From Sensors in General,

to Chemical Sensors,

to Optical Sensors,

to Oxygen:

Join me on an Exciting Trip!

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TUM; 17 March, 2012

Sensors

Sensors are

(a) miniaturized devices that can deliver

(b) real-time and on-line information on

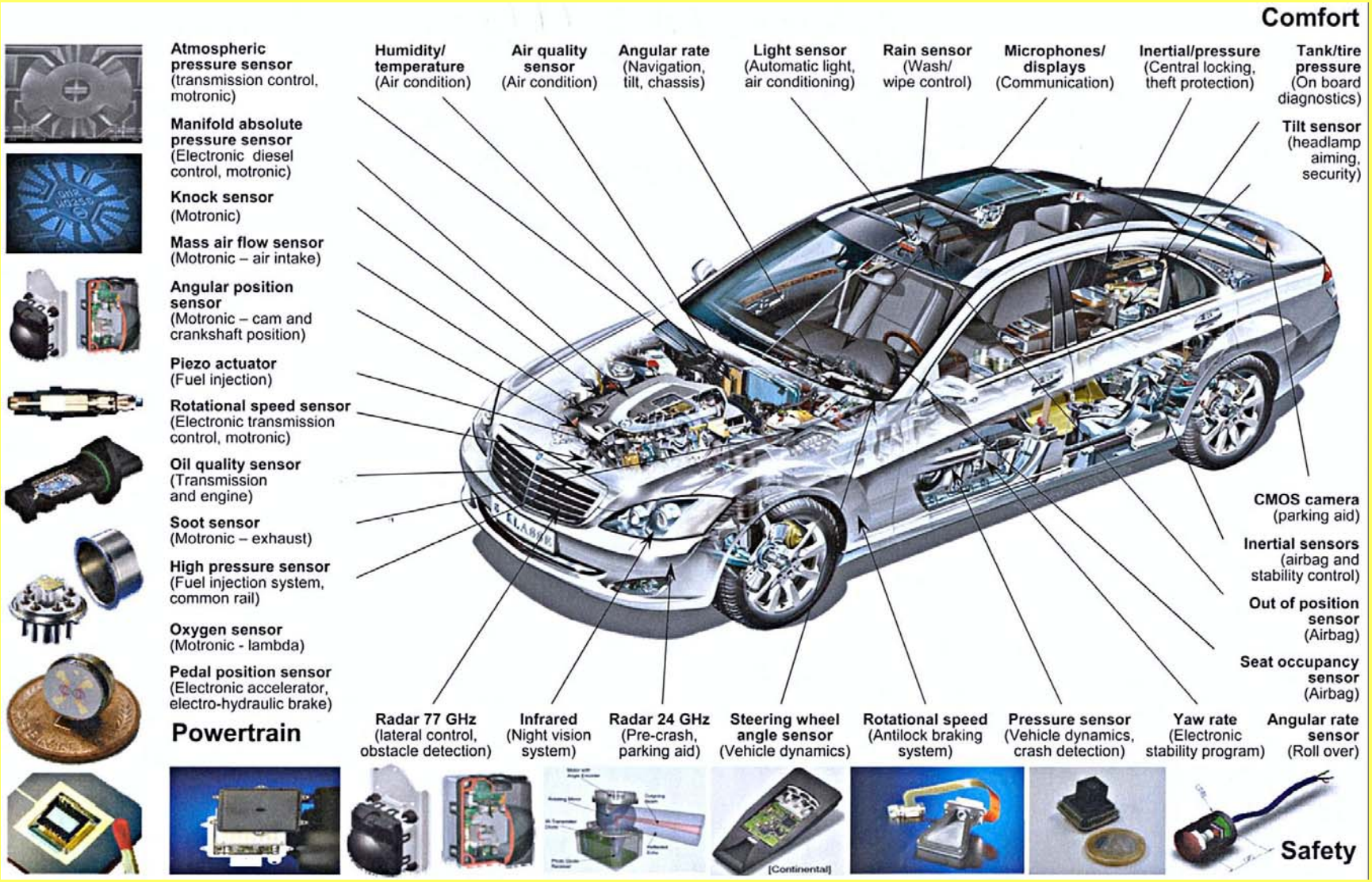
(c) a specific physical or chemical parameter

Sensors

We are hardly aware of the many sensors that surround us to ...

***control the temperature of refrigerators; *turn on and off city lights; *control heating; *determine our position (=> navigation systems); *measure distance; *monitor the quality of drinking water; *detect moving objects; *measure the altitude of aircrafts; * measure ozone in the stratosphere and NO_x in city centers; ....**

Sensors in the Automotive Industry



Sensors in the Automotive Industry

Examples of <u>physical</u> sensors in cars:

Tire pressure, oil pressure, oil level; temperature of -cooling water, -oil, -wind screen (frost!), -air (air condition), -exhaust gas, etc.; daylight sensors (brightness), altitude of chassis, rotation, distance, recognition of persons (for assistant systems); recognition of streets and traffic signs, position (GPS); movement and speed (navigation); air bags; antiblocking systems (ABS),

and numerous others we are only aware of <u>if they do not work</u>.

Chemical Sensors

- by analogy to physical sensors - are

(a) miniaturized devices that can deliver
(b) real-time and on-line information on
(c) a specific (bio)chemical parameter.

Dear organic chemists:

Indicators and molecules are not yet "sensors", even if you like to call them so or believe that synthesis is the greatest of all arts ....

Chemical Sensors in the Automotive Industry

Fuel: Ethanol, O_2 ("lambda probe"), urea, NOx,

Environment: Smell in a driver's cabin; ethanol (drunken driver detection)

Air (in and out): NOx (in tunnels;)

Motor oil: gegree decomposition

New (or better) chemical sensors are needed for:

Battery management

Hydrogen, methane, oxygen, ...

Note: This is a multi-billion € market!

