Bridging the Gap from Semiconductors to Medical Technologies:

GE Advances in Multiparameter Gas, Physiological, Biological Sensing

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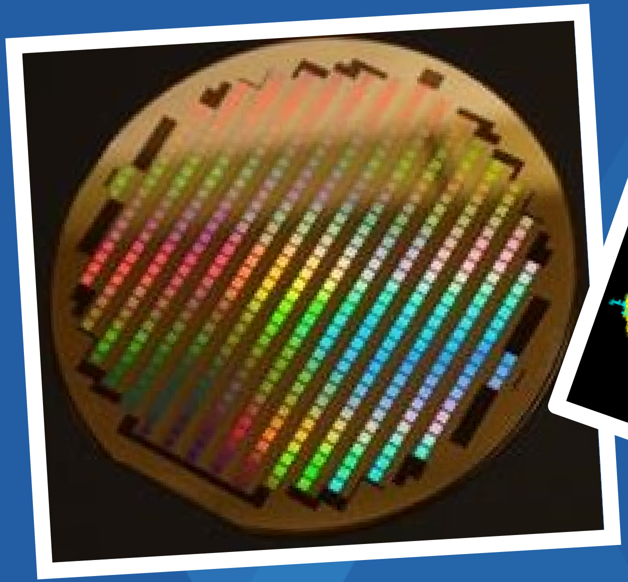

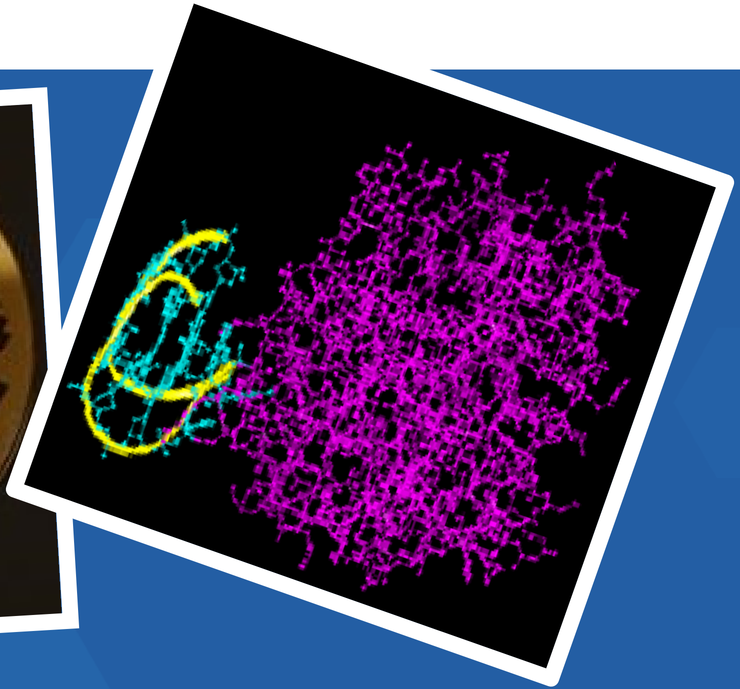

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SEMICONDUCTORS DRIVE SMART

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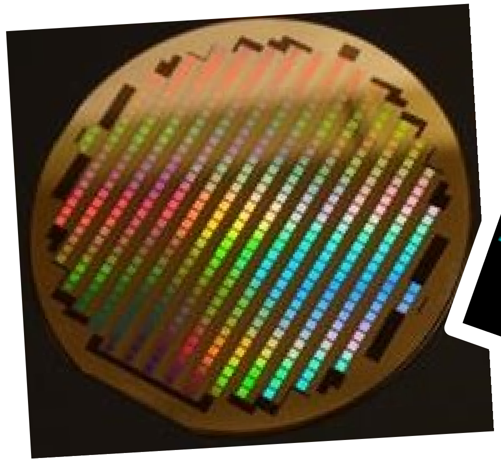
Outline

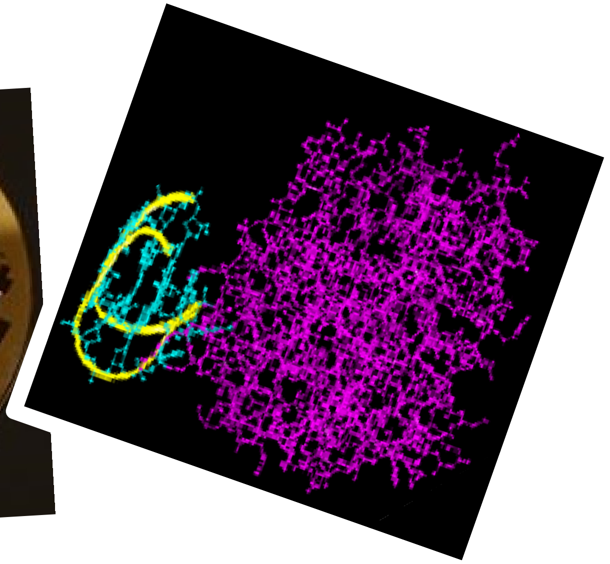
Current state and remaining challenges in wearable sensors

Value of high-performance sensors

Examples of GE advances:

- Multiparameter gas sensing
- Physiological sensing
- Biological sensing





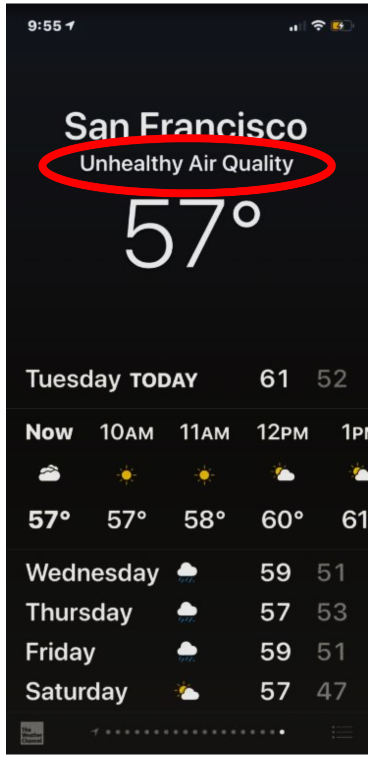
Future developments

I like my mobile phone

- ✓ Microphone / speaker
- ✓ Touch screen
- ✓ Screen orientation
- ✓ GPS
- ✓ Weather
- ✓ Air pollution
- ✓ Etc….

Use of internal sensors

Display of readings of other sensors



Reliable sensors on board,
wireless connectivity to reliable knowledge

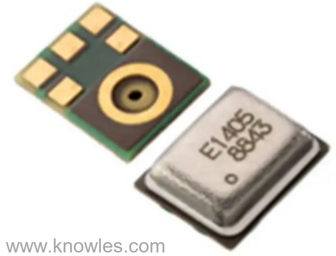
Physical sensors for mobile applications

Examples of sensors with annual sales of billions of units

Pressure sensors

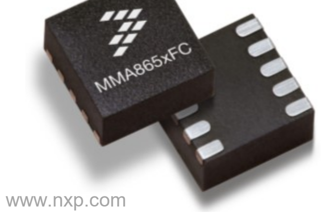
www.st.com

Microphones



www.knowles.com

Accelerometers



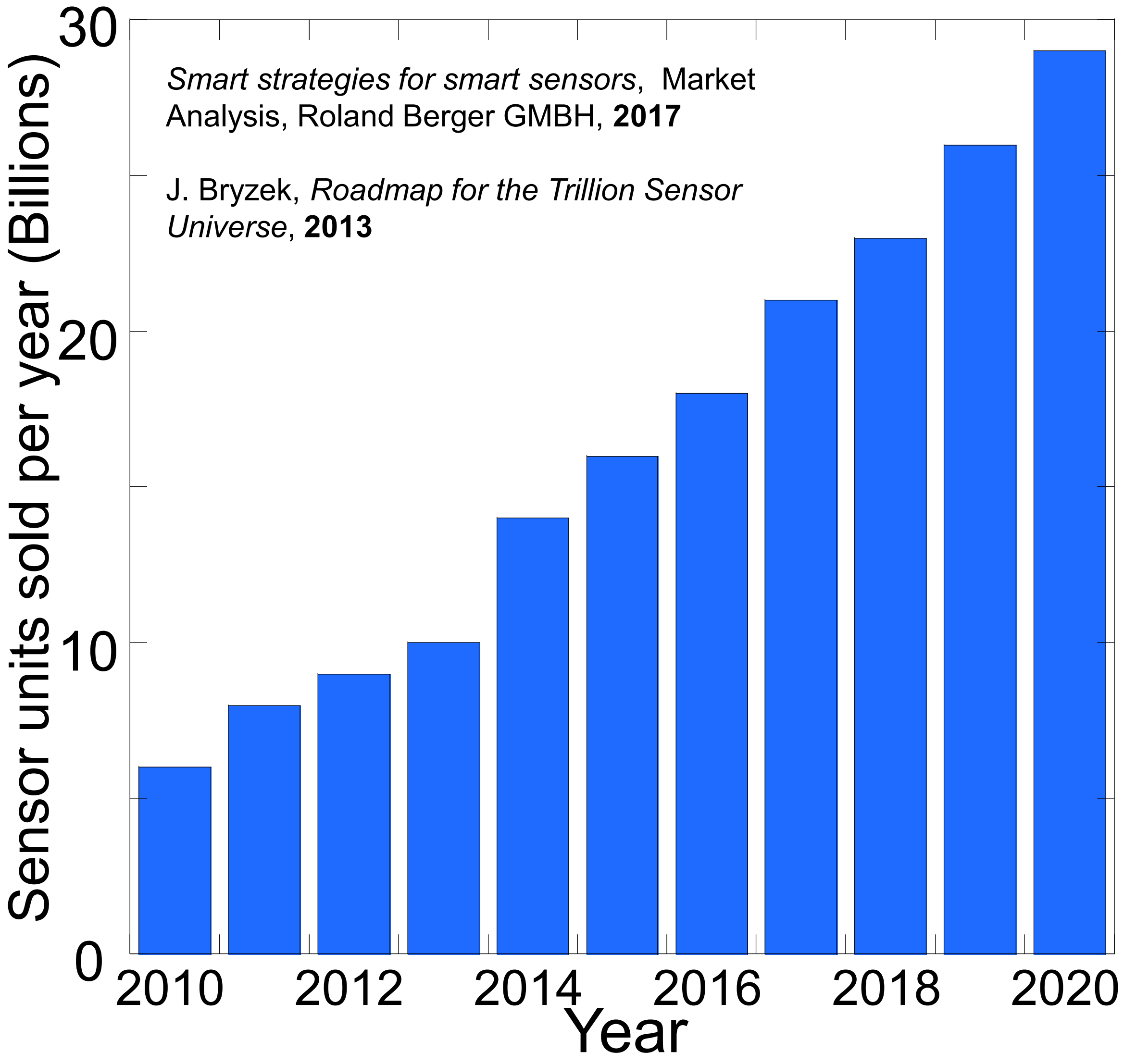
www.nxp.com

Gyroscopes

www.bosch-sensortec.com

Compasses

www.st.com



High sensor reliability leads to demand of billions of sensors per year

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I like my wearable heart rate monitor

Garmin Forerunner 235

amazon.com

Apple Watch

Great gadgets to motivate me to do workout…

I like my wearable heart rate monitor

Garmin Forerunner 235

Apple Watch

amazon.com

Great gadgets to motivate me to do workout…

For The Wearable Revolution To Take Off, Accuracy Must Improve

CVC, *Inside Activity Tracking*, **2013**

http://www.insideactivitytracking.com/tracking-accurately-how-is-it-done-why-is-it-difficult/

Fitness Wearables Lack Accuracy

C.Van Hoof, *EE Times*, **2014**

http://www.eetimes.com/author.asp?section_id=36&doc_id=1321976

The Struggle for Accurate Measurements on Your Wrist

R. Metz, *MIT Technology Review*, **2015**

https://www.technologyreview.com/s/538416/the-struggle-for-accurate-measurements-on-your-wrist/

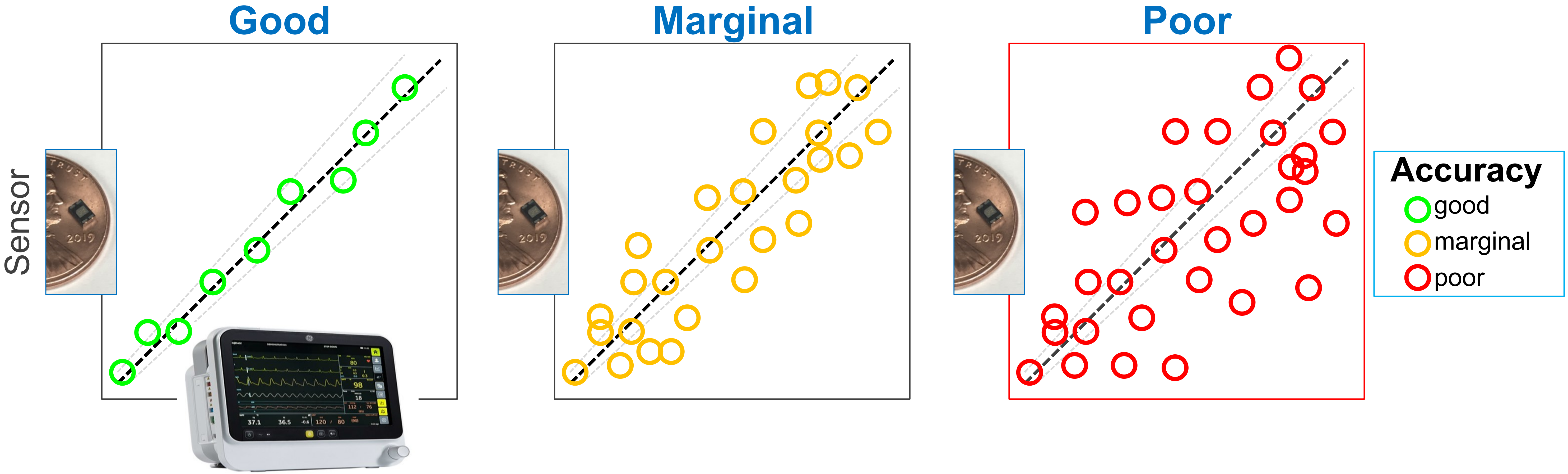
Real world wrist-based heart rate monitor test: Are they accurate enough?

