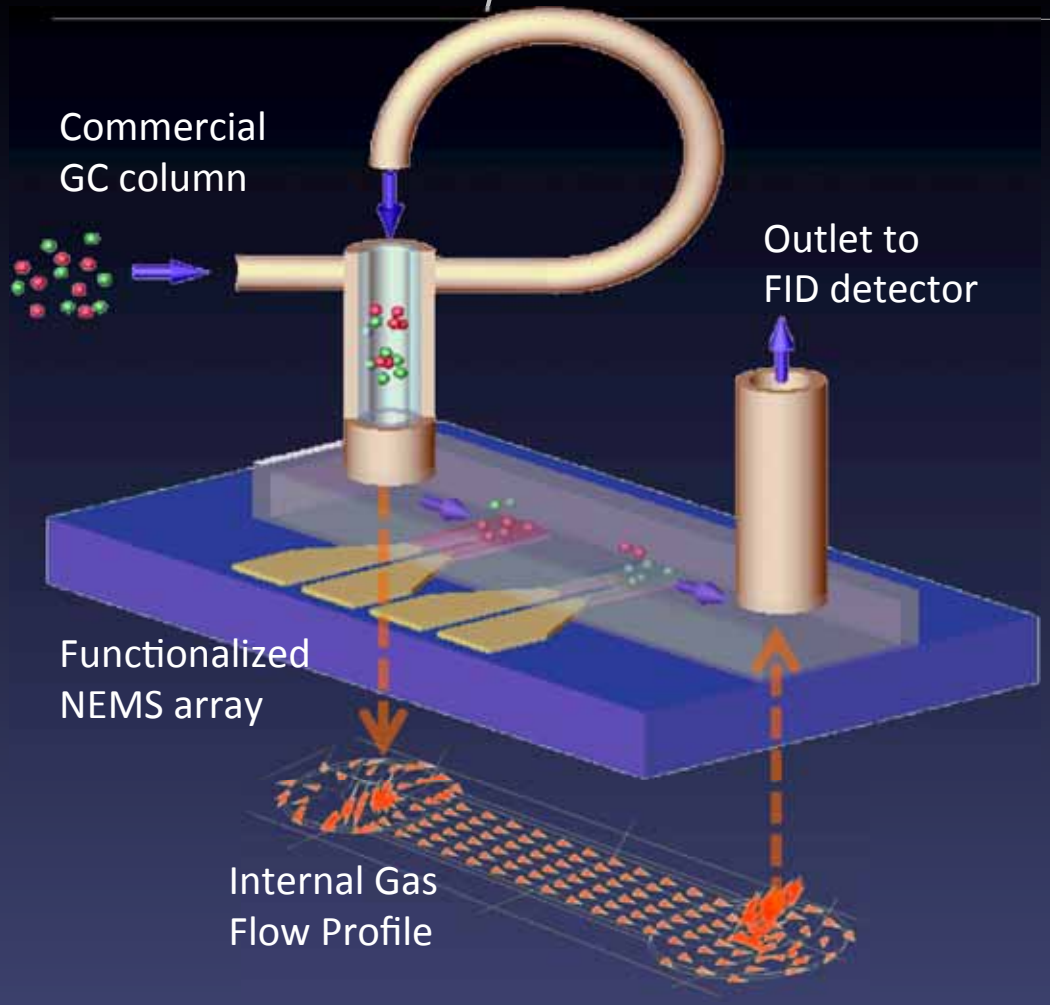
Miniscule NEMS footprint: state-of-the-art sensing in chip-scale GC columns



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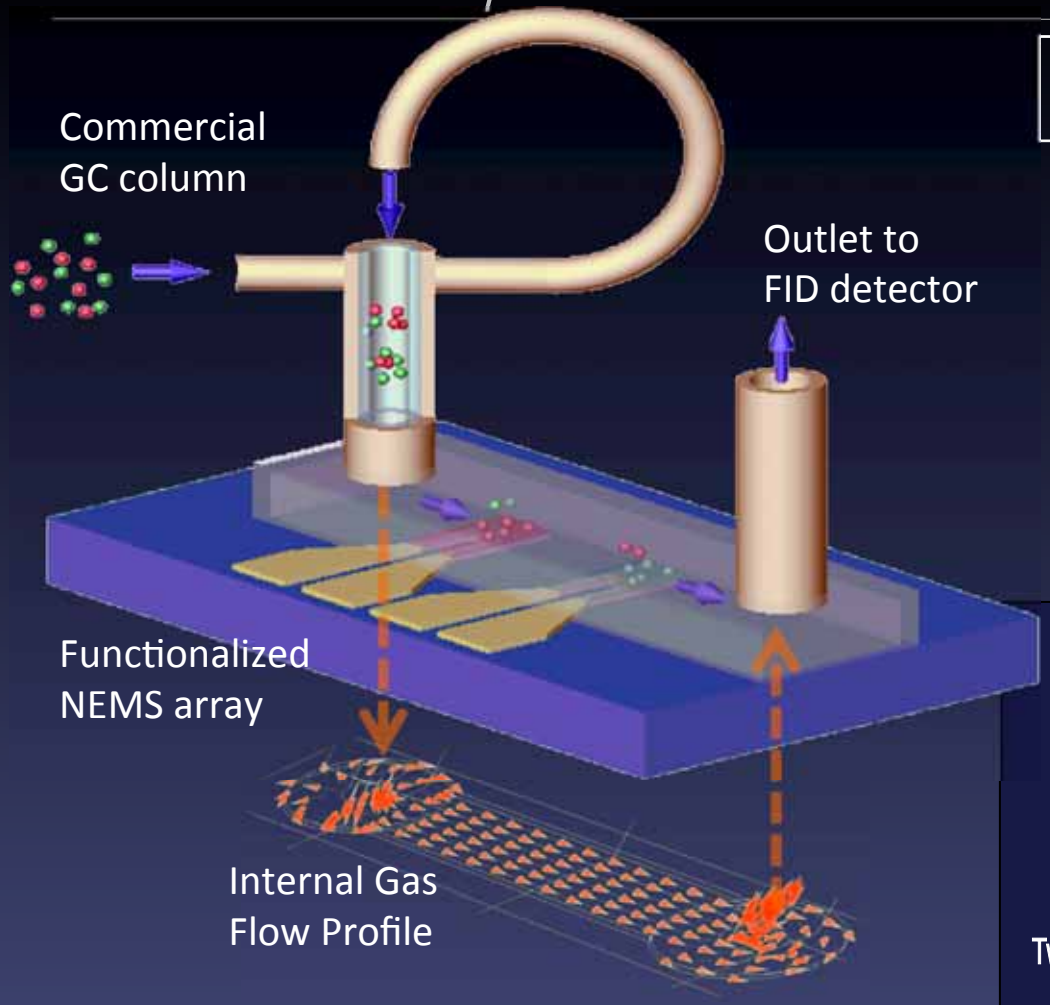
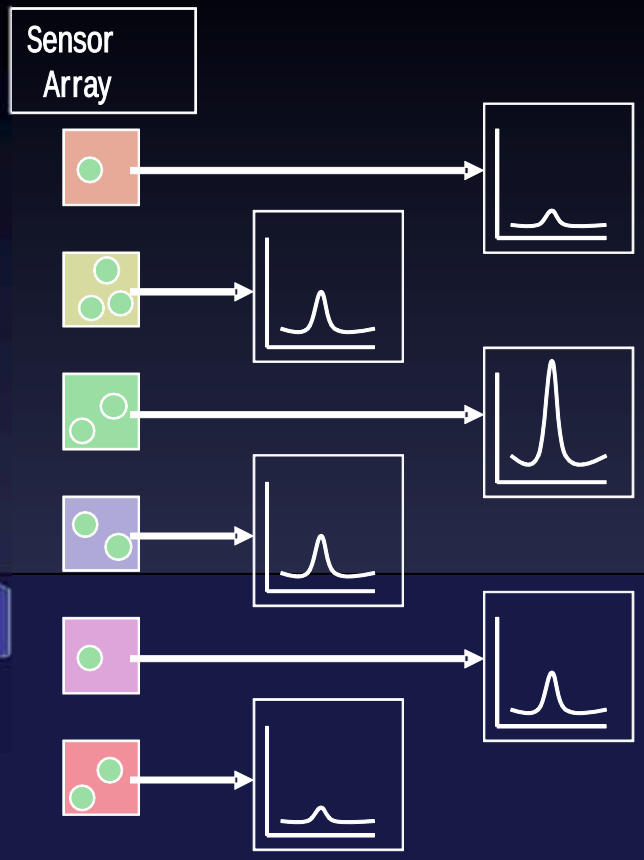
Miniscule NEMS footprint: state-of-the-art sensing in chip-scale GC columns