Regensburg

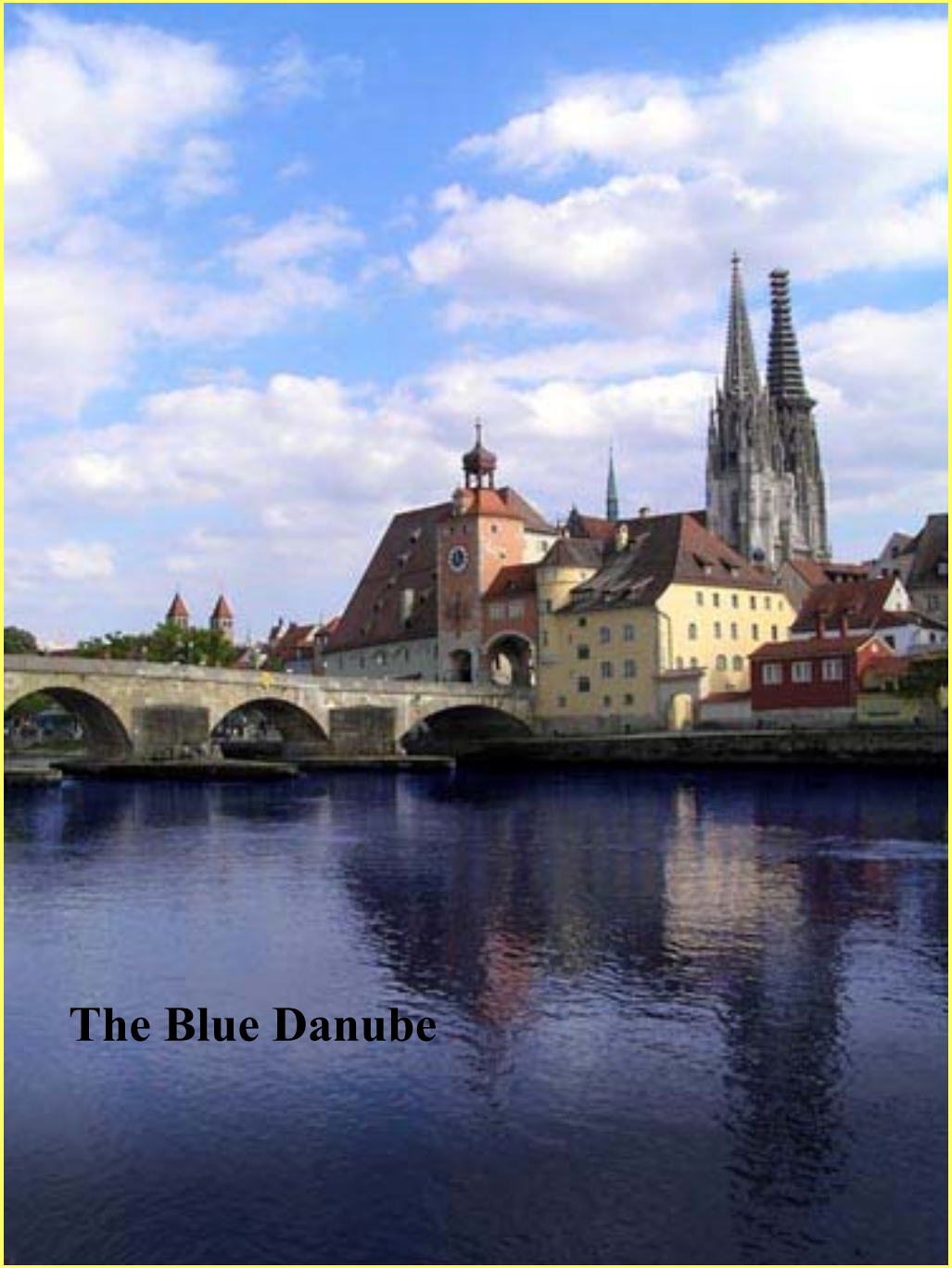
* 150,000 inhabitants

* 2500 years of history: from Celts to Romans to "Bavarians"

* city of the first all-German parliament (1582 - 1804)

* where the 300-series of BMWs is fabricated;

* has to be blamed for the current pope.



The University of Regensburg (Ratisbona)

*** 18,000 students; * largest (bio)analytical school in Germany**

Types of Chemical Sensors

Electrochemical Sensors
(based on amperometry, potentiometry, coulometry, conductivity; impedimetry ...)

Optical Sensors
(based on absorption, fluorescence, Raman, infrared (gas) sensing, surface plasmon resonance, fiber optic sensors, remote imagers;

Mass-sensitive devices (such as the quartz microbalance);

Sensors based on surface acoustic waves, on thermal effects (calorimetric sensors), and so forth.

Optical Sensing of Oxygen: A (Hi)story of Success

Why Oxygen?

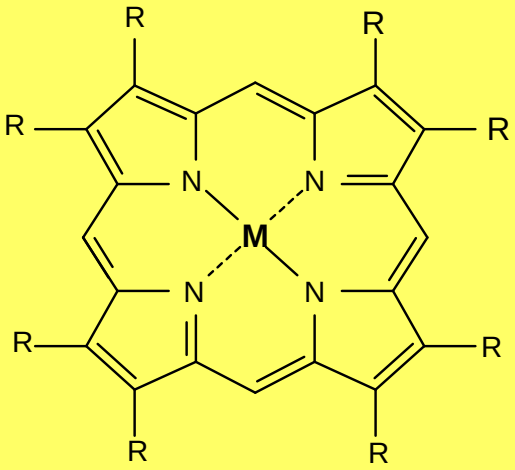
Oxygen is present in

- in the atmosphere (up to 30 km)
- in seawater (from the arctic to the antarctic)
- in blood
- in car exhaust
- in bioreactors
- in breath air (inhaled and exhaled)
- in industrial gases and in chemical plants
- almost everywhere

Quenchable Probes for Oxygen

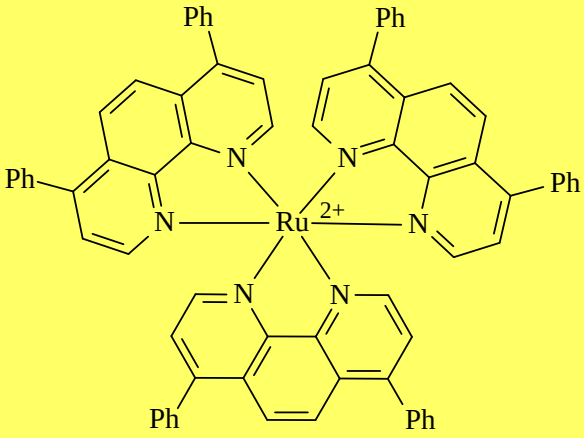
Probes (Indicators) for Oxygen

Metallo-Porphyrins (also fluorinated)



Ruthenium-Diimine Complexes such as Ru(dpp)