S. Richmond, *Wareable*, **2015**

http://www.wareable.com/fitness-trackers/heart-rate-monitor-accurate-comparison-wrist

The remaining challenge in wearable sensors:
"For the wearable revolution to take off, accuracy must improve"

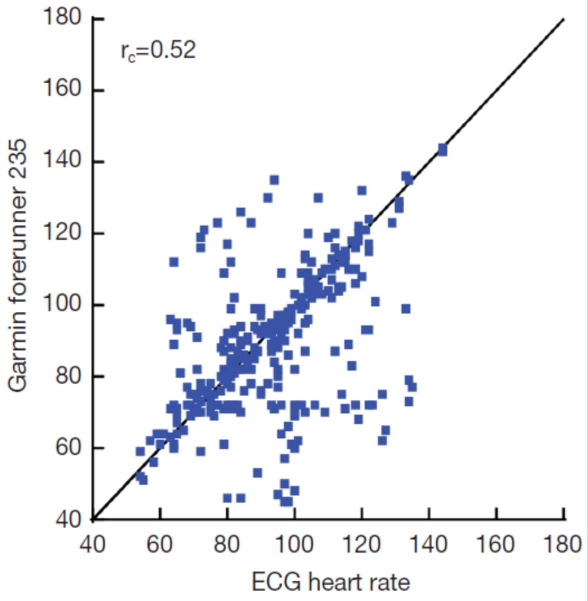
Accuracy:
Correlation between benchmark instruments and new sensors



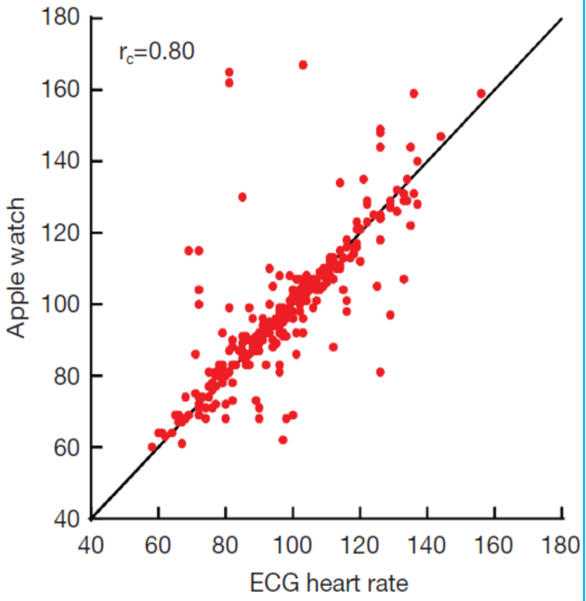
Benchmark instrument

Accuracy demands in wearable sensors

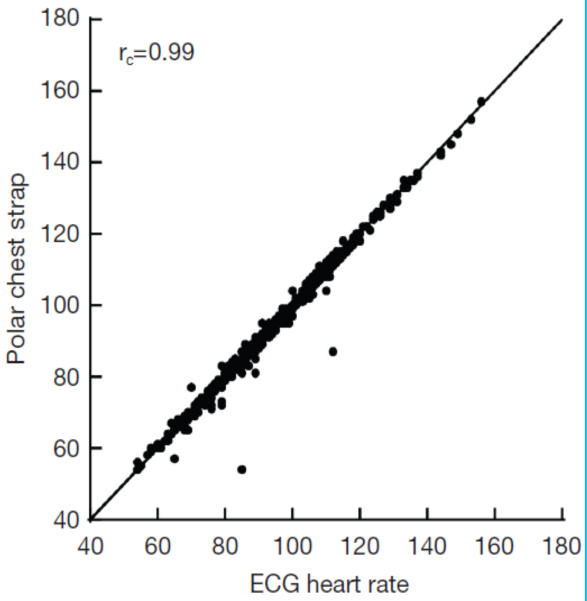
Garmin Forerunner 235



Apple Watch



Polar H7 chest strap



Value of high-performance sensors:

- Reliable detection of undesired conditions
- More convenient and effective screening and diagnosis
- More effective clinical research
- All – at cost-effective solutions

Etiwy et al., Accuracy of wearable heart rate monitors in cardiac rehabilitation, *Cardiovasc. Diagn. Ther.* **2019**, *9*, 262-271

Accuracy demands in wearable sensors

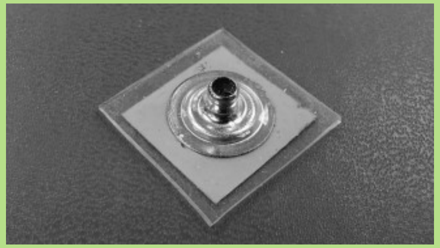
More accurate readings without the goop

Y. Zhu, *NC State Engineering FALL/WINTER,* **2015**

https://news.engr.ncsu.edu/2015/10/more-accurate-readings-without-the-goop/

Silver nanowire wearable sensors match hospital ‘wet electrode’ accuracy

J. Ford, The Engineer, **2015**



http://www.theengineer.co.uk/silver-nanowire-wearable-sensors-match-hospital-wet-electrode-accuracy/

Forbes Billionaires Innovation Leadership Money Consumer

31,964 views | Sep 14, 2018, 01:15pm

Apple Watch 4 Is Now An FDA Class 2 Medical Device: Detects Falls, Irregular Heart Rhythm

https://www.forbes.com/sites/jeanbaptiste/2018/09/14/apple-watch-4-is-now-an-fda-class-2-medical-device-detects-falls-irregular-heart-rhythm/#3513aae82071

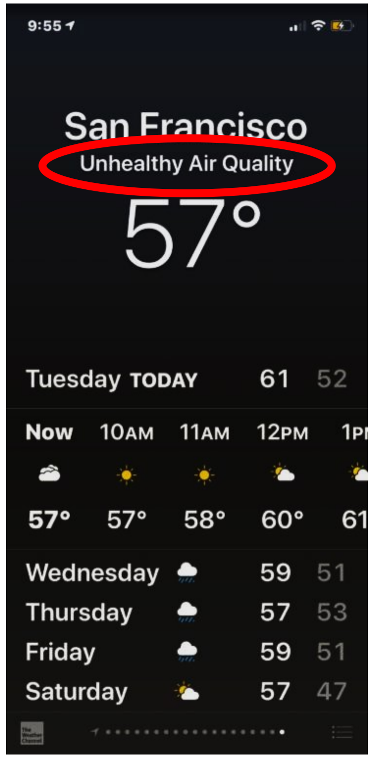
The wearable revolution took off because of the improved accuracy

Air quality index of ambient air: accepted metric

Air Quality Index Levels of Health Concern	Numerical Value	Meaning
Good	0 to 50	Air quality is considered satisfactory, and air pollution poses little or no risk
Moderate	51 to 100	Air quality is acceptable; however, for some pollutants there may be a moderate health concern for a very small number of people who are unusually sensitive to air pollution.
Unhealthy for Sensitive Groups	101 to 150	Members of sensitive groups may experience health effects. The general public is not likely to be affected.
Unhealthy	151 to 200	Everyone may begin to experience health effects; members of sensitive groups may experience more serious health effects.
Very Unhealthy	201 to 300	Health warnings of emergency conditions. The entire population is more likely to be affected.
Hazardous	301 to 500	Health alert: everyone may experience more serious health effects

Air Sensor Guidebook, EPA/600/R-14/159 June 2014 www.epa.gov/ord

Display of readings of other sensors



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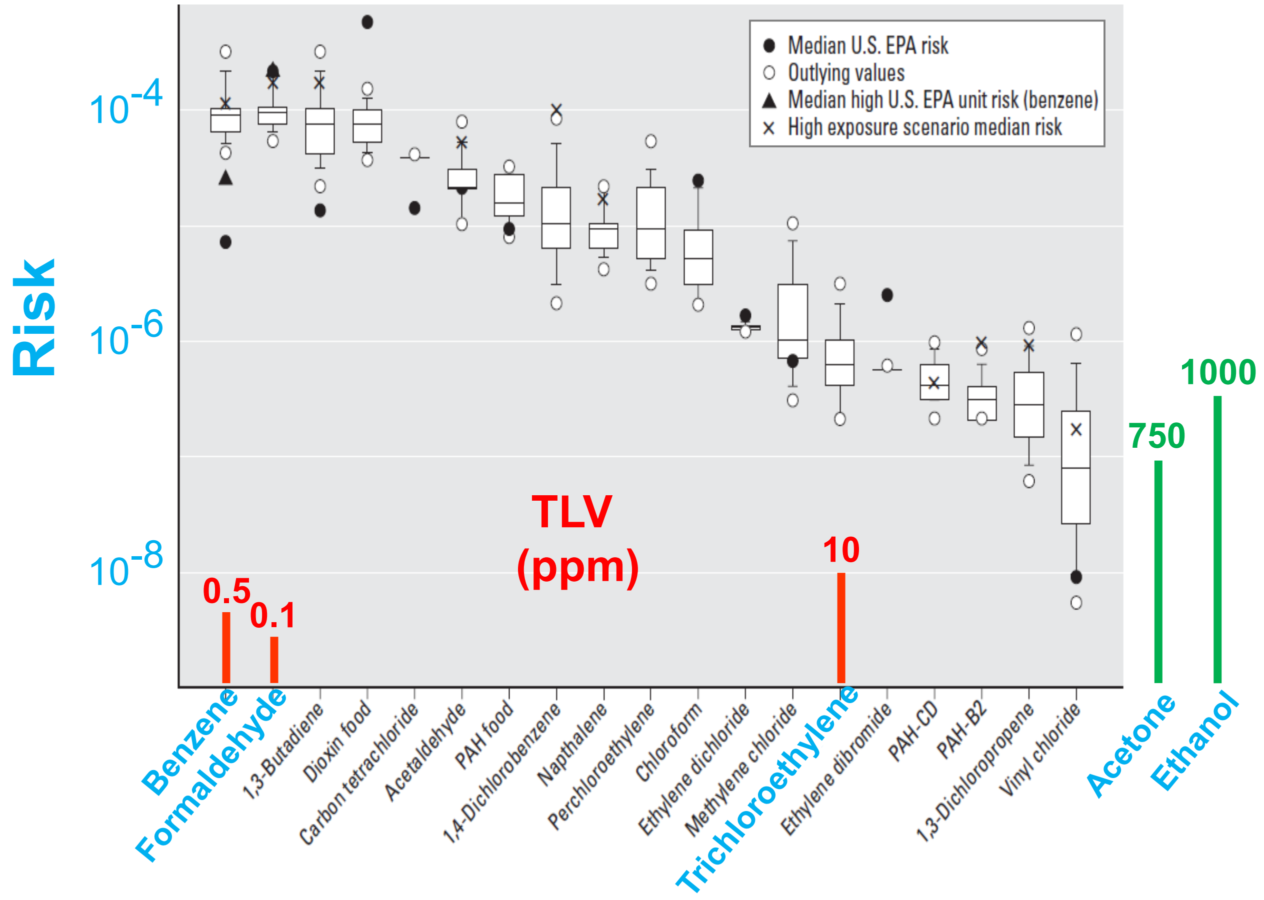
Important health-related volatiles: outdoor and indoor environments

Major outdoor volatile pollutants

Ozone	< 0.1 ppm
Nitrogen dioxide	< 0.2 ppm
Sulfur dioxide	< 0.2 ppm
Carbon monoxide	<30 ppm

Brunekreef, Holgate, *Lancet* **2002**, 360, 1233–1242
who.int/ceh/capacity/Outdoor_air_pollution.pdf
euro.who.int/document/e71922.pdf
who.int/airpollution/ambient/pollutants/en/

Indoor volatiles of importance



Risks from: Loh et al., *Environmental Health Perspectives*, **2007**, 115, 1160-1168

TLV (Threshold Limit Values) from: Permissible Exposure Limits / OSHA

- Some volatiles are much more toxic than others
- Toxic volatiles often are at much lower levels than benign volatiles
- Need to detect toxic volatiles in complex background of benign volatiles

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Air quality index:
determined from measurements by high performance instruments

AQI	AQI	O_3 (ppb)	CO (ppm)	SO_2 (ppb)	NO_2 (ppb)
I_{low} - I_{high}	Category	C_{low} - C_{high} (avg)	C_{low} - C_{high} (avg)	C_{low} - C_{high} (avg)	C_{low} - C_{high} (avg)
0-50	Good	-	0.0-4.4 (8-hr)	0-35 (1-hr)	0-53 (1-hr)
51-100	Moderate	-	4.5-9.4 (8-hr)	36-75 (1-hr)	54-100 (1-hr)
101-150	Unhealthy for Sensitive Groups	125-164 (1-hr)	9.5-12.4 (8-hr)	76-185 (1-hr)	101-360 (1-hr)
151-200	Unhealthy	165-204 (1-hr)	12.5-15.4 (8-hr)	186-304 (1-hr)	361-649 (1-hr)
201-300	Very Unhealthy	205-404 (1-hr)	15.5-30.4 (8-hr)	305-604 (24-hr)	650-1249 (1-hr)
301-400	Hazardous	405-504 (1-hr)	30.5-40.4 (8-hr)	605-804 (24-hr)	1250-1649 (1-hr)
401-500		505-604 (1-hr)	40.5-50.4 (8-hr)	805-1004 (24-hr)	1650-2049 (1-hr)

Technical Assistance Document for the Reporting of Daily Air Quality – the Air Quality Index (AQI). US EPA Office of Air Quality Planning and Standards. EPA-454/B-09-001, **2009**
Revised Air Quality Standards For Particle Pollution And Updates To The Air Quality Index (AQI). US EPA Office of Air Quality Planning and Standards. **2013**

Reference and Equivalent Methods Used to Measure National Ambient Air Quality Standards (NAAQS) Criteria Air Pollutants – Vol. 1, EPA/600/R-16/139, **2016**

UV absorption

Non-dispersive IR

UV fluorescence

Chemiluminescence

Traditional analytical instruments are used for required high-quality measurements