Two devices with diff. selectivities:

1) DKAP: specifically sensitive to phosphonate nerve agents
2) PCL: highly absorptive, but unselective, polymer

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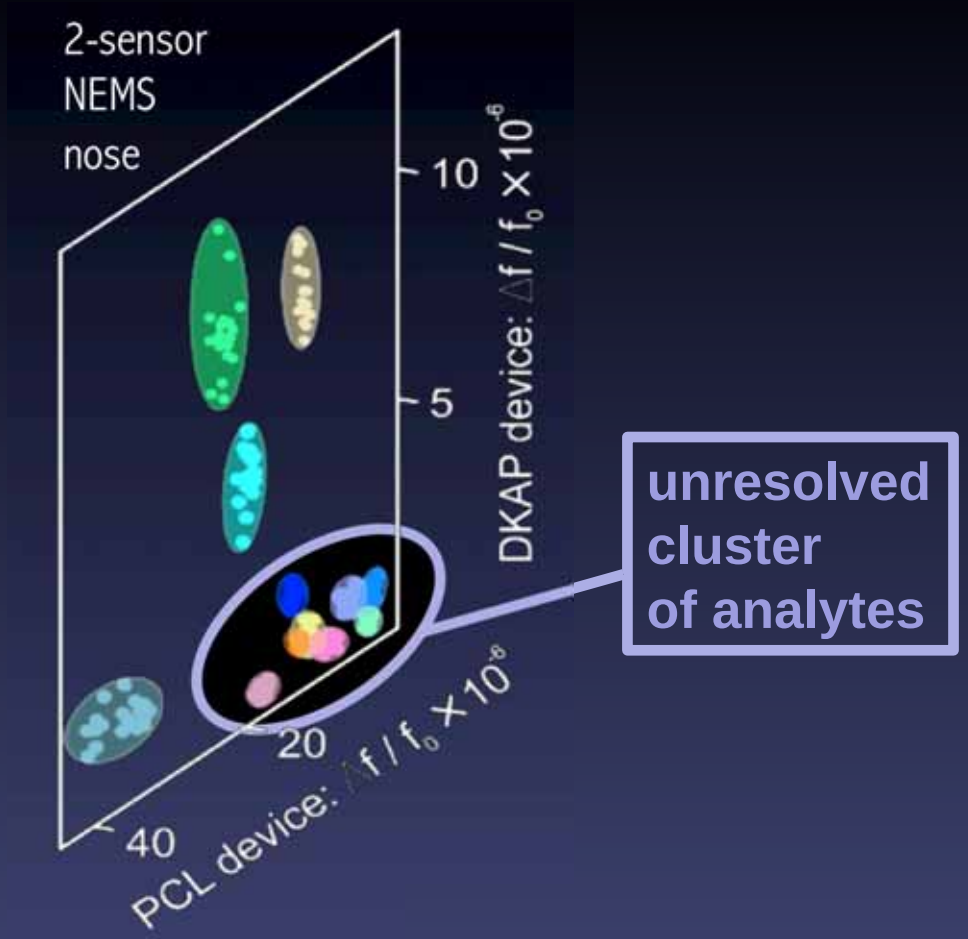
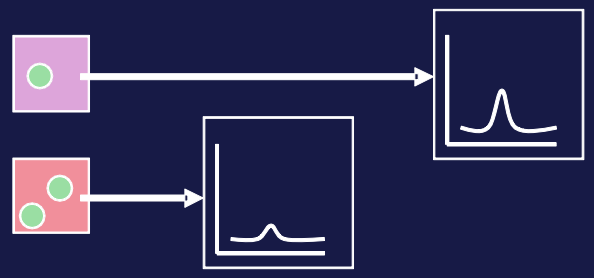
Conventional "e-nose" paradigm is inadequate



unresolved cluster of analytes



Two devices with diff. selectivities:

1) DKAP: specifically sensitive to phosphonate nerve agents
2) PCL: highly absorptive, but unselective, polymer