Others: **decacyclene, pyrene**
Al-oxine complex
campher quinone



Visualization of the Quenching Effect

Probe: Ru (bathophenanthroline)$_3$ *("Ru-batho")*

↑ **Ru(batho) in buffer**

fluorescence quenched due to O_2 in sample

↑ **addition of NaCl**

no change

↑ **addition of $Na_2S_2O_8$**

fluorescence enhanced due to consumption of O_2 by dithionite

↑ **after bubbling with air for 15 min**

fluorescence decreases again due to presence of O_2

The Stern-Volmer Relationship

(the equation may be derived from the mass action law)

$$F_0/F = \tau_0/\tau = 1 + K_{sv}[Q]$$

where

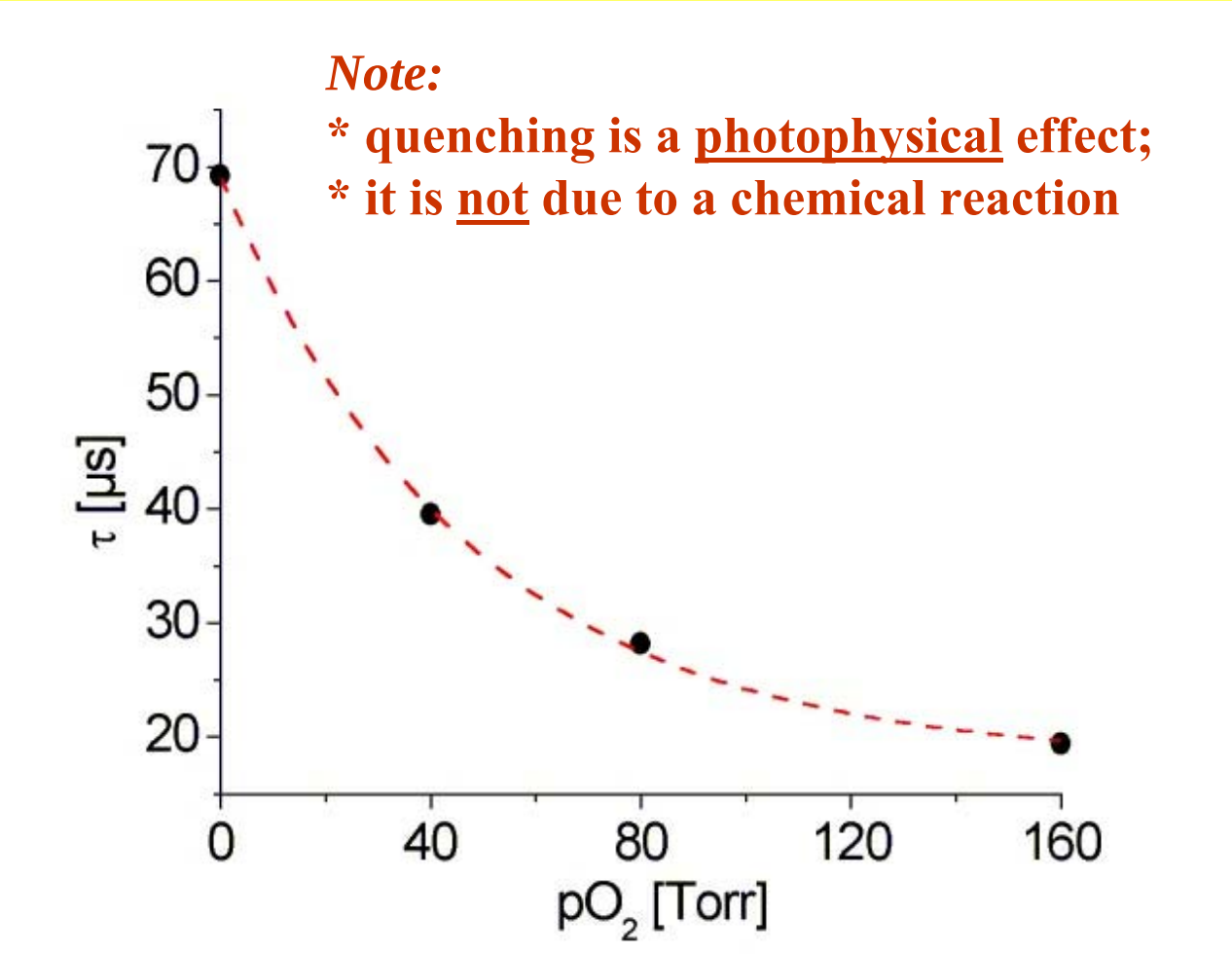
F_0	**is the fluorescence intensity in absence of a quencher**
F	**is the fluorescence intensity in presence of a quencher**
τ_0	**is the fluorescence decay time in absence of a quencher**
τ	**is the fluorescence decay time in presence of a quencher**
[Q]	**is the concentration of the quencher**

May be applied to all sensors for dynamic quenchers of luminescence (oxygen, halides, nitro compounds, etc.)