Examples of field-deployed monitoring solutions

https://blog.aclima.io
http://eis-me.com
https://uk-air.defra.gov.uk

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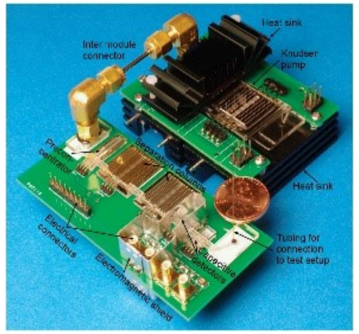
Design principles of high performance analytical instruments:
Diverse designs to reject known and unknown interferences

Chemiluminescence *

UV fluorescence

Reference and Equivalent Methods Used to Measure National Ambient Air Quality Standards (NAAQS)
Criteria Air Pollutants – Vol. 1, EPA/600/R-16/139, **2016**

Gas chromatography



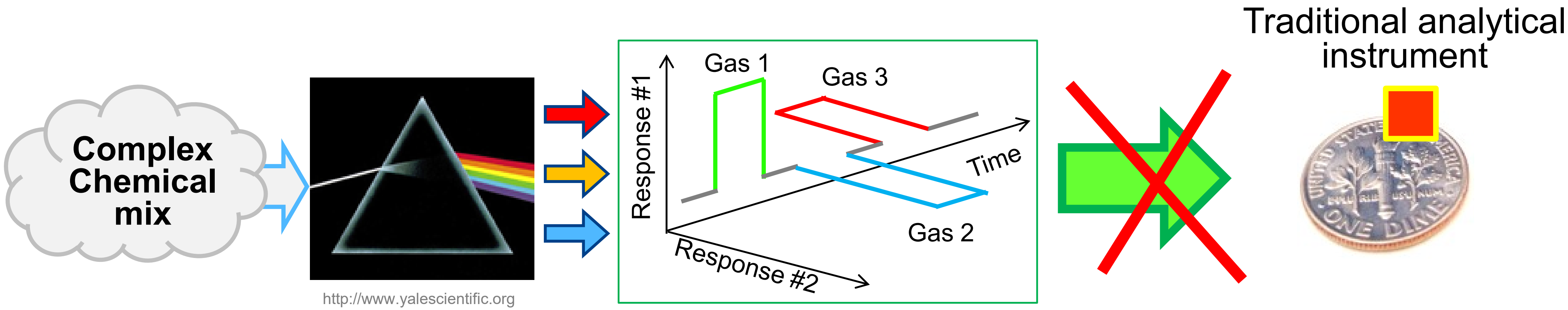
Qin, Gianchandani,
Microsyst. Nanoeng. **2016**

Mass spectrometry

May 28, **2018**

Laser spectroscopy

https://alliedscientificpro.com



http://www.yalescientific.org

Diverse instrument-design rules to operate in complex conditions

* Cross-flow modulated semi-decompression chemiluminescence

Current state-of-the-art in gas sensing

alphasense.com
figaro.com
sgxsensortech.com

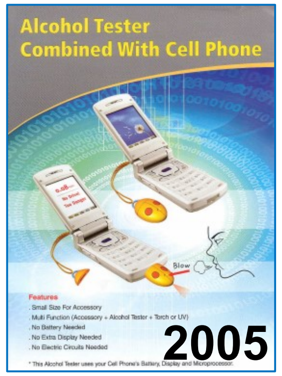
- ✓Miniaturization
- ✓Packaging
- ✓Reduced power

Wearables

https://www.treehugger.com

https://www.itri.org.tw/eng/

Cell phone integrated

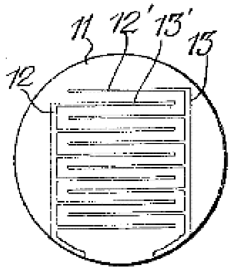


Expo at TRANSDUCERS'05, S.Korea

https://www.catphones.com

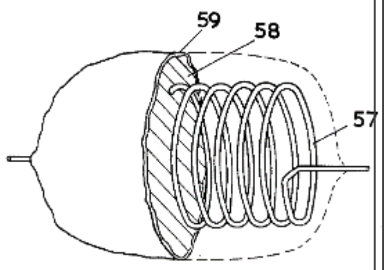
Conventional sensors: single-output devices for expected gases

Polymeric blends for humidity



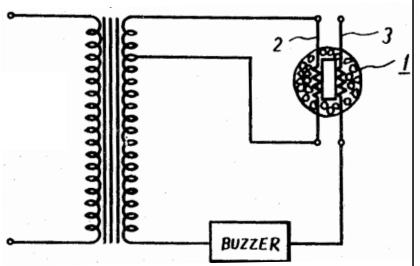
US Pat. 2047638, **1936**

Catalysts for combustible gases



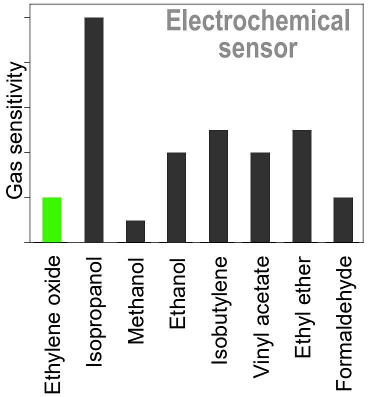
US Pat. 3092799, **1963**

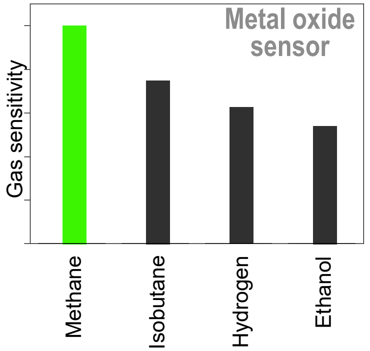
Metal oxides for diverse gases

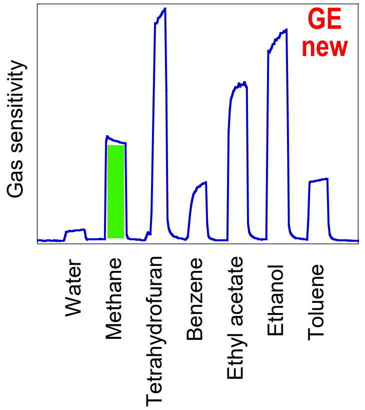


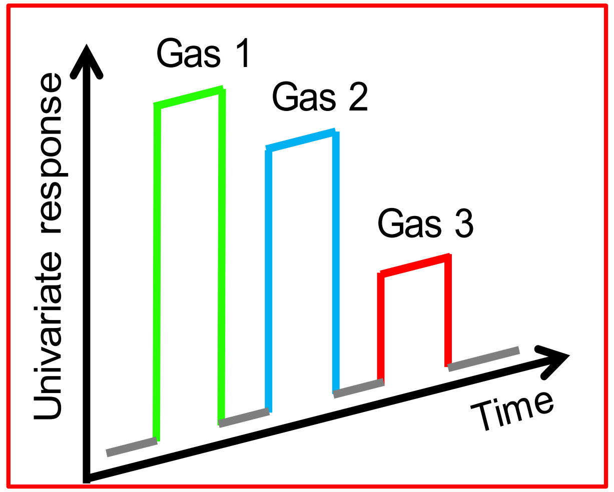
US Pat. 3644795 **1972**

Gas cross-sensitivity: undesired response to interfering gases









> "Simple sensors perform best when pollution levels are high and when the compound of interest swamps others"
> Lewis, Edwards, *Nature* **2016**

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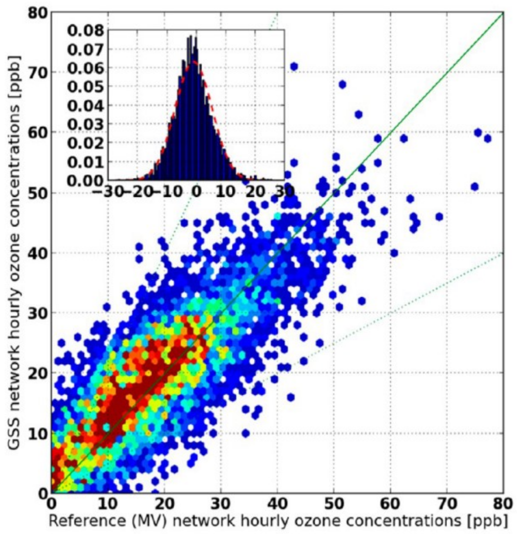
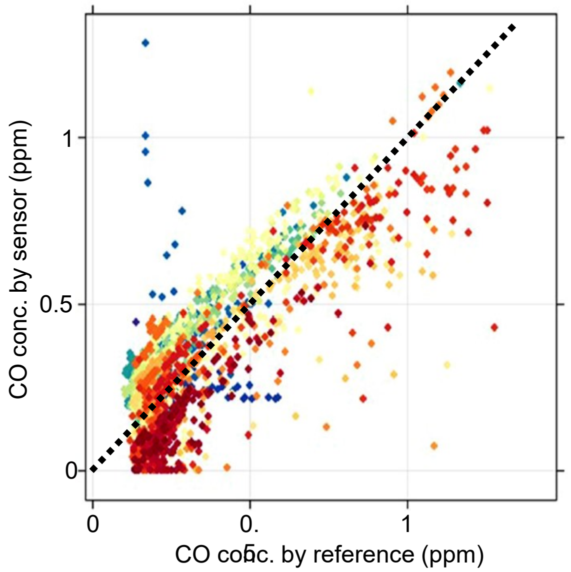
Examples + learnings: gas cross-sensitivity of existing sensors

Ozone O_3



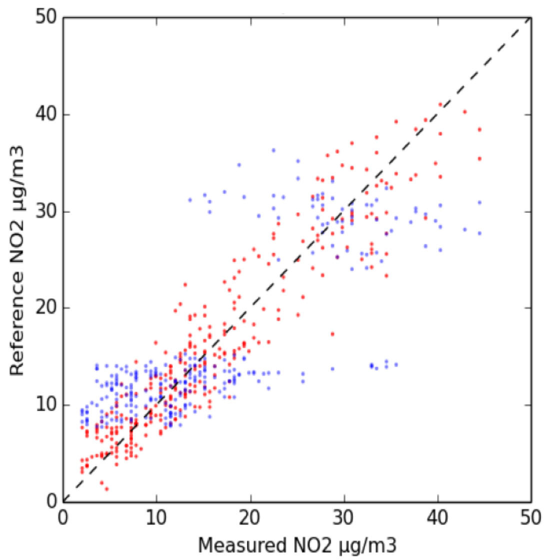
Bart et al., *Environ. Sci. Technol.* **2014**, *48*, 3970

Carbon monoxide CO



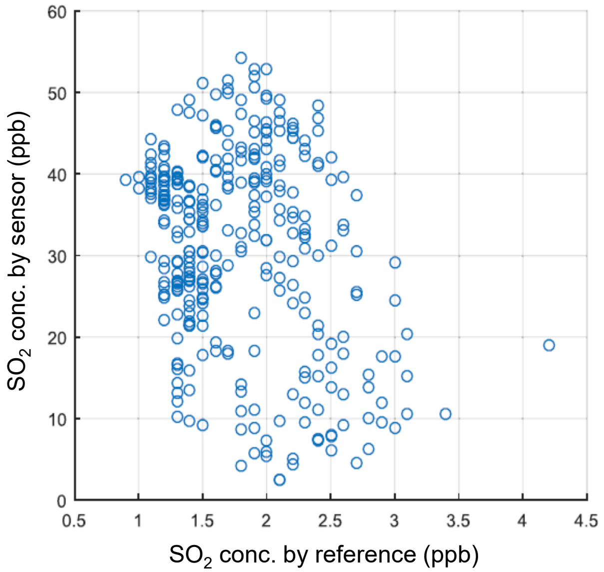
Hagler et al., *Atmospheric Meas. Tech.* **2016,** 9, 5281

Nitrogen dioxide NO_2



Peterson et al., *Sensors* **2017**, 17, 1653

Sulfur dioxide SO_2



Borrego et al., Atmospheric Environment **2016**, 147, 246

The biggest headaches are caused by interfering chemicals
Lewis, Edwards, *Nature* **2016**

ehstoday.com/sponsored/understanding-cross-sensitivities-can-help-keep-workers-safer

EPA

It must be stated that no low cost sensors meet the Regulatory Monitoring requirements
Air Sensor Guidebook, EPA/600/R-14/159 2014