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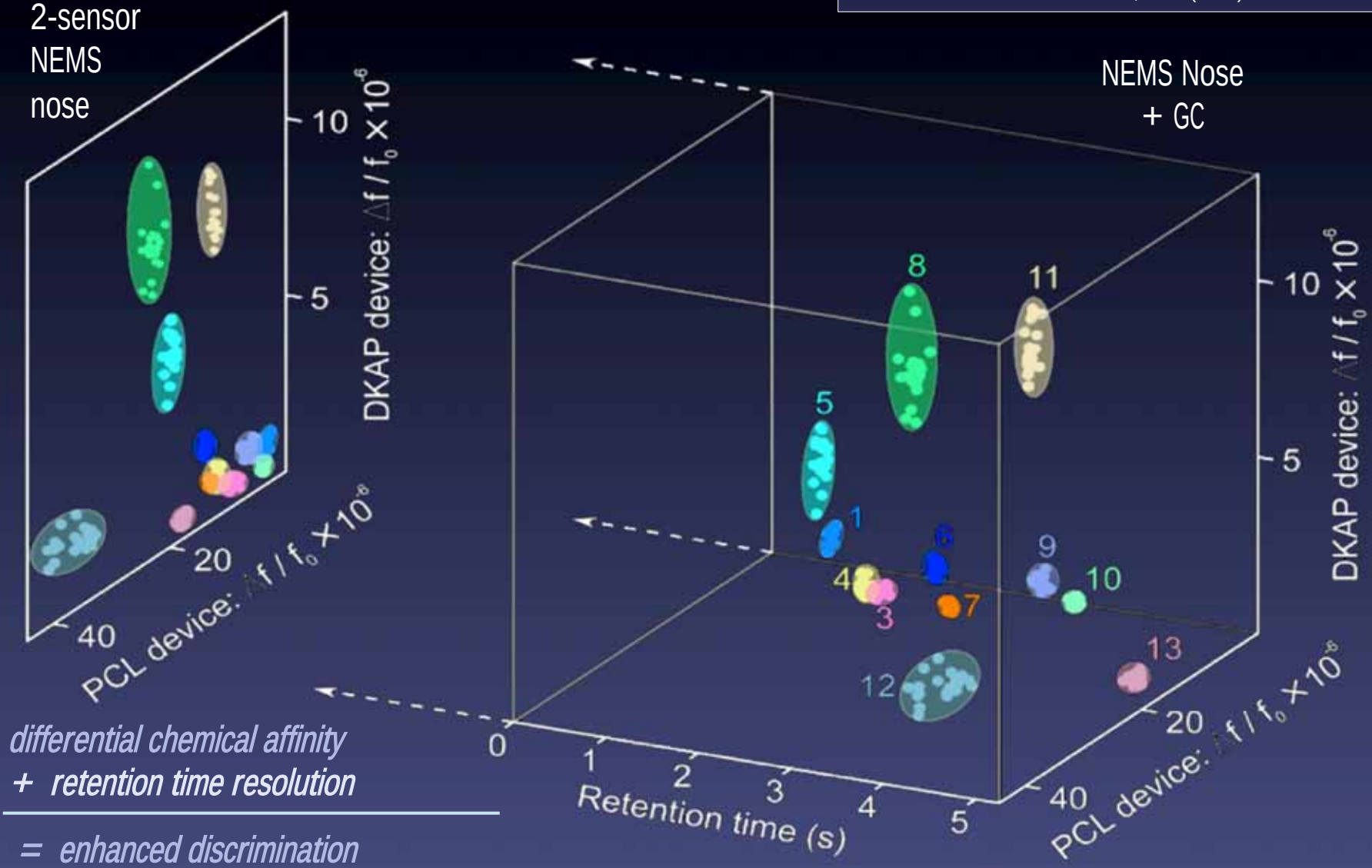
(hard) lessons learned

- (c) complex combinations of real-world analytes are unlikely to be resolved by any “one-stop” generic approach;

GC+"NEMS nose" provides superior performance

Nanoelectromechanical Resonator Arrays for Ultrafast, Gas-Phase Chromatographic Chemical Analysis
Mo Li, EB Myers, HX Tang, SJ Aldridge, HC McCaig, JJ Whiting, RJ Simonson, NS Lewis, ML Roukes,
Nano Letters **10**, 3899 (2010)



differential chemical affinity
+ retention time resolution

= enhanced discrimination

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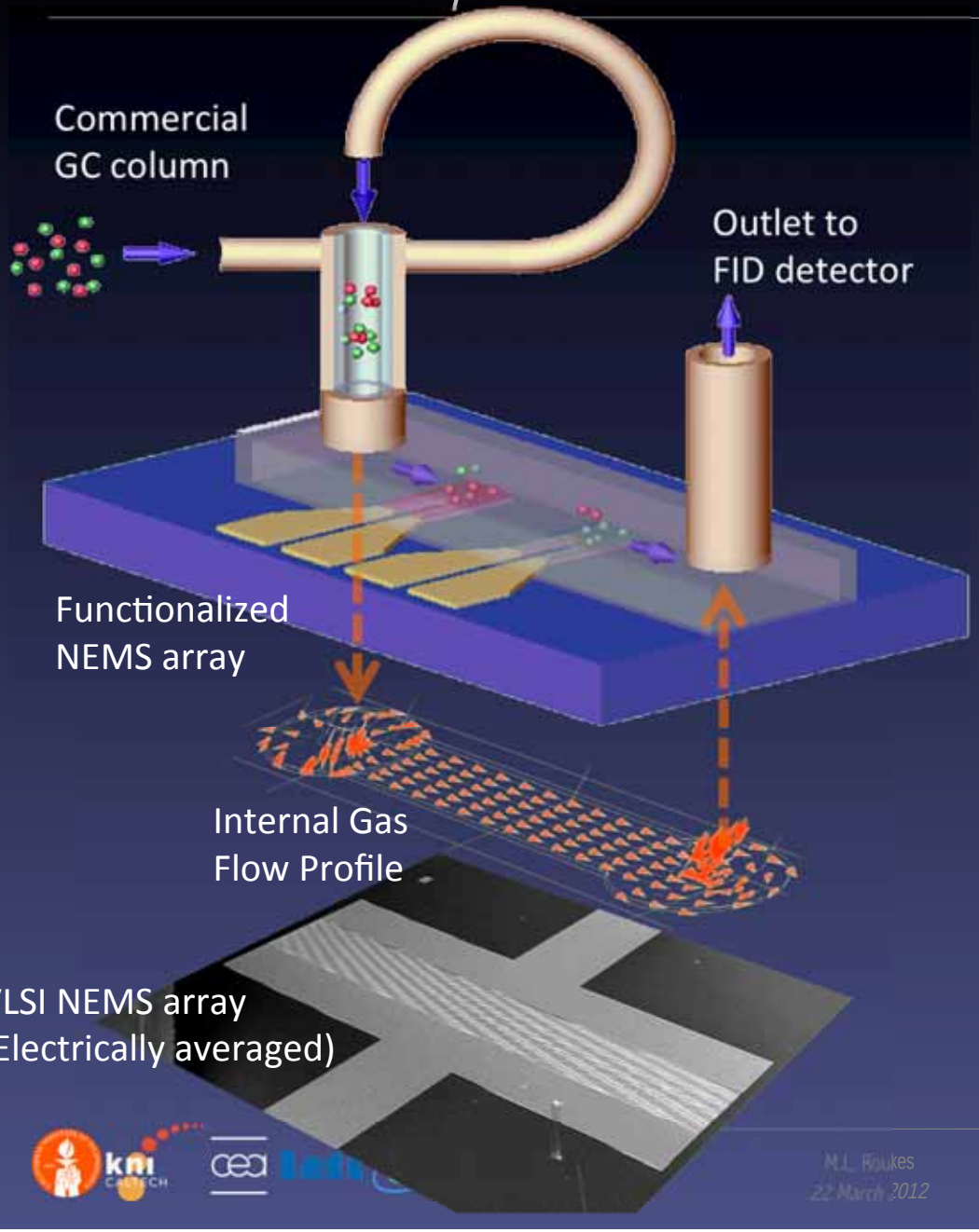
Miniscule NEMS footprint allows for massive scale-up