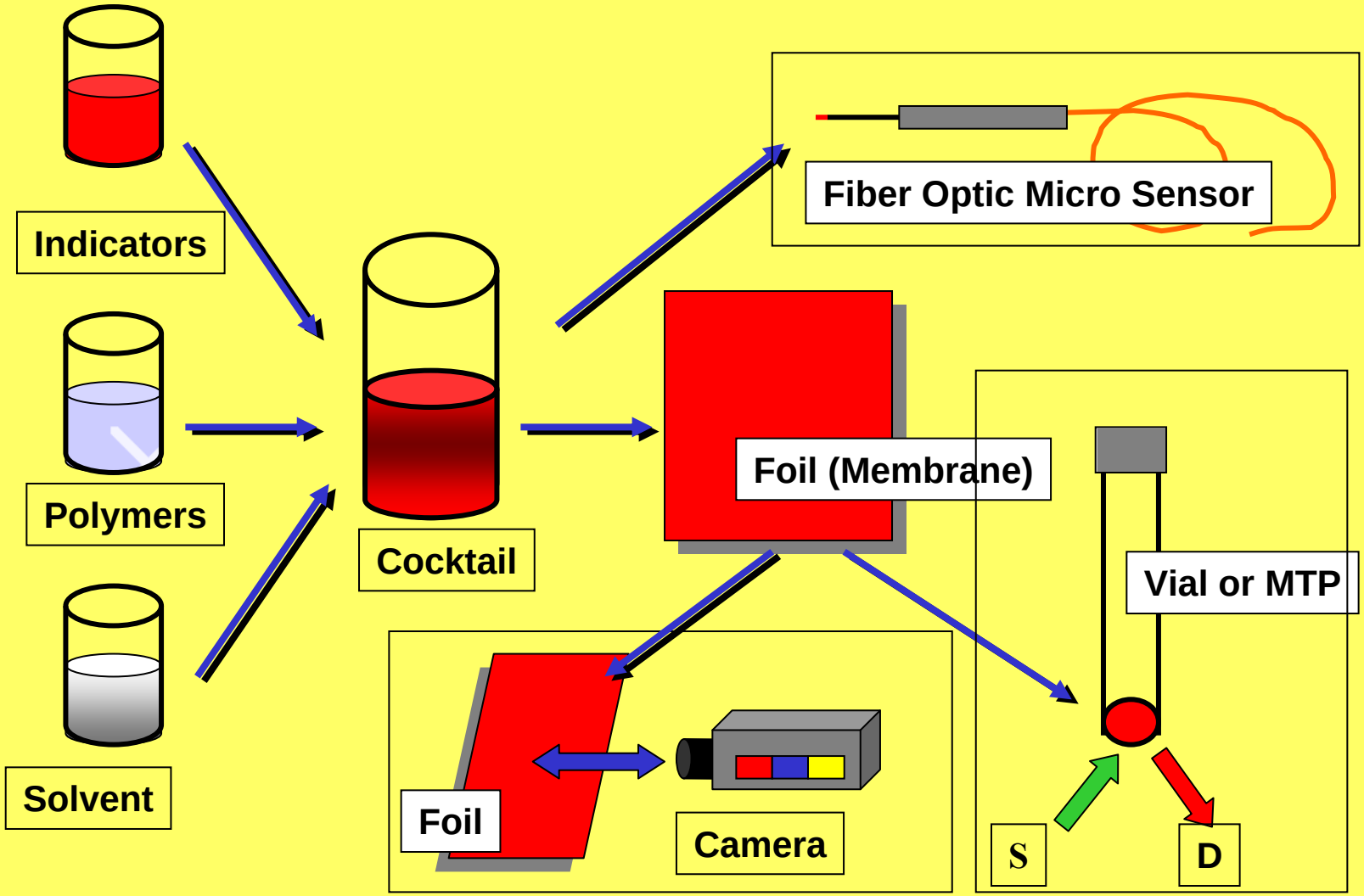
Dynamic Quenching of Luminescence

A: Decrease in Luminescence Decay Time Due to Quenching by Oxygen

➔ Basis for all Practically Used Optical Oxygen Sensing Schemes at Present

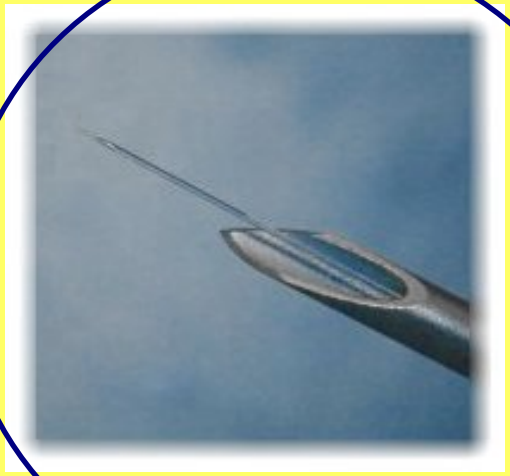


Making and Deposition of "Cocktails"



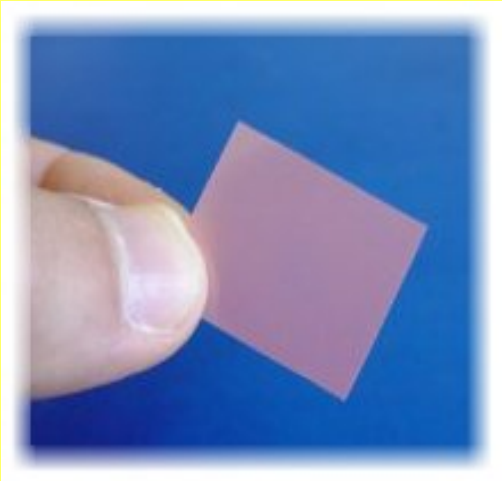
Sensing Formats

sensor cocktails



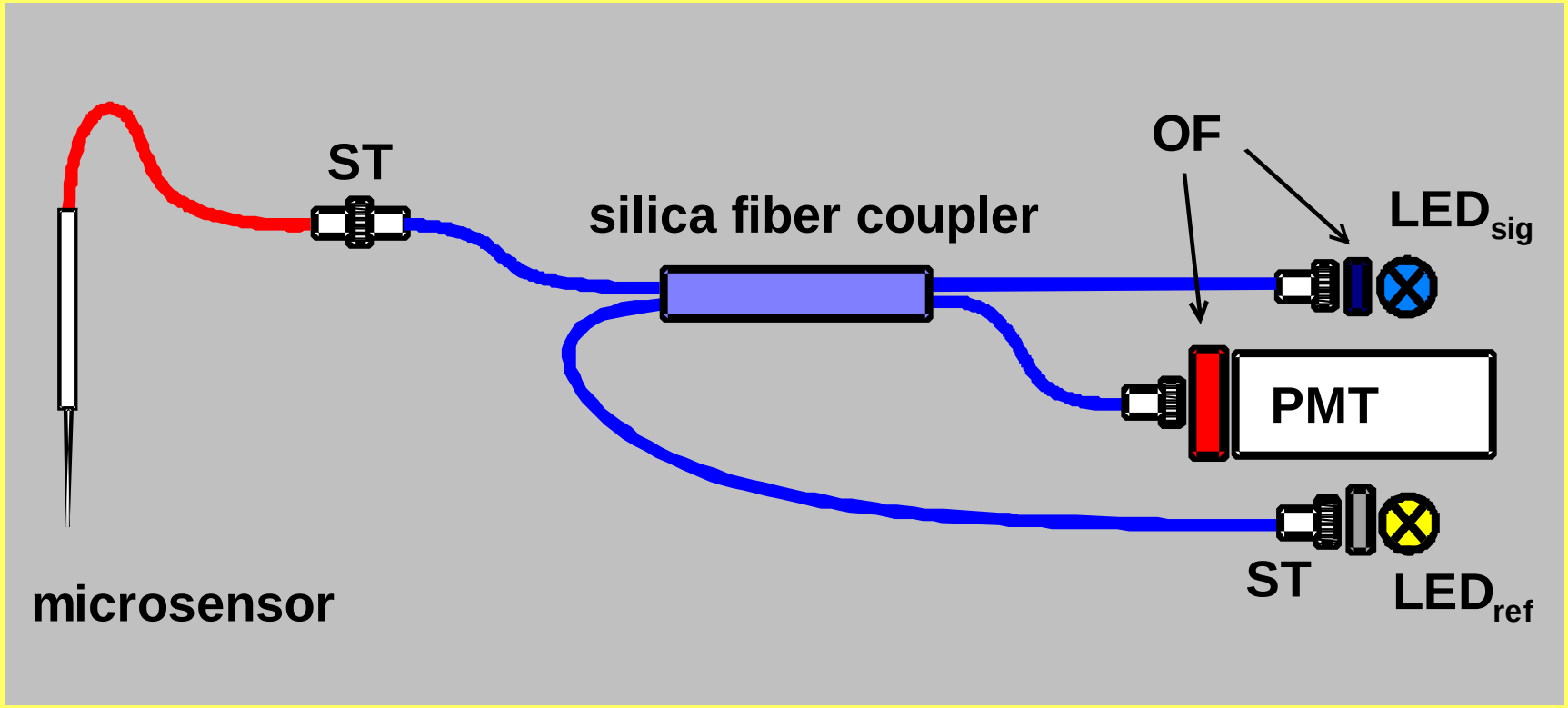
fiber optic microsensor

microplate



planar

Fiber Optic Oxygen Microsensor



Fast Response Oxygen Micro-Optodes Based on Novel Soluble Ormosil Glasses,

I. Klimant, F. Ruckruh, G. Liebsch, A. Stangelmayer, O. S. Wolfbeis, *Microchim. Acta* 131 (1999) 35

Fiber Optic Oxygen Microsensor

Let us make an experiment, Mr. Fischer!