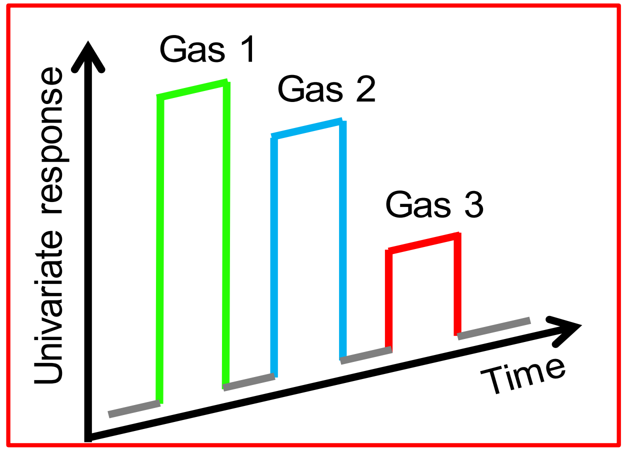
EPA

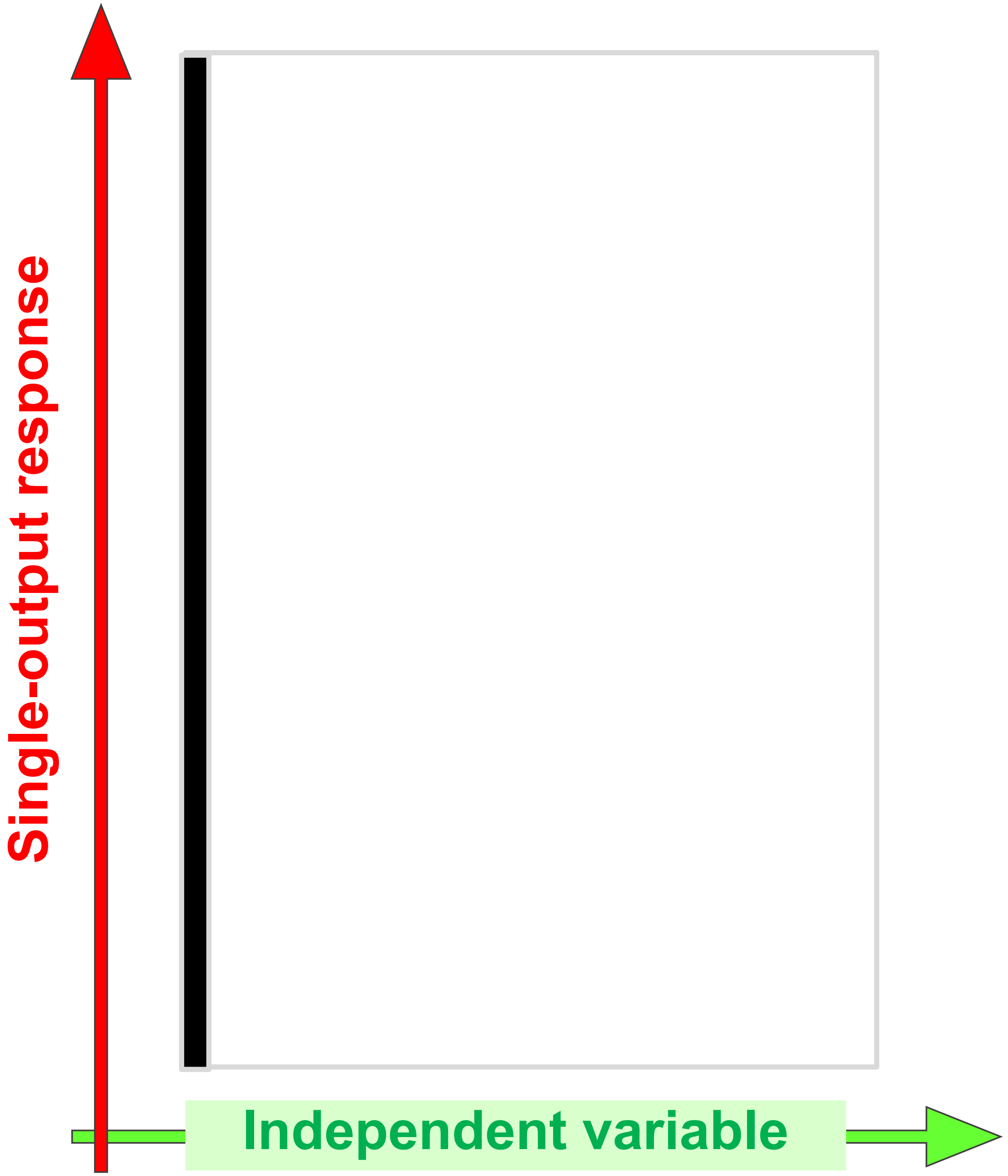
R^2 versus reference monitors widely variable (0.01 to ~ 0.8) in field evaluations
New Paradigm for Air Pollution Monitoring, Air and Energy Research Program, EPA 2018

For gas sensors revolution to take off, accuracy must improve

GE Vision: Boosting dimensionality of sensor response

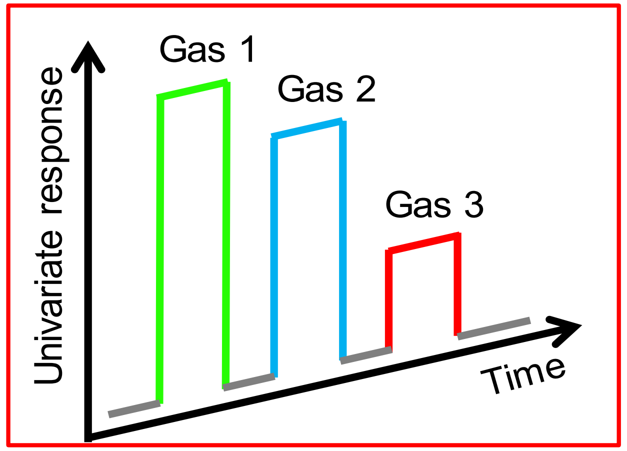
Conventional single-output sensor





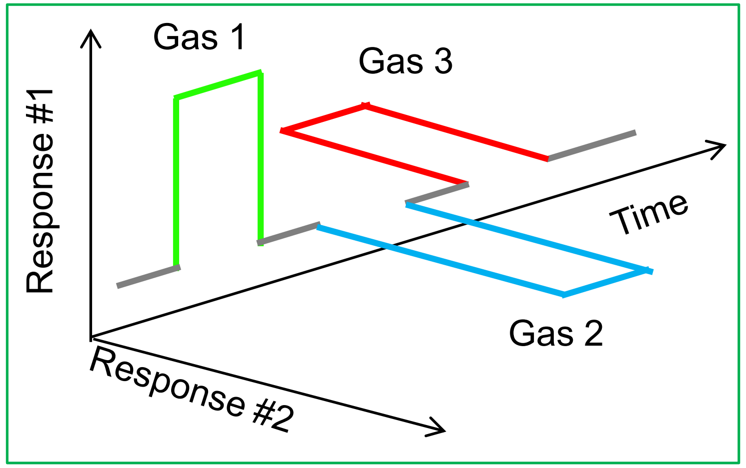
GE Vision: Boosting dimensionality of sensor response

Conventional single-output sensor

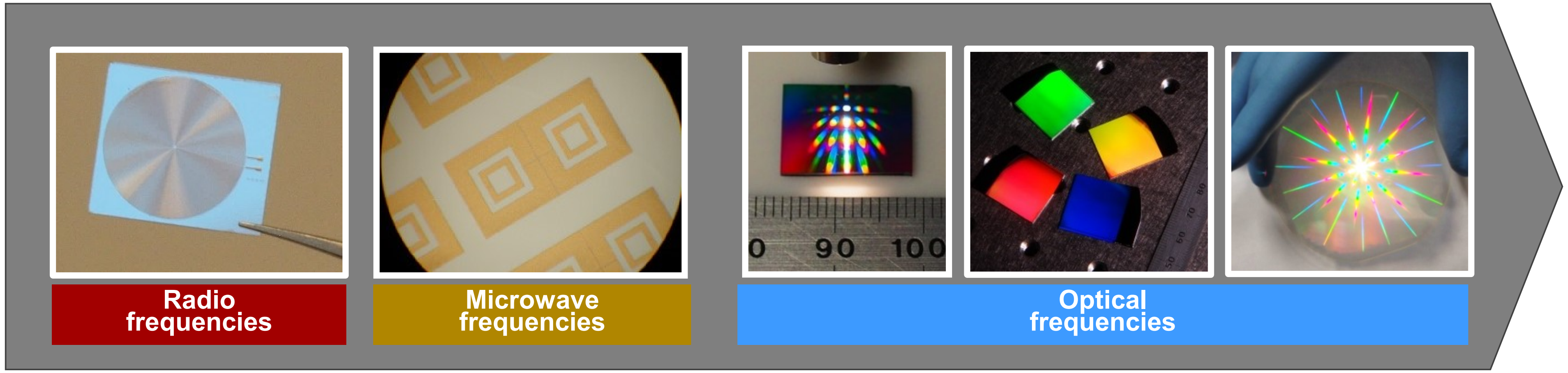


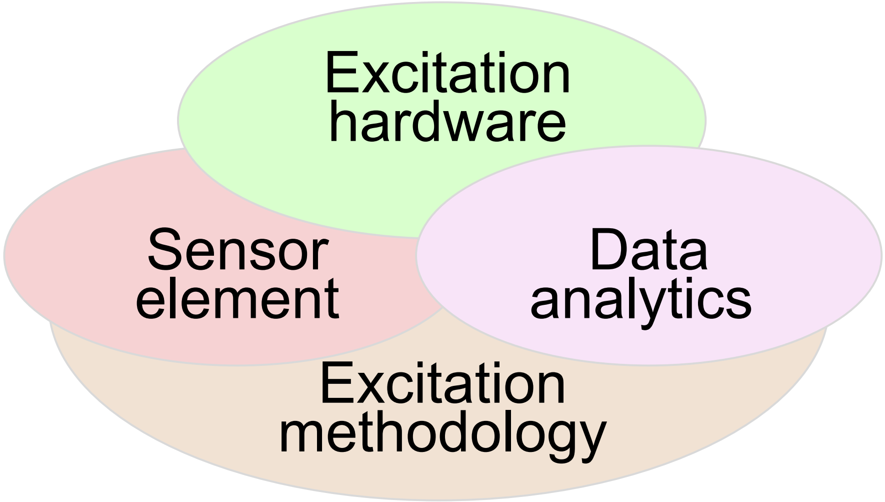
Types of independent variables

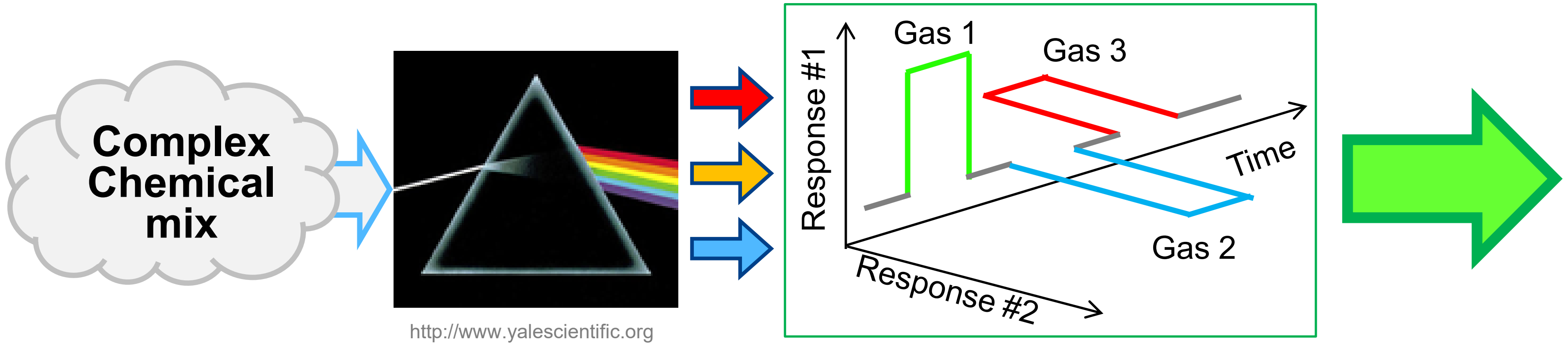
- Electrical modulation
- Optical modulation



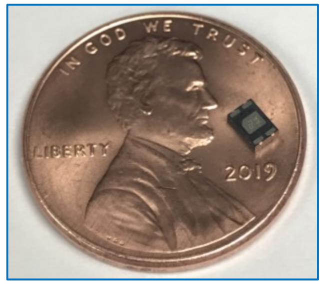
Our roadmap: electromagnetic multivariable sensors







Example of GE multivariable sensor



Present developments in gas sensing: Data analytics

a.k.a. chemometrics, multivariate statistics, machine learning (ML)

Tools for diverse applications

Supervised learning
Artificial neural network
Bayesian statistics
Case-based reasoning
Gaussian process regression
Gene expression programming
Group method of data handling
Inductive logic programming
Instance-based learning
Lazy learning
Learning Automata
Learning Vector Quantization
Logistic Model Tree
Minimum message length
Probably approximately correct learning
Random Forests
Support vector machines
Symbolic machine learning

Unsupervised learning
Expectation-maximization algorithm
Vector Quantization
Generative topographic map
Information bottleneck method
Self-organizing map
Association rule learning
Hierarchical clustering
Single-linkage clustering
Conceptual clustering
Cluster analysis
K-means algorithm
Fuzzy clustering

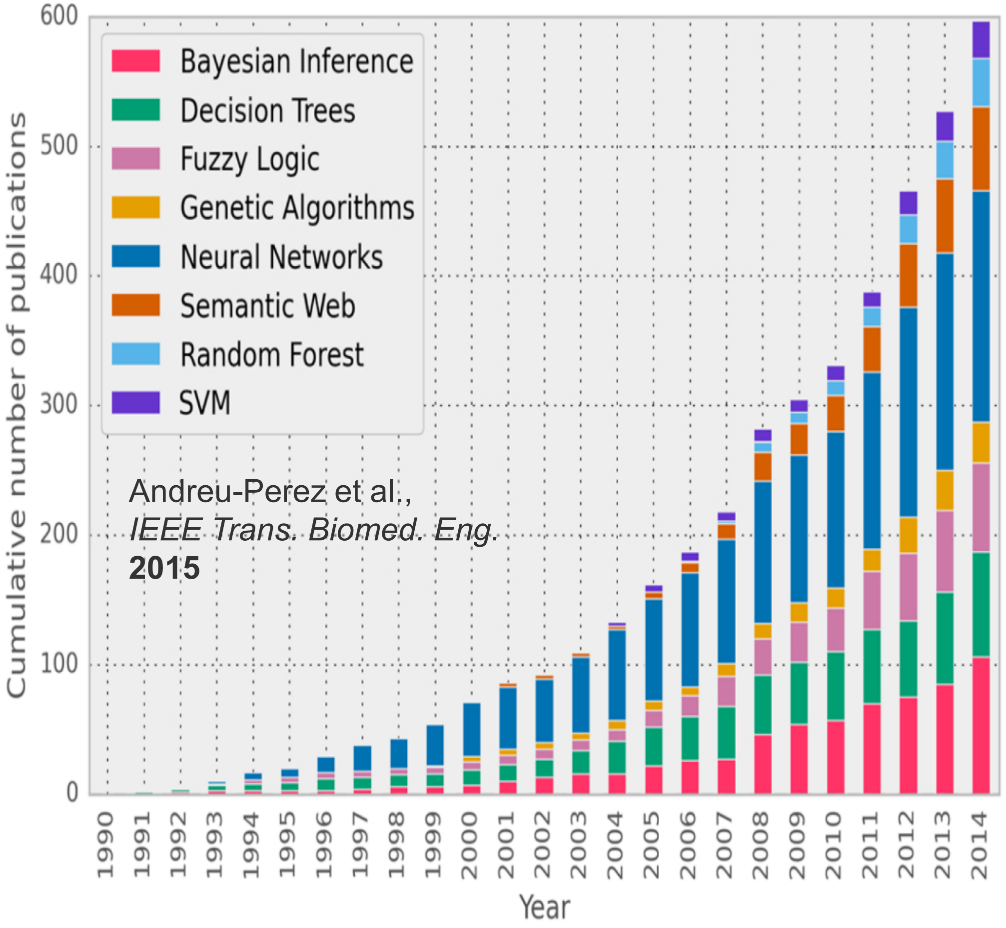
Semi-supervised learning
Generative models
Low-density separation
Graph-based methods
Co-training