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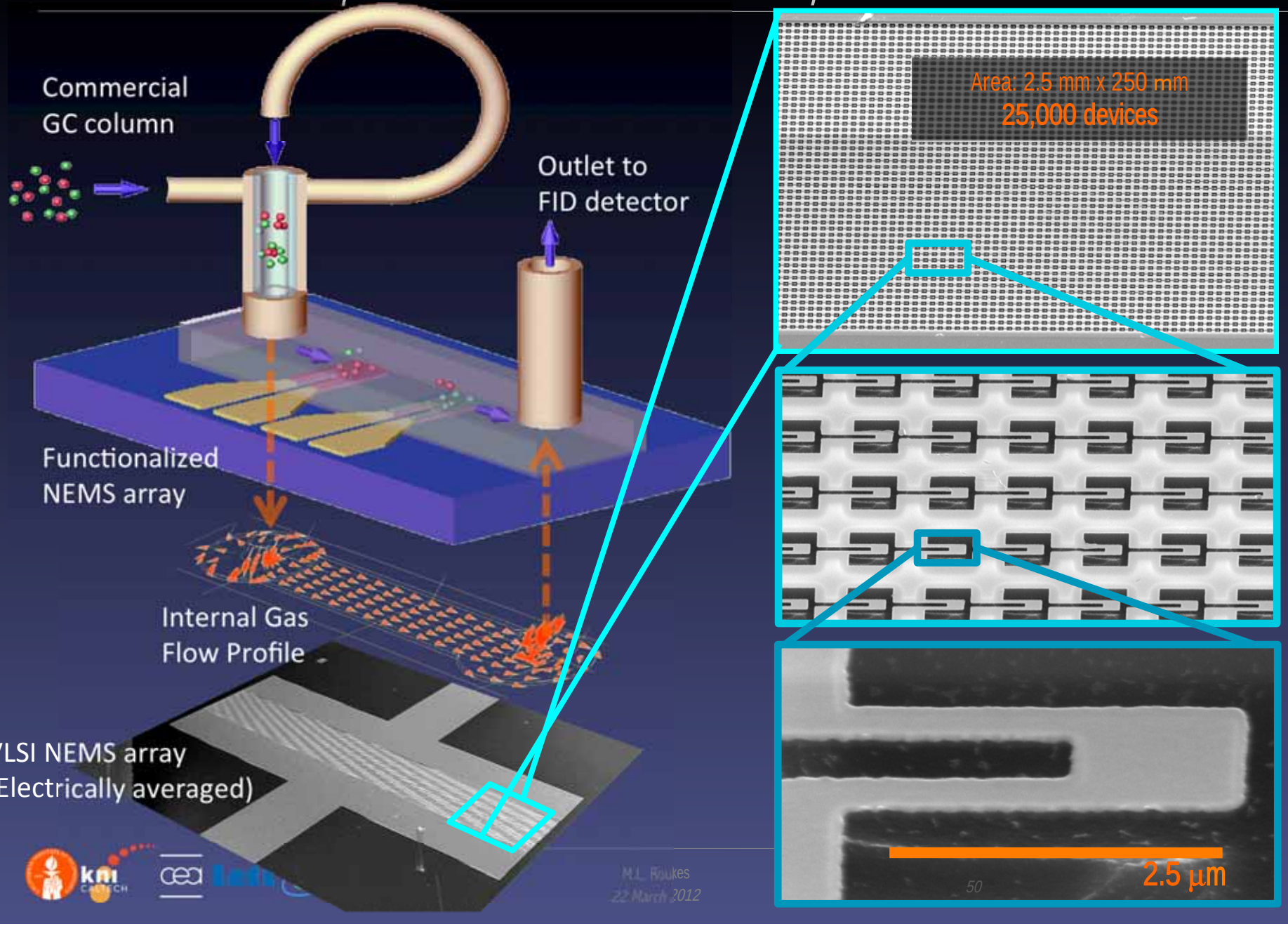
Miniscule NEMS footprint allows for massive scale-up



(hard) lessons learned

- (d) arrays of sensors can often give enhanced performance over individual devices, but achieving such gains may require exceptionally careful attention to device variances;

Nano Letters **12**, 1269-1274 (2012)

NANO LETTERS
Letter
pubs.acs.org/NanoLett

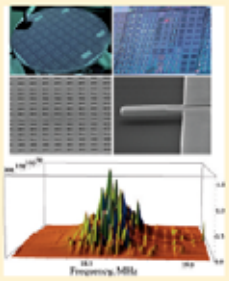
Large-Scale Integration of Nanoelectromechanical Systems for Gas Sensing Applications

I. Bargatin,[†,‡,§] E. B. Myers,[†] J. S. Aldridge,[†,∥] C. Marcoux,[‡] P. Brianceau,[‡] L. Duraffourg,[‡] E. Colinet,[‡] S. Hentz,[‡] P. Andreucci,[‡] and M. L. Roukes*[,†]

[†]Kavli Nanoscience Institute and Department of Physics, Caltech, Pasadena, CA
[‡]CEA/LETI - MINATEC, Grenoble, France

Supporting Information

ABSTRACT: We have developed arrays of nanomechanical systems (NEMS) by large-scale integration, comprising thousands of individual nanoresonators with densities of up to 6 million NEMS per square centimeter. The individual NEMS devices are electrically coupled using a combined series-parallel configuration that is extremely robust with respect to lithographical defects and mechanical or electrostatic-discharge damage. Given the large number of connected nanoresonators, the arrays are able to handle extremely high input powers (>1 W per array, corresponding to <1 mW per nanoresonator) without excessive heating or deterioration of resonance response. We demonstrate the utility of integrated NEMS arrays as high-performance chemical vapor sensors, detecting a part-per-billion concentration of a chemical warfare simulant within only a 2 s exposure period.