For details: see www.preses.de

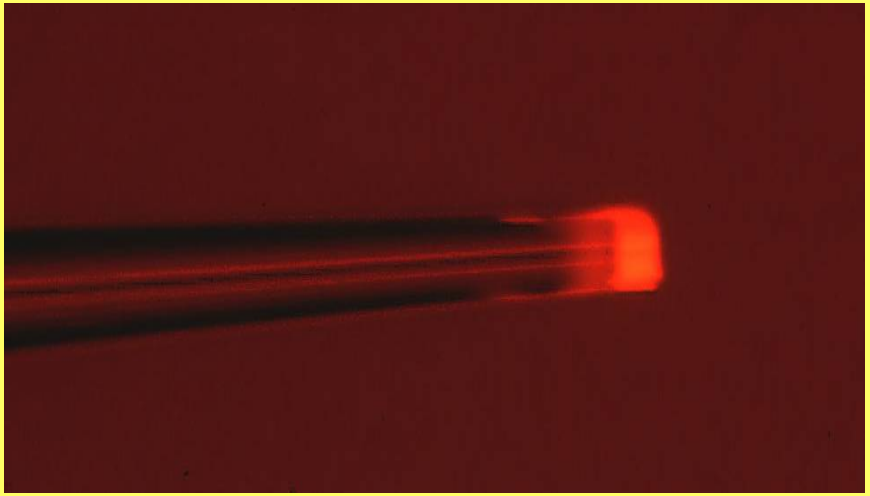
Presens GmbH:

73 coworkers in 2012,

9 M€ turnover in 2011

Products: sensors for oxygen, pH, CO_2

Fiber Optic Oxygen Microsensors



Review:

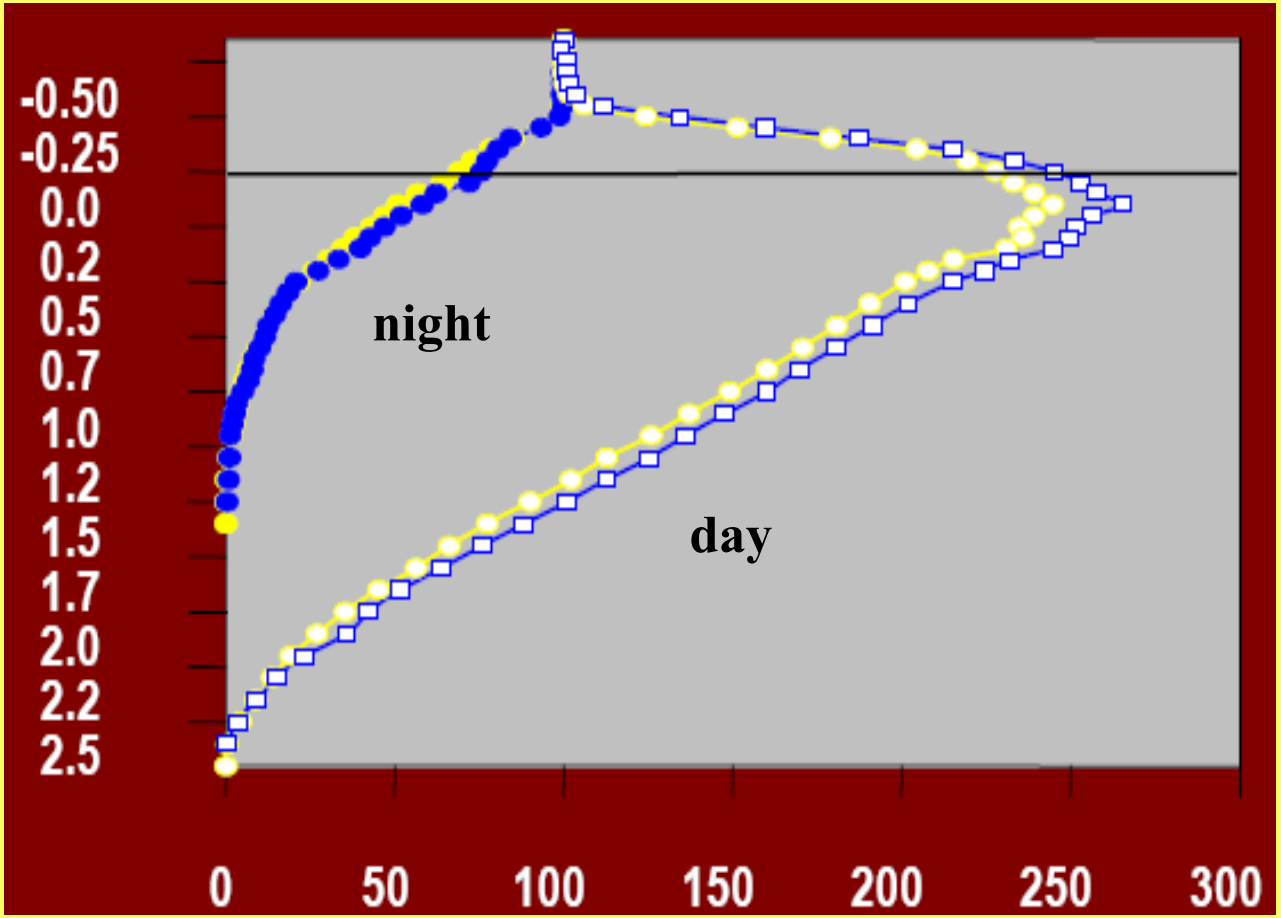
Fiber-Optic Chemical Sensors and Biosensors. O. S. Wolfbeis; *Anal. Chem.* (2008), *80*, 4269-4283.