Reinforcement learning
Temporal difference learning
Q-learning
Learning Automata

Deep learning
Deep belief networks
Deep Boltzmann machines
Deep Convolutional neural networks
Deep Recurrent neural networks
Hierarchical temporal memory

Wikipedia.org

Tools for sensor data processing



Examples of GE Research tools

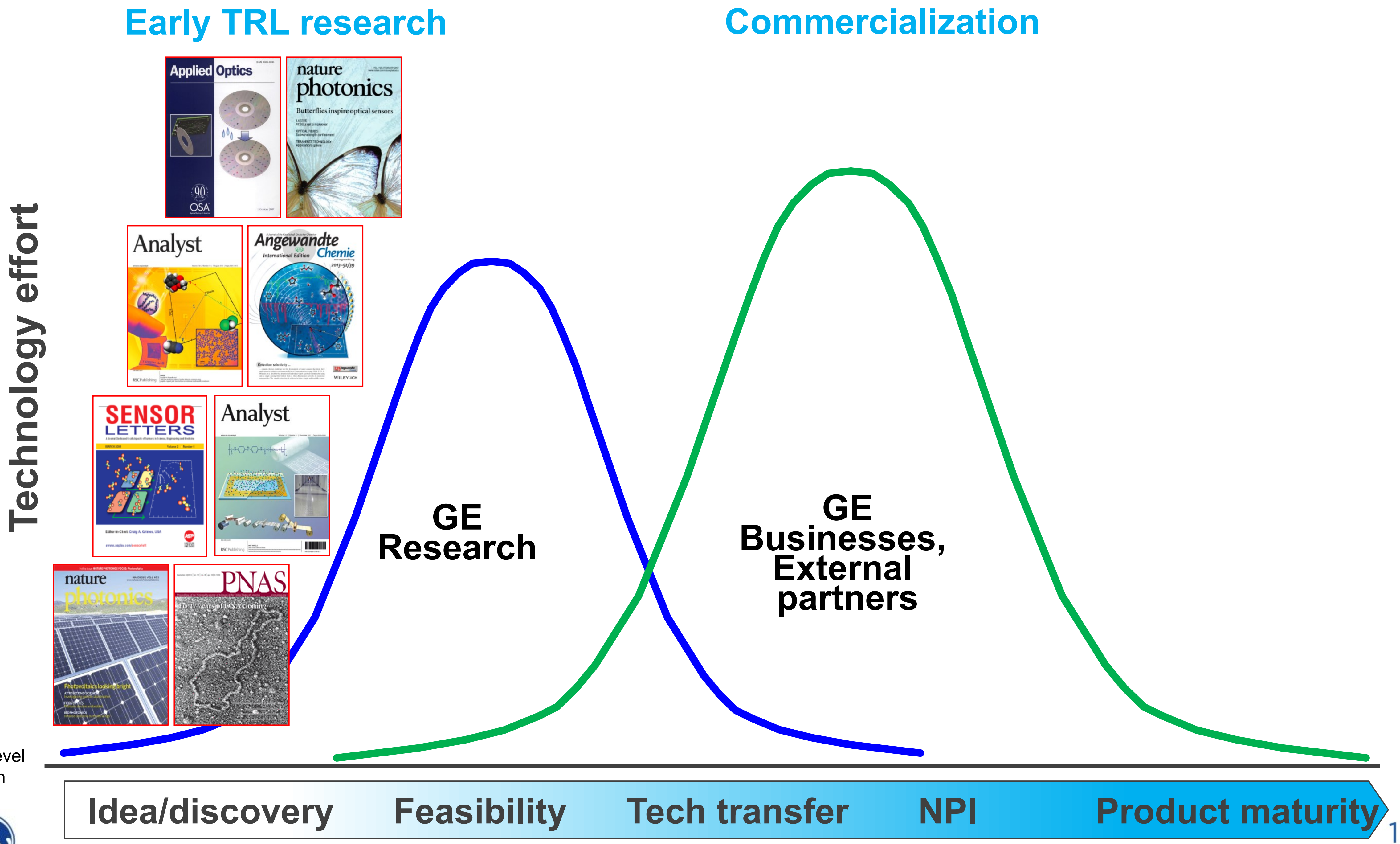
- Support Vector Machines (SVM)
- Principal component analysis (PCA)
- Hierarchical cluster analysis (HCA)
- Discriminant Analysis (DA)
- Artificial Neural Network (ANN)
- Independent Component Analysis (ICA)
- Partial least squares (PLS) regression
- Principal Component Regression (PCR)
- **New tools for boosting sensor stability**

R. A. Potyrailo, Multivariable sensors for ubiquitous monitoring of gases in the era of Internet of Things and Industrial Internet, *Chem. Rev.* **2016**, *116*, 11877–11923

Appropriate sensor + appropriate data analytics = high performance sensing

Our industrial R&D goal:

Develop technologies with new capabilities, transition for commercialization



TRL = technology readiness level
NPI = new product introduction

Our industrial R&D goal:

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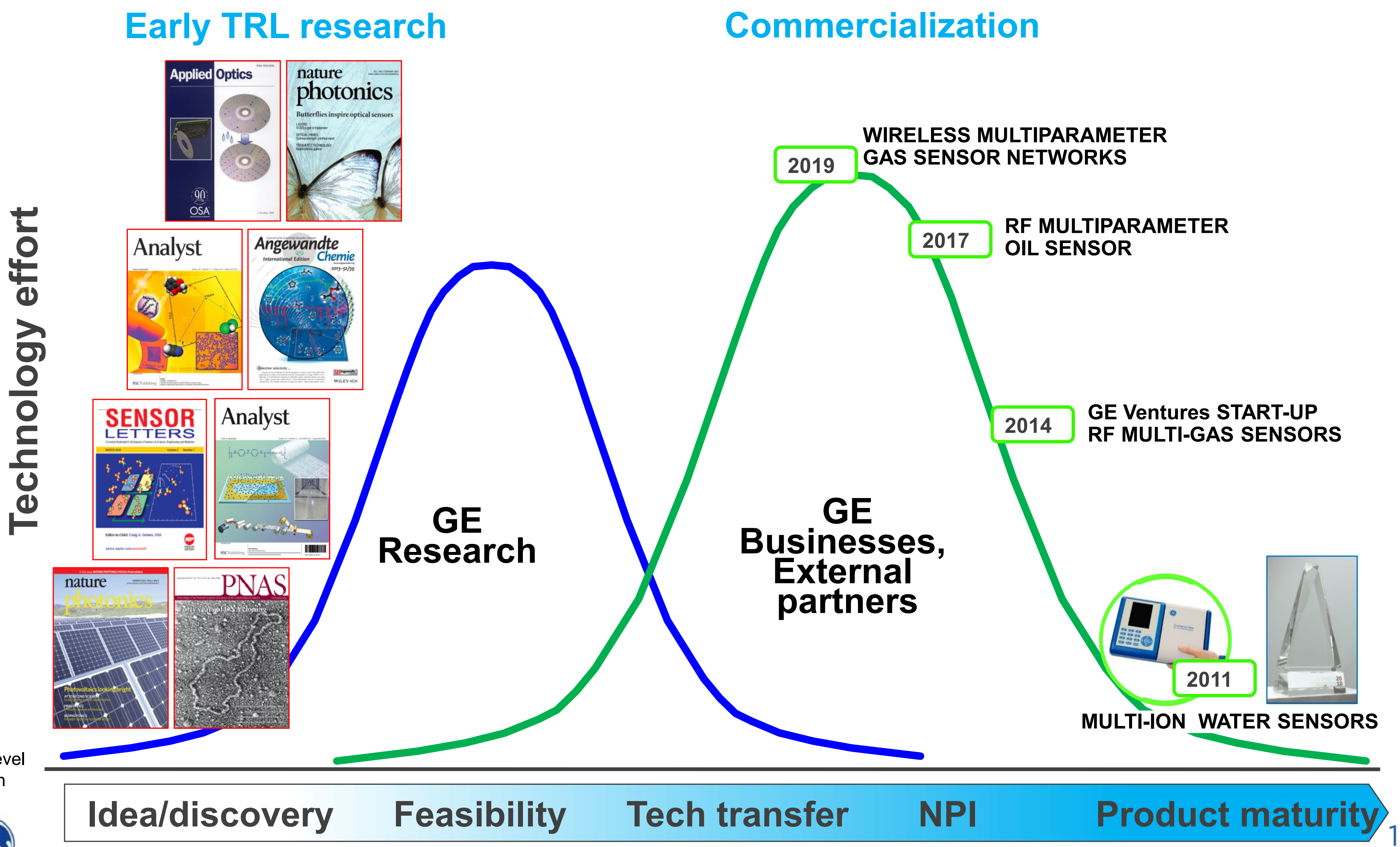
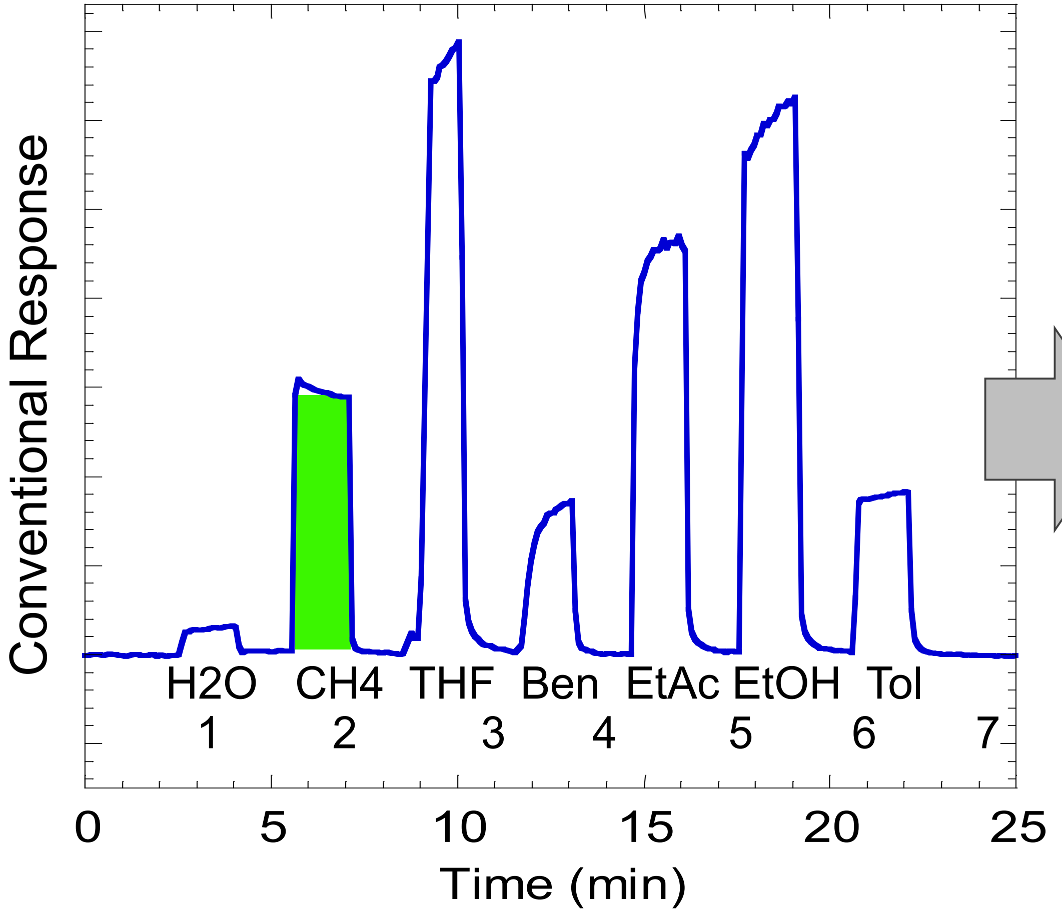


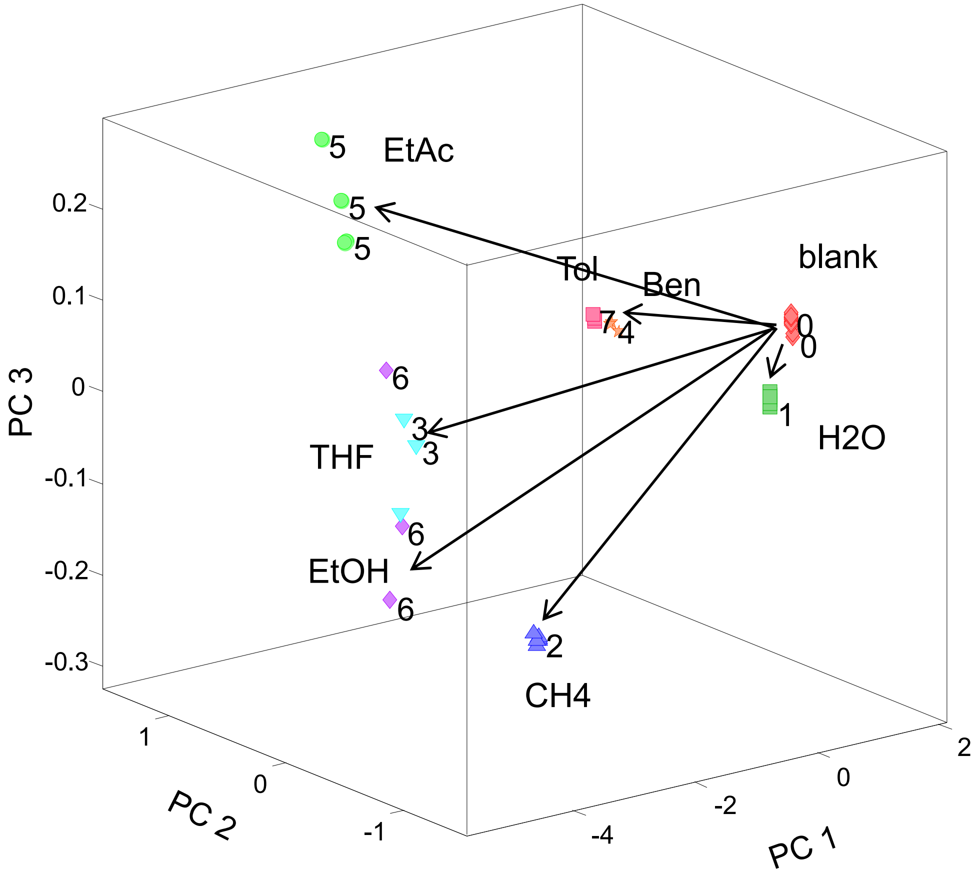
TRL = technology readiness level
NPI = new product introduction