Electrically averaged NEMS arrays

NANO LETTERS Letter
Nano Letters **12**, 1269-1274 (2012)

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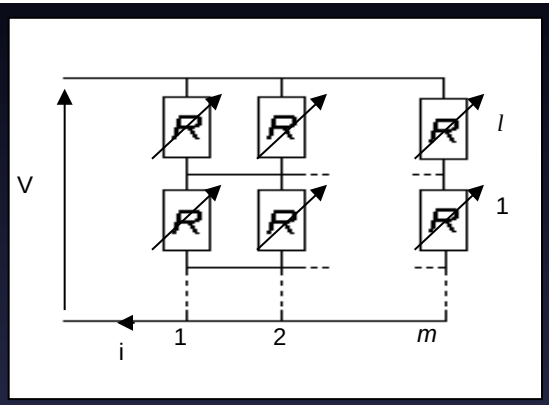
$$R_{tot} = \sum_{j}^{l} \frac{1}{\sum_{k}^{m} \frac{1}{R_{0,jk}(1+\delta_{jk})}} \approx \sum_{j}^{l} \frac{1}{\sum_{k}^{m} \frac{1}{R_0(1+\delta_{jk})}} \approx \frac{l}{m} R_0 \left(1 + \sum_{j,k} \frac{\delta_{jk}}{lm}\right)$$

$$V_{out} = C_{\det} V_{bias} \frac{\Delta R_{tot}}{R_{tot}} = C_{\det} V_{bias} \sum_{j,k} \frac{\delta_{jk}}{lm}$$



In terms of dissipated power *per device*:

$$P_{device} = \frac{V_{bias}^2}{l^2 R_0}.$$

$$V_{out} = C_{\det} \sqrt{P_{device} R_0 l^2} \left(1 + \sum_{j,k} \frac{\delta_{jk}}{lm}\right)$$

$$V_s = C_{\det} \sqrt{P_{device}\, R_0} \sum_{j,k} \frac{\delta_{jk}}{m} = C_{\det} \sqrt{P_{device}\, R_{tot}} \sum_{j,k} \frac{\delta_{jk}}{\sqrt{N}}, \; where \; N = lm$$

Best-case scenario: All N resonator signals add coherently: **signal ~ N**

Noise adds incoherently: **total noise ~ √N**

Arrays can yield up to √N enhancement of S/N
(~160x for 25,000 devices!)

Scale-up with minimization of variance provides immense SNR improvement

NANO LETTERS
Letter
Nano Letters **12**, 1269-1274 (2012)

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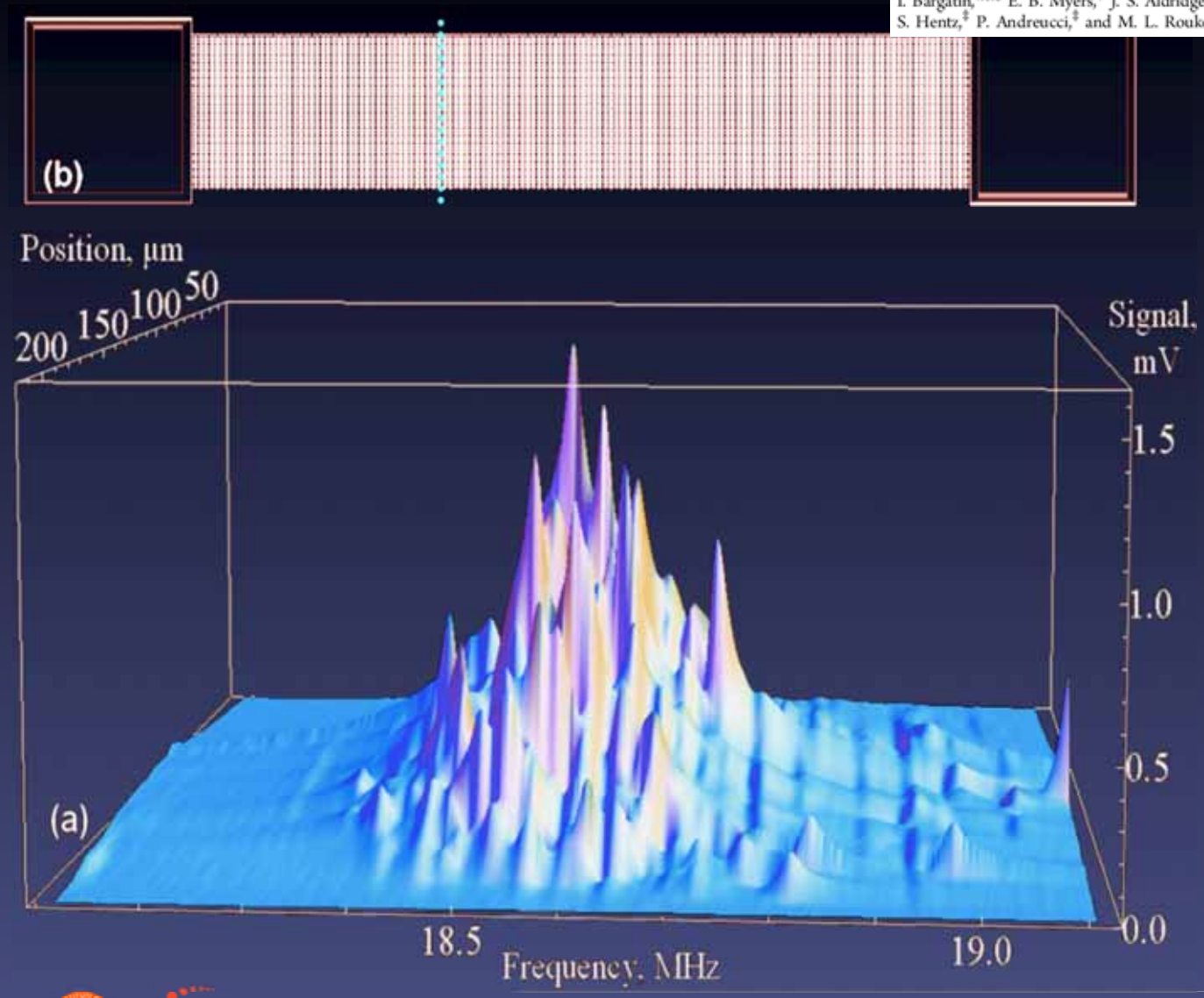

(a) Top-view schematic of a 140 × 20 cantilever array. Individual devices are not visible in this image. The dotted red line shows the trajectory of the laser-based displacement transduction system used to acquire the spectra.

(b) Optically detected spectra of from cantilevers within the array as a function of the position of the laser readout beam. (Beam width is approximately 10 μm).