Fiber Optic Microsensors in Marine Sciences

Studying the Oxygen Profile in a Marine Mat

(cooperation with MPI for Marine Microbiology, Bremen)

Oxygen Profiles in Marine Mats



% air saturation

<= seawater

<= sand mat with hierarchical order:

* photosynthetic cyanobacteria

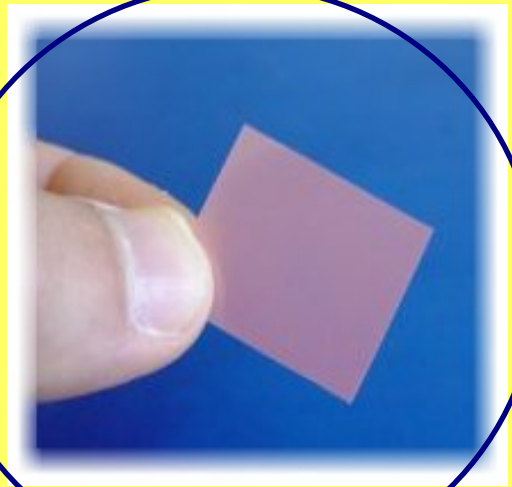
* sulfur bacteria

Sensing Formats, 2: Planar Sensors

sensor cocktails

fiber optic microsensor

microplate



planar

Clinical Applications

Sampler with integrated sensor spots for

pH,
O_2
CO_2
Na, K, Ca,
or Cl or glucose
or lactate or creatinine

Clinical Applications

Portable Single Shot Blood Analyzer

Measures
O_2, CO_2, pH, Na, K, Cl, Hb; Hc; S_{O2} Glucose, Ca^{2+}

AVL
➔ Roche
➔ Osmetech

Clinical Applications

* portable
* ready in 7 min
* requires 80 µL of whole blood
* disposable sensors

Clinical Applications of Oxygen Sensors

Test Tube for Detection of *Microbacillus tuberculosis*

(Becton-Dickinson)

http://www.bd.com/clinical/products/bc/index.asp

Becton Dickinson's BacTec Series

The *BACTEC* 9000 System is the only blood culturing system that provides truly non-invasive technology.

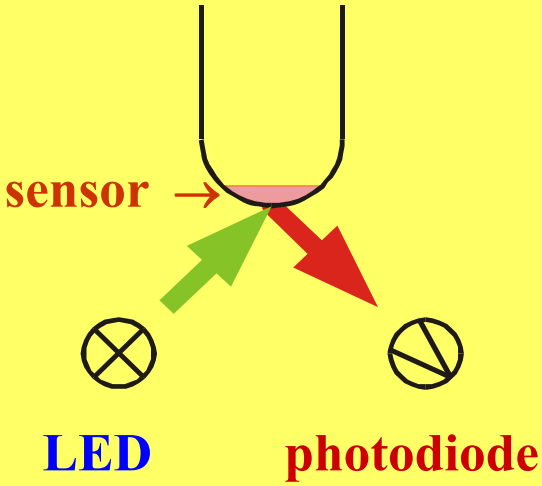
Also detects slow growing organisms such as *Haemophilus* and *Neisseria*.

http://www.bd.com/clinical/products/bc/index.asp

Sensor Spots for Microbioreactors

* oxygen sensors integrated into small bottles or microplates

* allows respriration to be monitored through bottle glass;
  ➔ no risk of contamination