Discrimination between multiple gases and vapors

Conventional response:
Gas cross-sensitivity



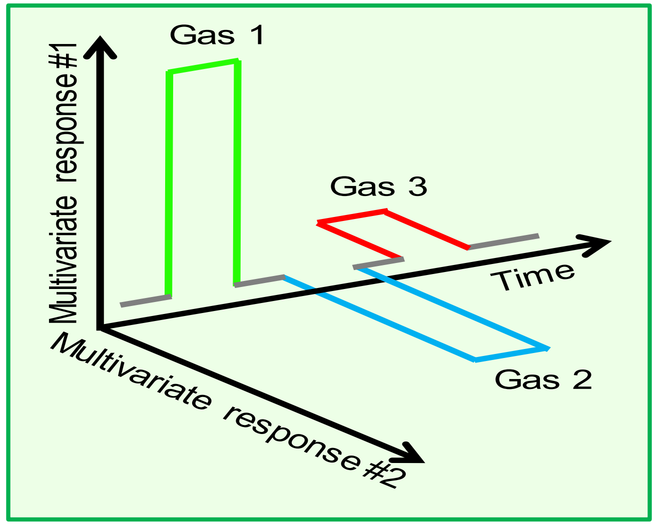
GE response:
Multi-gas resolution



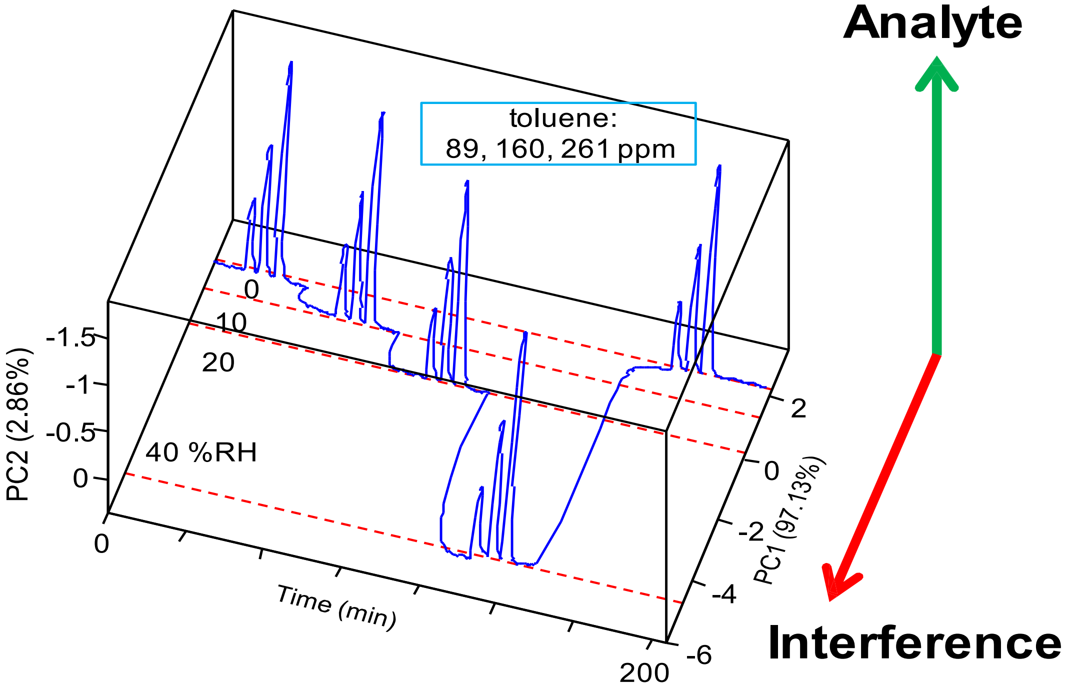
H2O = water
CH4 = methane
THF = tetrahydrofuran
Ben = benzene
EtAc = ethyl acetate
EtOH = ethanol
Tol = toluene

High performance sensing = appropriate sensor + appropriate data analytics

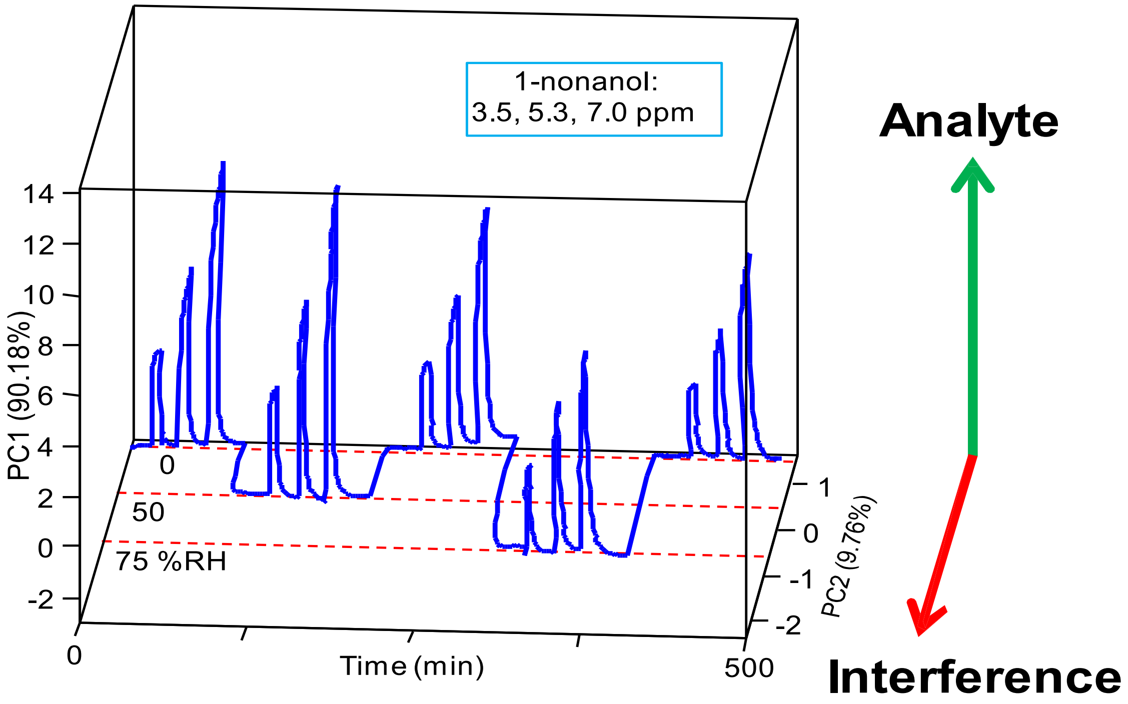
Interference rejection at 10,000 – 2,000,000 fold



10,000 fold rejection



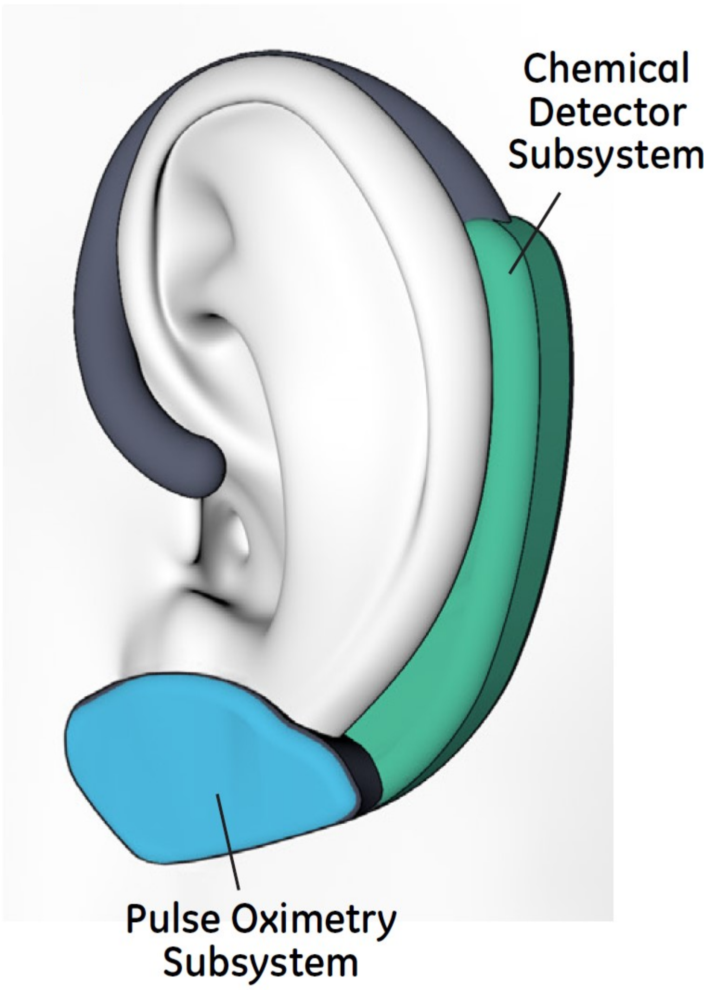
2,000,000 fold rejection

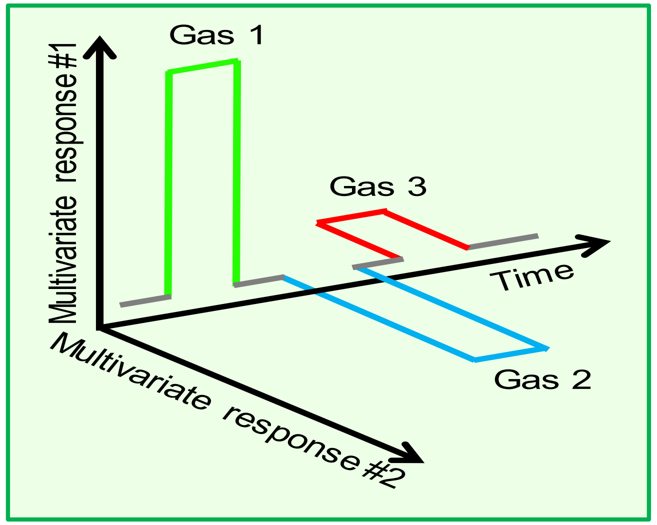


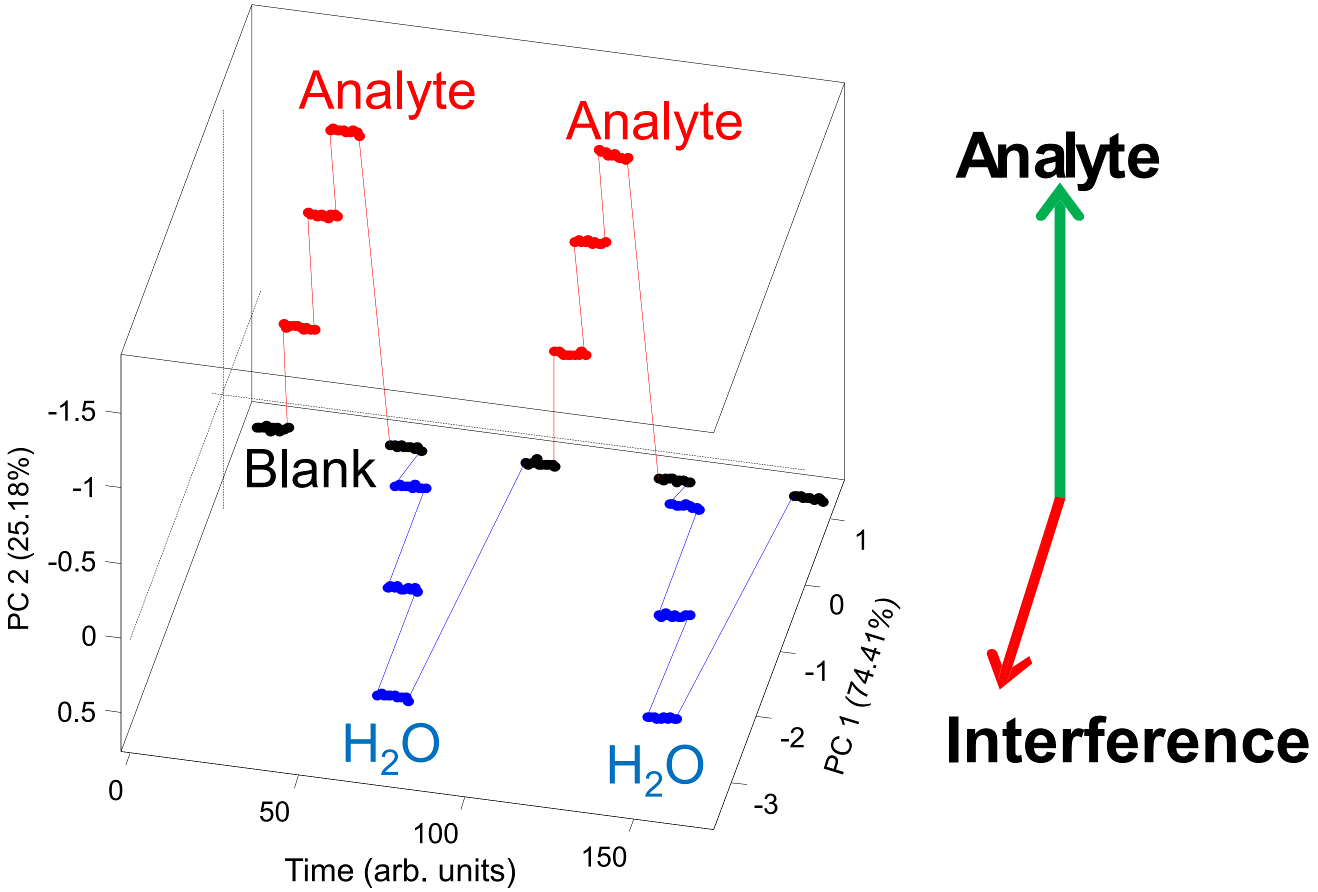
Immunity to interferences by applying new sensing philosophy