Scale-up with minimization of variance provides immense SNR improvement

NANO LETTERS
Letter
Nano Letters **12**, 1269-1274 (2012)

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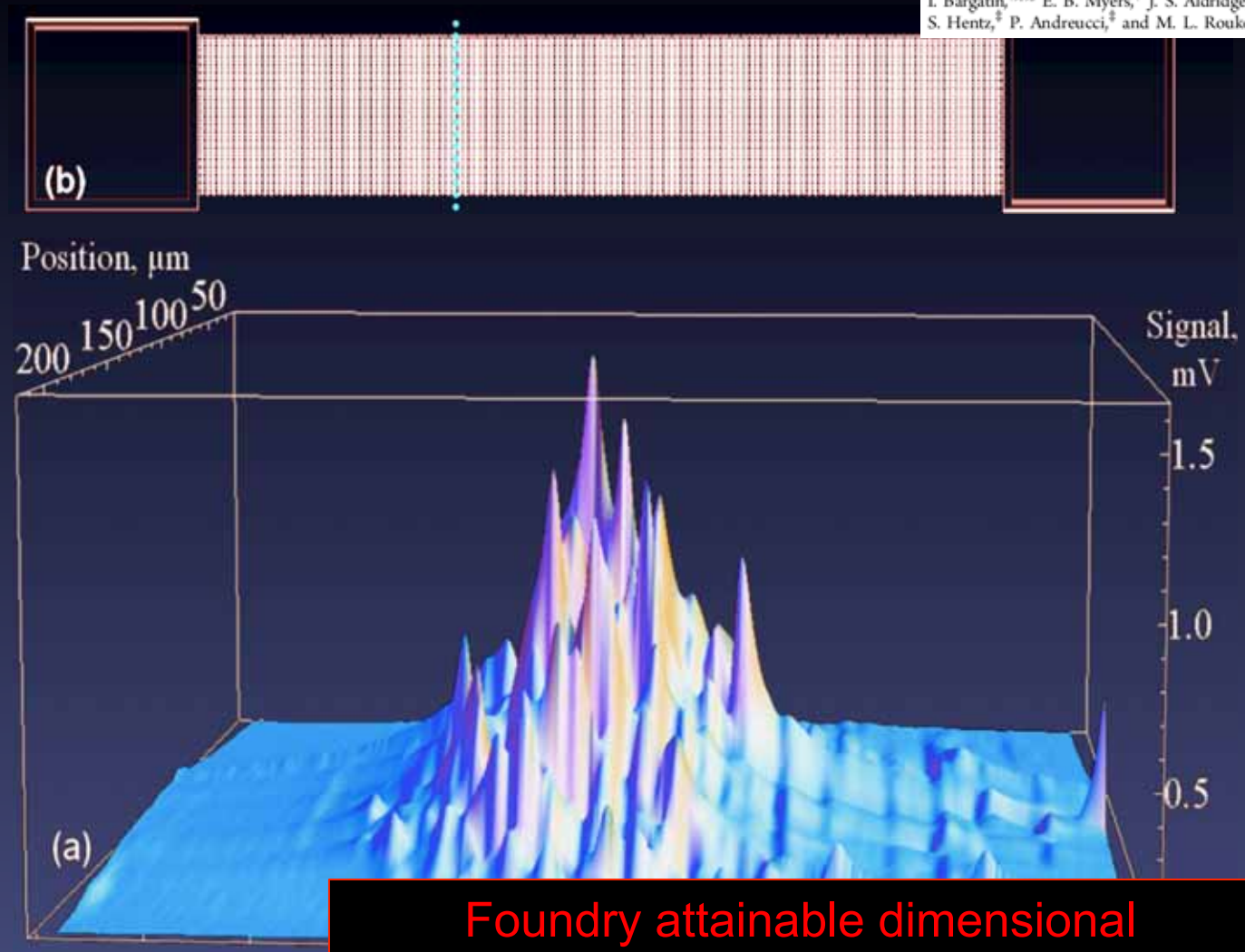


(a) Top-view schematic of a 140 × 20 cantilever array. Individual devices are not visible in this image. The dotted red line shows the trajectory of the laser-based displacement transduction system used to acquire the spectra.

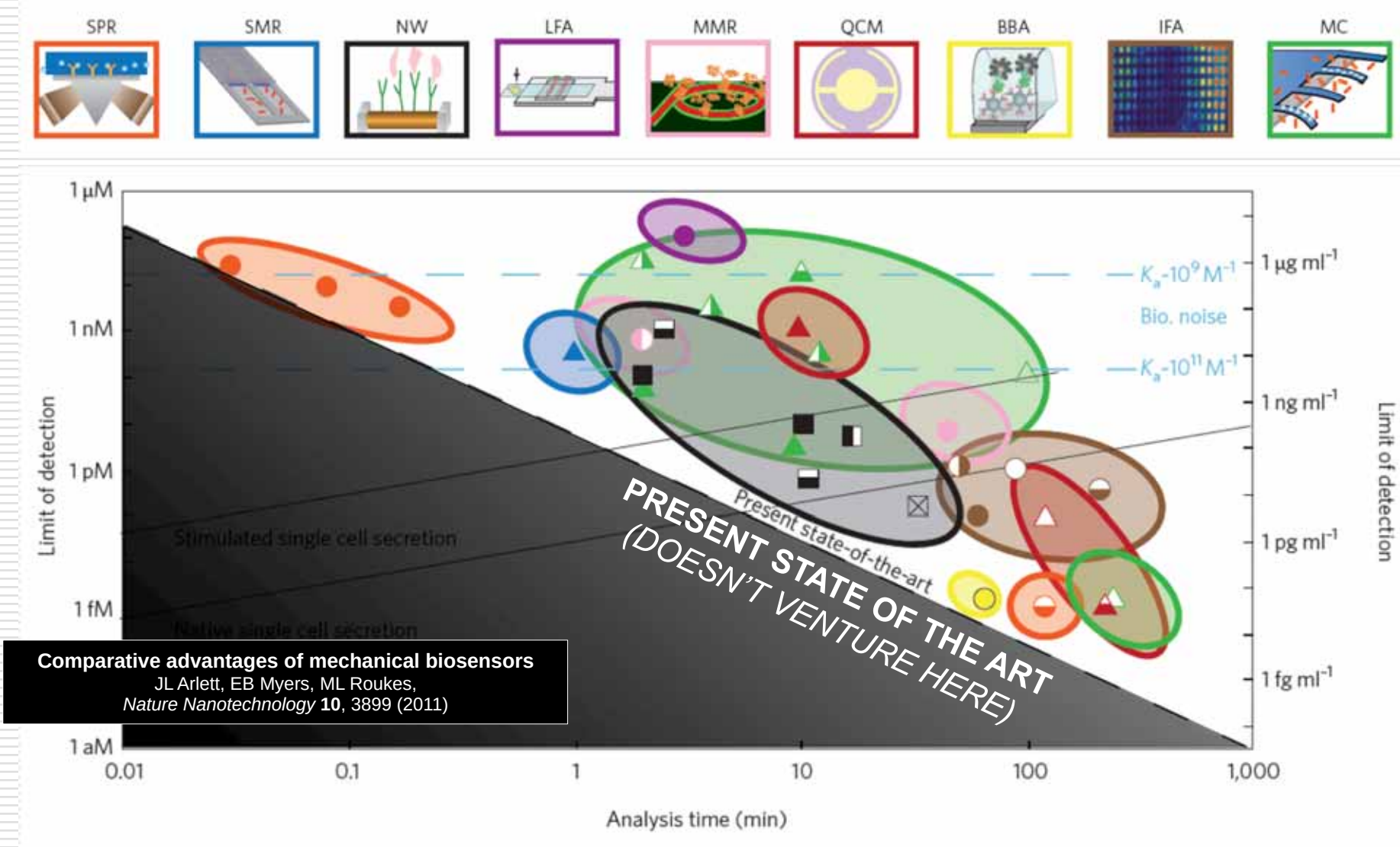
(b) Optically detected spectra of from cantilevers within the array as a function of the position of the laser readout beam. (Beam width is approximately 10 μm).