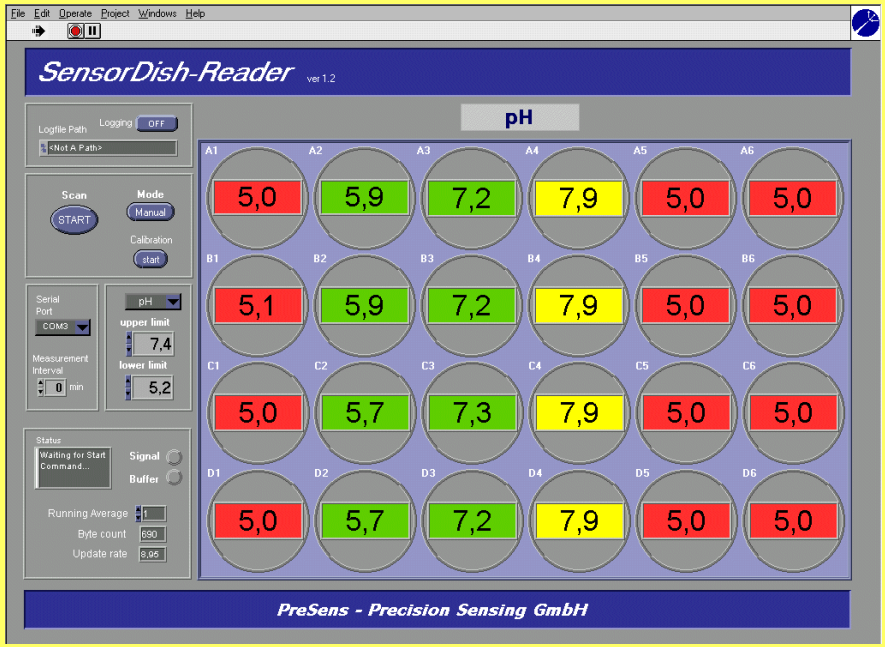


24 well array (top down); note the colored sensor spots

Fluorescent Sensing Using Microtiterplates

* fluorescent pH sensors integrated into small bottles or microplates

* read out by photodiodes after excitation by blue LEDs



Software Surface

LED-based 24 well array reader

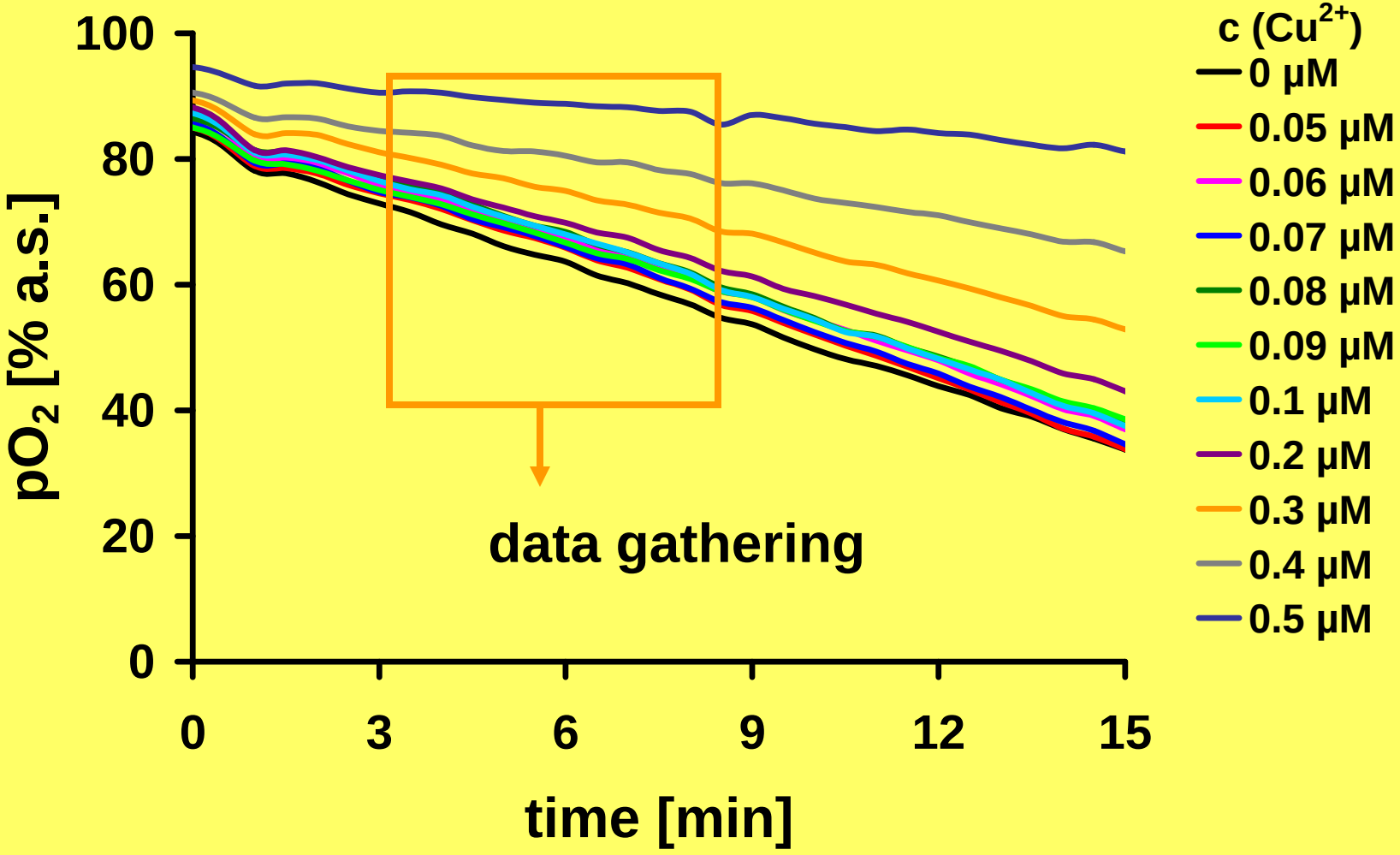
Sensor Spots for Microbioreactors

Let us make another experiment, Mr. Fischer!

Sensing oxygen in a micro-bioreactor

(www.presens.de)

Oxygen Uptake of *Ps. putida* in Presence of Cu^{2+}



If one can sense oxygen, ...

... one can make biosensors

by using enzymes that

cause the <u>consumption</u> or <u>production</u> of oxygen.

Examples:

Enzyme-Based Sensing of Glucose

(1) glucose + O_2 ==(GOx)==> gluconolactone + H_2O_2

(2) gluconolactone + H_2O ===> gluconate + H^+

Note:

4 Million Germans suffer from diabetes mellitus! (= >4M tests per day)

Review: **Optical Methods for Sensing Glucose. M.-S. Steiner, A. Duerkop, O. S. Wolfbeis; *Chem. Soc. Rev.* (2011), *40*, 4805**

Enzyme-Based Optical Biosensing

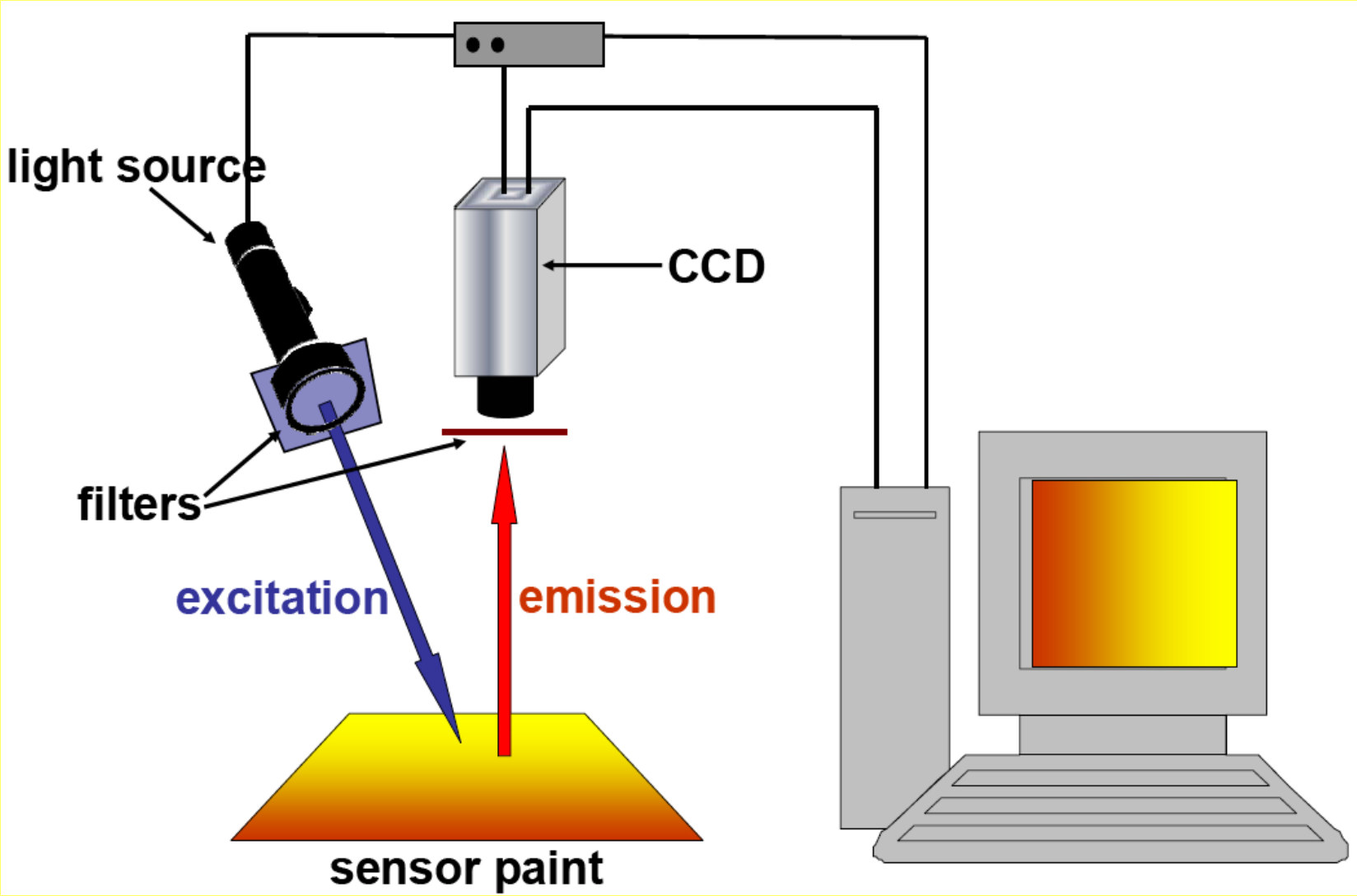
can be applied to the determination of ..