Potyrailo, *Chem. Soc. Rev.* **2017**

Wearable physiological sensor components for gas sensing



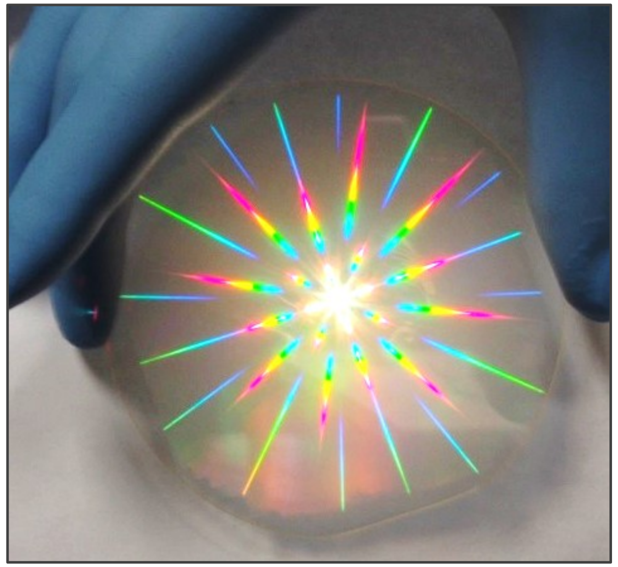


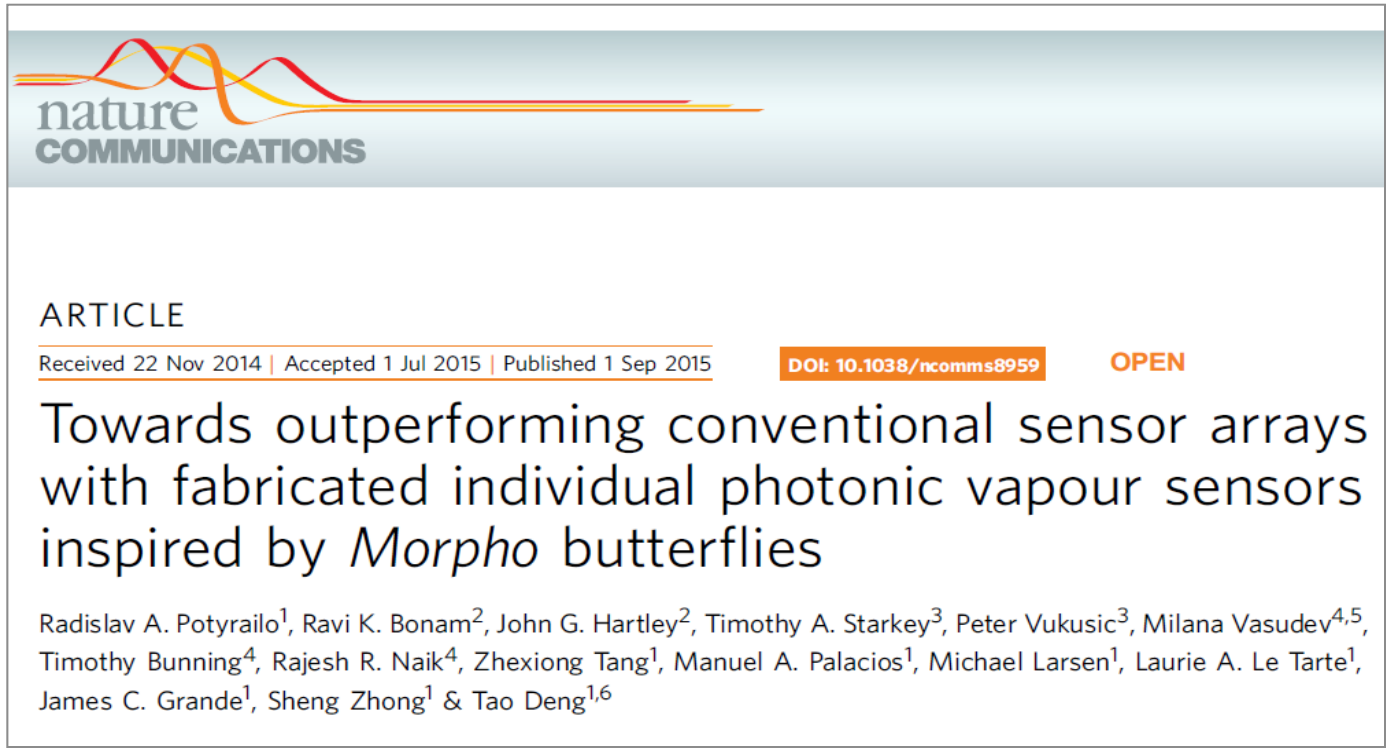


Potyrailo et al, submitted to USPTO, **2019**

Rejection of humidity on par with more bulky multivariable sensor systems

Single multivariable sensor outperforms sensor arrays




nature COMMUNICATIONS

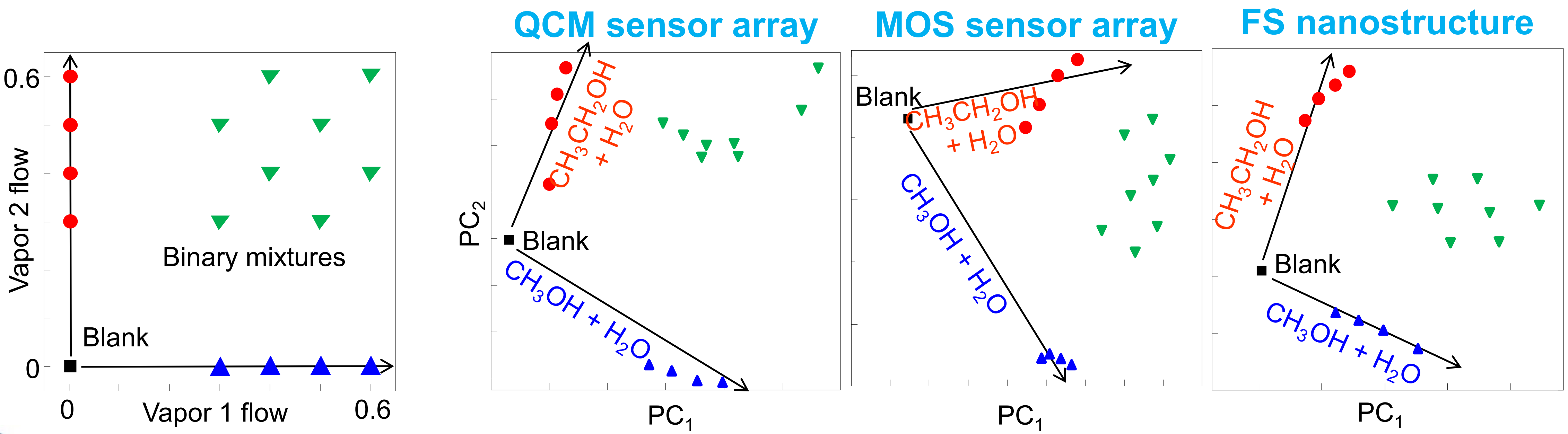
ARTICLE

Received 22 Nov 2014 | Accepted 1 Jul 2015 | Published 1 Sep 2015

DOI: 10.1038/ncomms8959 OPEN

Towards outperforming conventional sensor arrays with fabricated individual photonic vapour sensors inspired by *Morpho* butterflies

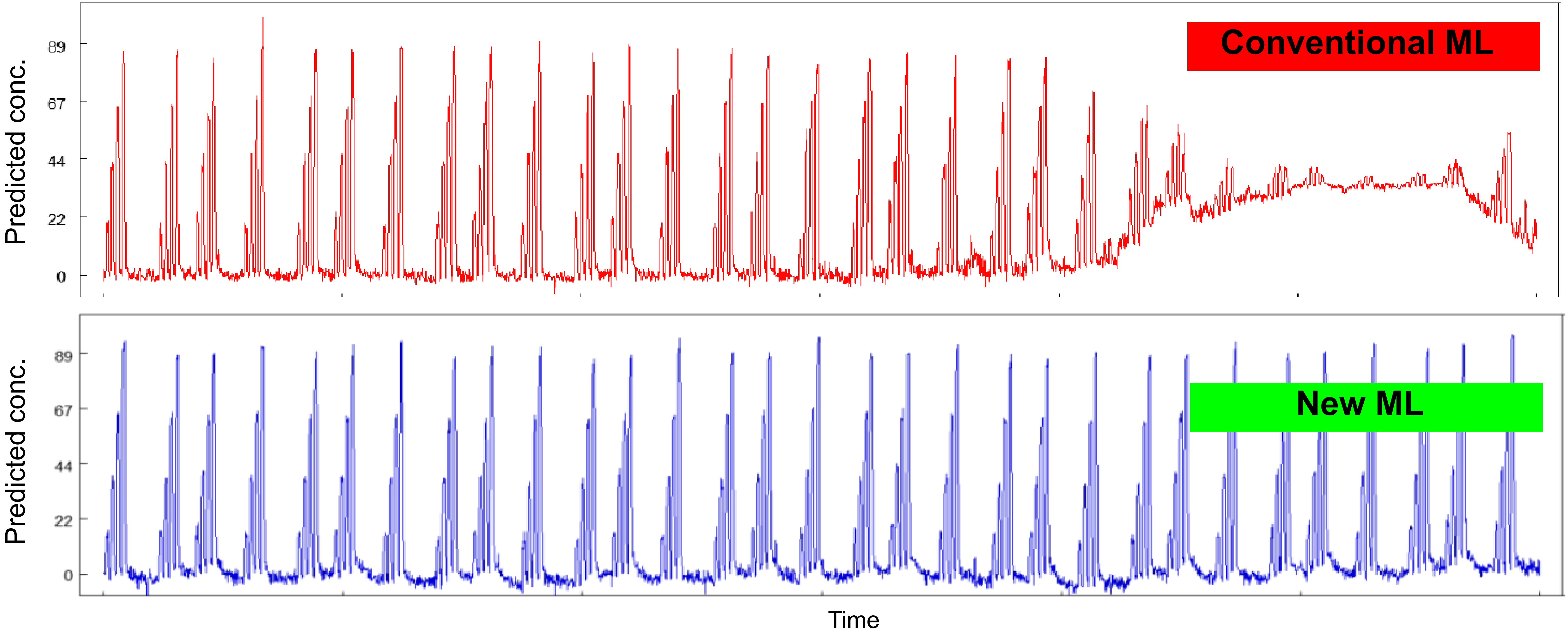
Radislav A. Potyrailo[1], Ravi K. Bonam[2], John G. Hartley[2], Timothy A. Starkey[3], Peter Vukusic[3], Milana Vasudev[4,5], Timothy Bunning[4], Rajesh R. Naik[4], Zhexiong Tang[1], Manuel A. Palacios[1], Michael Larsen[1], Laurie A. Le Tarte[1], James C. Grande[1], Sheng Zhong[1] & Tao Deng[1,6]



FS = nonafluorohexyl-trimethoxysilane
QCM = quartz crystal microbalance
MOS = metal oxide semiconductor

Potyrailo et al.
Nature Communications
2015

Sensor stability boost:
using new machine learning (ML) tools

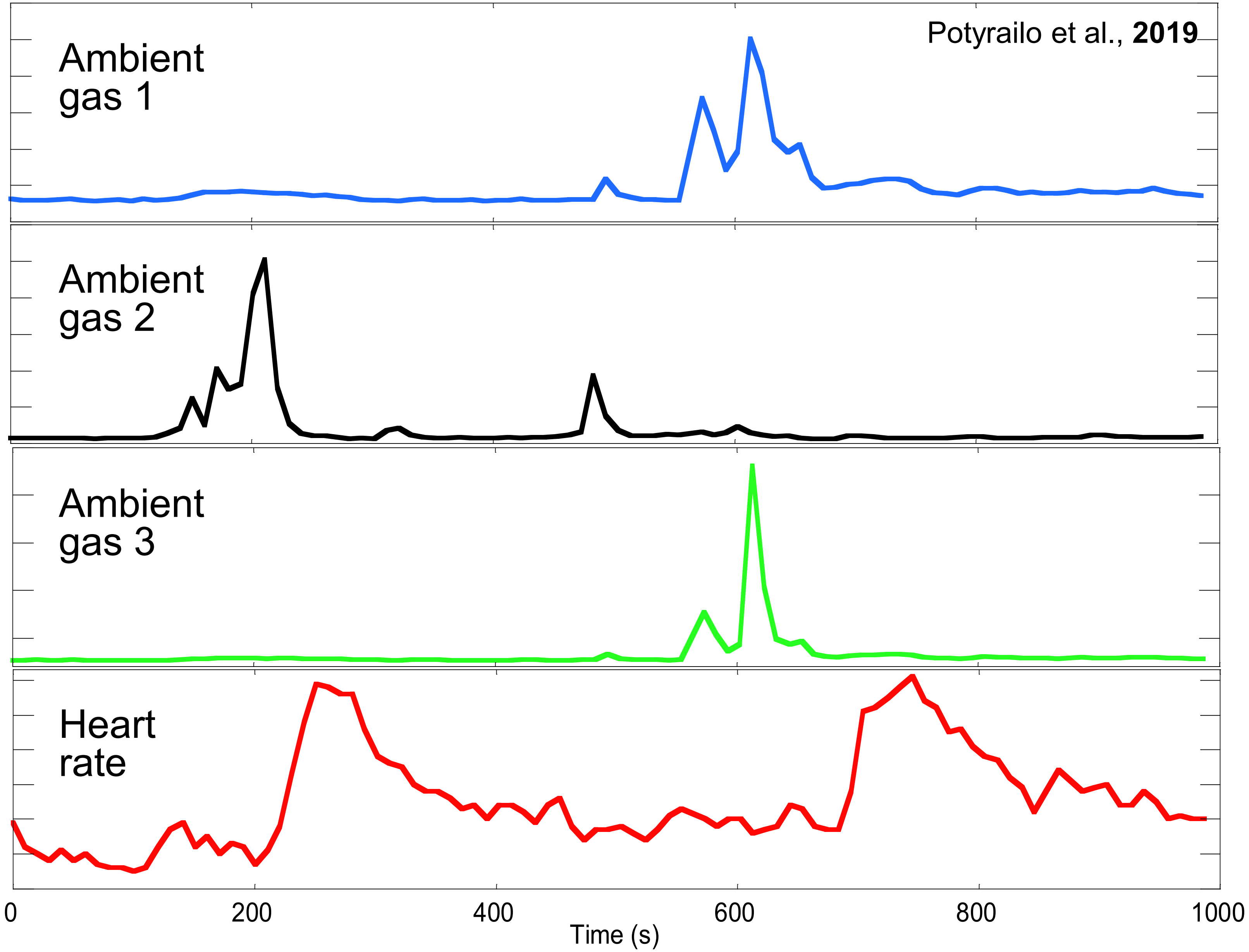


Classic vs GE ML to predict sensor response in the presence of drift

Potyrailo et al, NETL-DOE SOFC Project Review Meeting **2018**

Fusion of high-performance gas and physiological sensors: new valuable capabilities