Foundry attainable dimensional tolerances **below 1%** provide access to majority of array-based enhancement

(hard) lessons learned

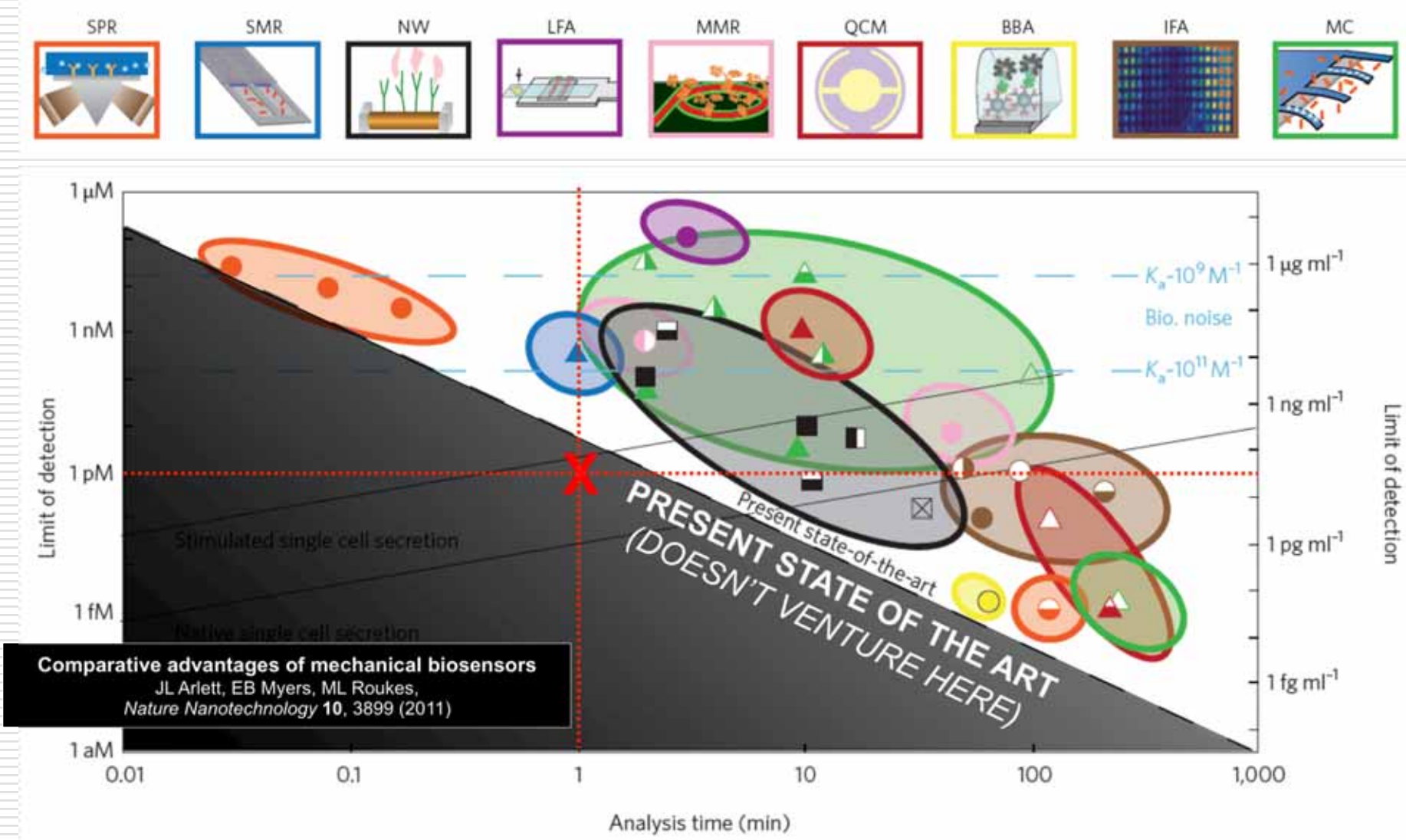
- (c, revisited for fluidic sensors) any stand-alone sensor is unlikely to be up to the full dynamic range of challenges posed in the real world;

Fluidic biosensors: the present "landscape"

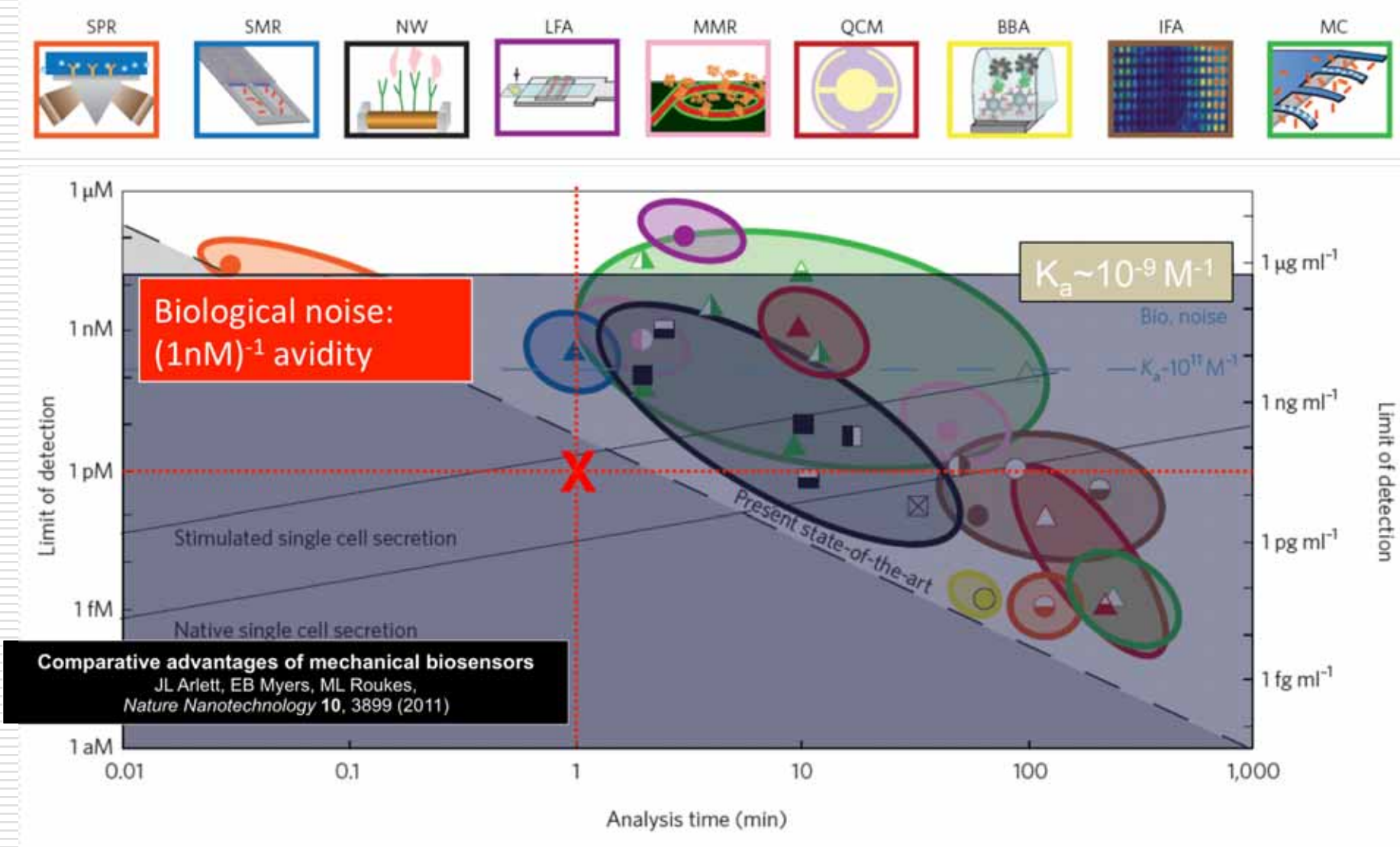


Comparative advantages of mechanical biosensors
JL Arlett, EB Myers, ML Roukes,
Nature Nanotechnology **10**, 3899 (2011)

Fluidic biosensors: a worthy goal – 1pM LOD/1m

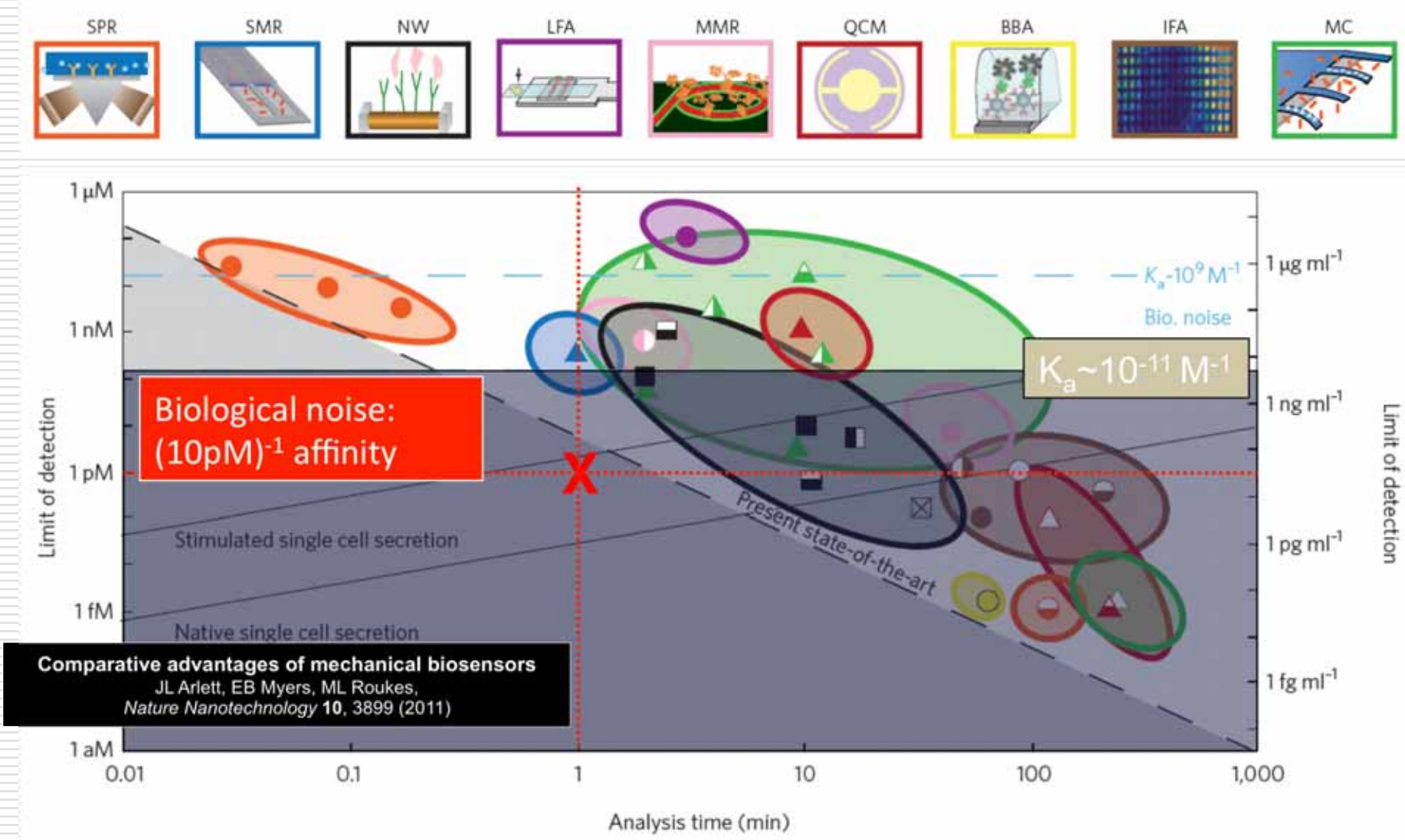


But (non-specific) biological noise is a problem



Comparative advantages of mechanical biosensors
JL Arlett, EB Myers, ML Roukes,
Nature Nanotechnology **10**, 3899 (2011)

Label-free capture probe affinity is also a challenge



…but, to end on a high note…

Although these sobering considerations may potentially force an initial downselection from amongst the exciting possibilities from within the emerging panoply of nanosensors…

…learning from the past, and considering real-world (not academic laboratory) conditions, will accelerate realization of practical nanosensor systems.