Graphic: GE Research



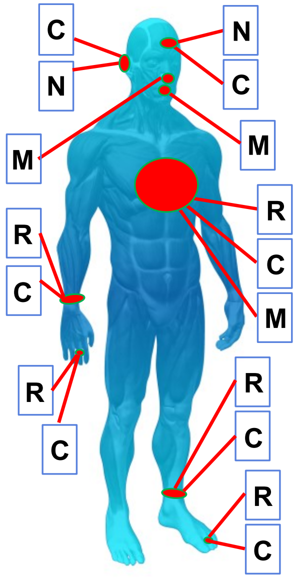
Toward prediction of undesirable human conditions

Undesirable Human Condition → **Measurement Tools** → **Machine Learning Tools** → **Prediction Time**

Physiological functions

- Neural (N)
- Respiratory (R)
- Circulatory (C)
- Metabolic (M)

Potyrailo , et.al., **2019**

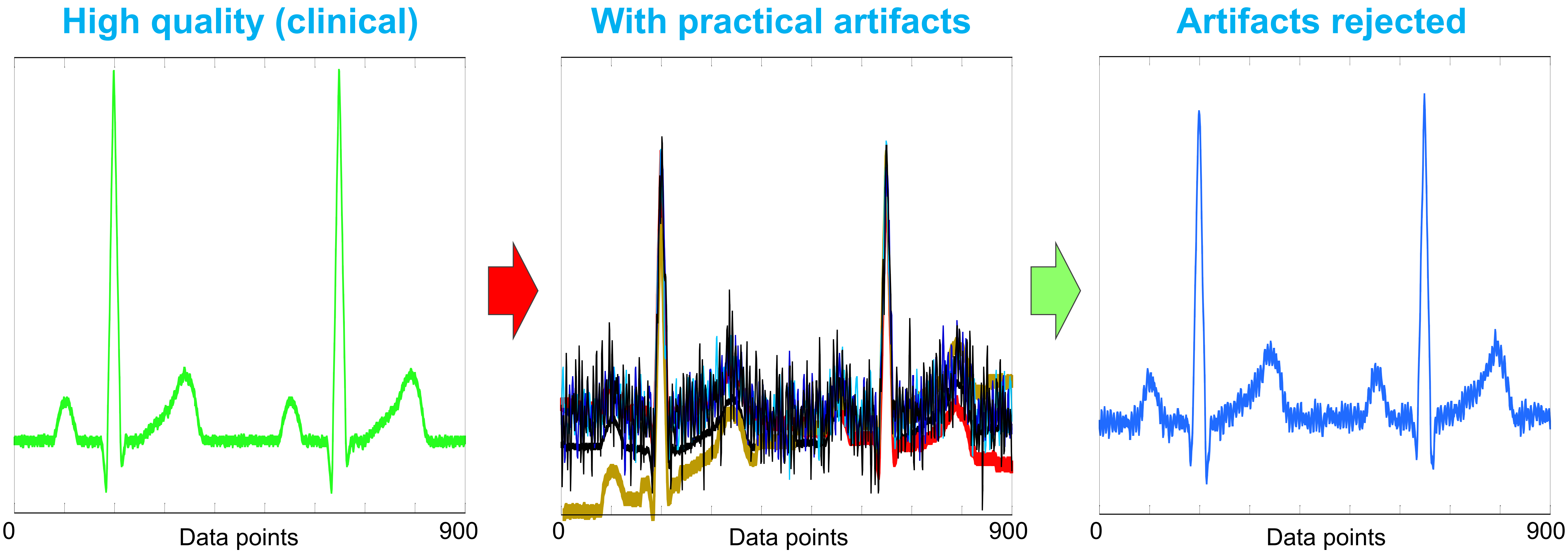


Graphic: GE Research

Diverse users of wearable sensors

All graphics: GE Research

Simplifying hardware + system with preserved ECG data quality



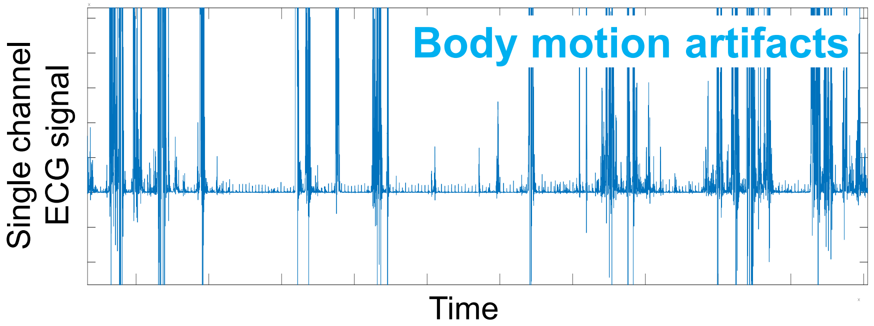
Rejection of poor electrode connection and electrode movements in ECG data

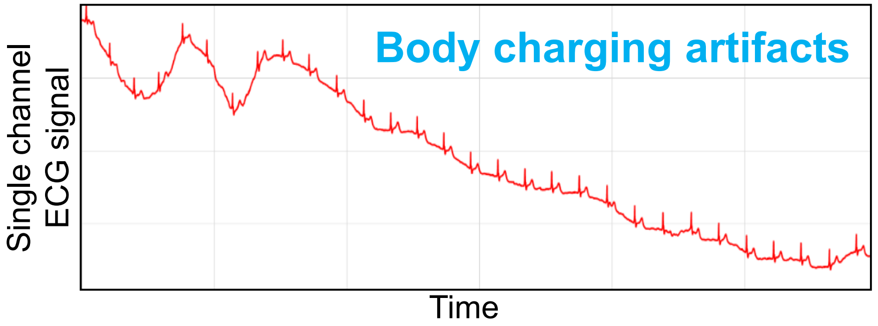
R. Potyrailo, A. Obi, **2019**

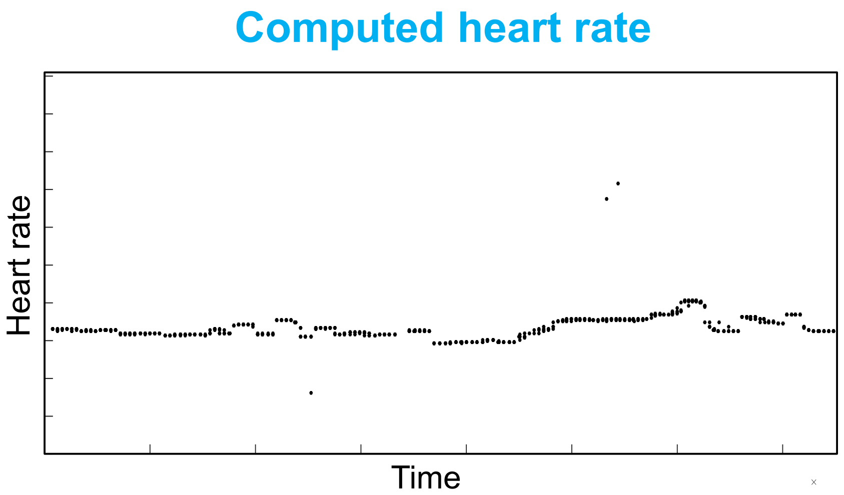
Non-contact ECG signal processing and fusion

Problems with non-contact ECG
- Extreme sensitivity to motion artifacts
- 30 heart beat recovery time after signal loss
- Clothing and subject variability

GE solutions for non-contact ECG
- Eliminated/reduced sensitivity to motion artifacts
- Signal recovery at next heart beat
- Clothing and subject robustness



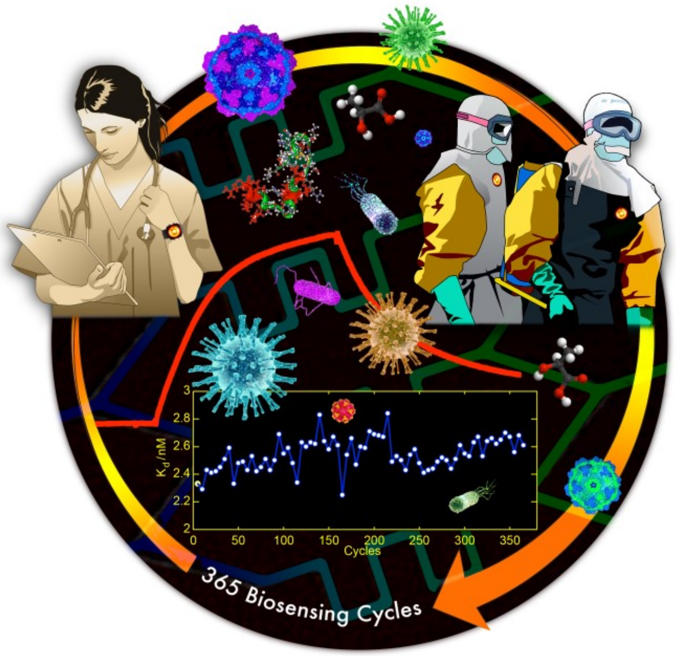


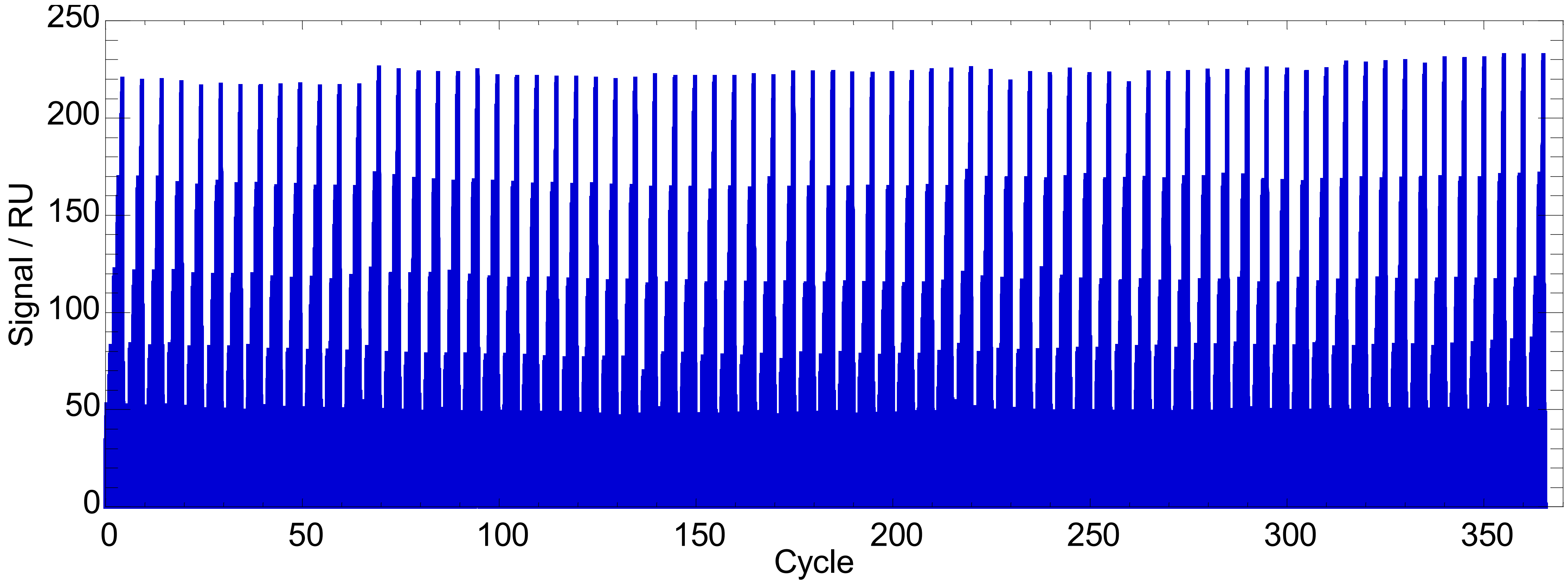


Multi-electrode design + neuromorphic algorithm = high performance sensing

P. Lorraine, Filed to USPTO

Reversible biorecognition for 365 bind/release cycles
Toward wearable reversible biosensing:





Highly stable binding affinity constant K_d over 365 bind/release cycles, $K_d = 2.5 \pm 0.1$ nM

Potyrailo et al. *Angew. Chem. Int. Ed.* **2015**

Thrombin concentrations: 0.5, 1, 2, 4, and 8 nM
Substrate: Streptavidin Biacore chips
Chemical deactivation: 50 mM NaOH/1M NaCl

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Future developments driven by multiple markets

Industrial Safety: $3B

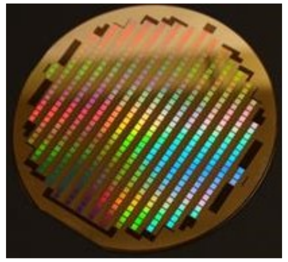
Health self-monitoring: $15B

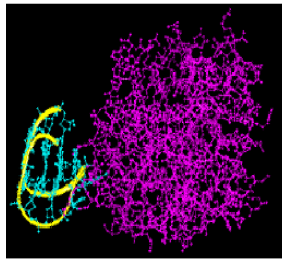
Wearable sensors: $7B (2017) → $24B (2023)

https://www.marketsandmarkets.com/PressReleases/safety-instrumented-system.asp

https://www.prnewswire.com/news-releases/health-self-monitoring-technologies-and-global-markets-300102733.html

https://www.mordorintelligence.com/industry-reports/global-wearable-sensors-market





Thank you !

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