.. enzyme substrates:	**Glucose (via O_2, H^+ or H_2O_2)** **Urea (via H^+ or NH_3/ammonium)** **Lactate (via O_2, H^+ or H_2O_2)**
.. enzyme inhibitors:	**Heavy Metals** **Cyanide, etc.**
.. enzyme activities:	**Esterases** **Phosphatases and kinases** **Amylases (Alzheimer)** **Proteases (HIV drugs!)**

Review: **Optical Biosensors.**
S. M. Borisov, O. S. Wolfbeis; *Chem. Rev*. (**2008**), *108*, 423

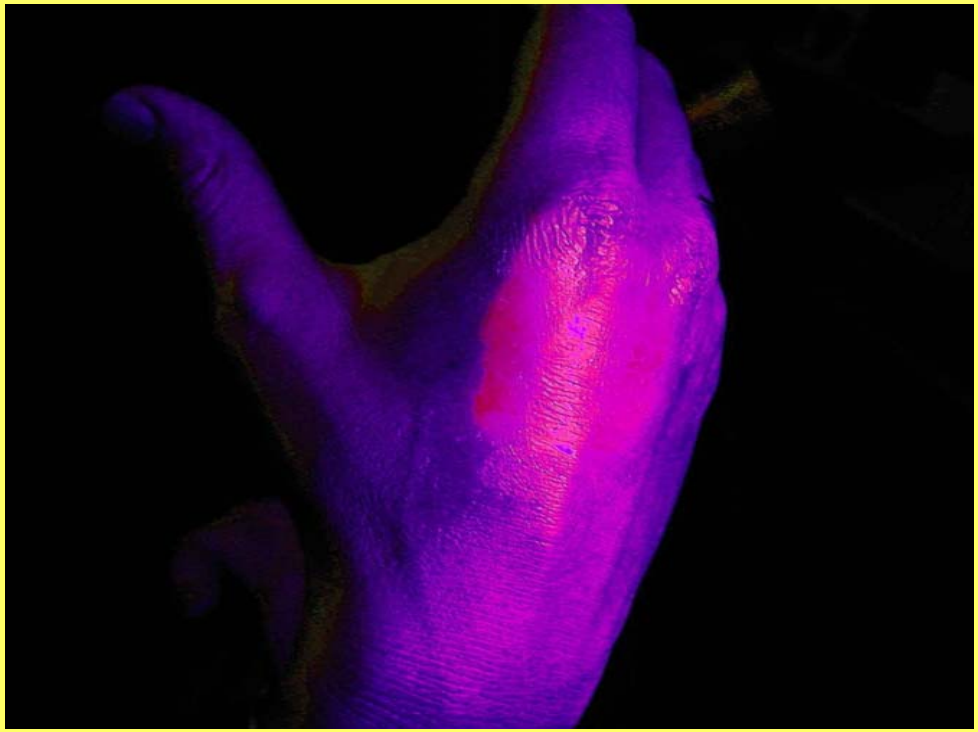
Next Section: Sens(ing)-Imaging

Experimental Setup for Imaging Sensor Paints



An Oxygen Sensor Spray

- made from layers of a polyalcohol and polyglycol
- contains an oxygen probe (a porphyrin)
- can be easily removed from skin

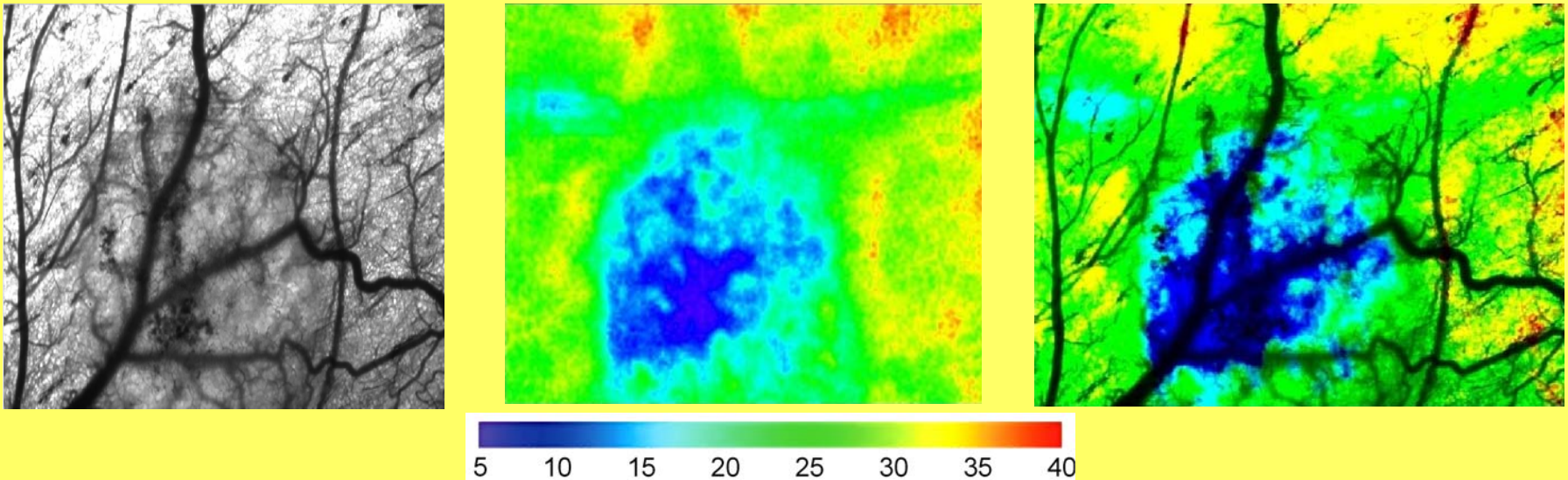


Sensor layer sprayed onto skin to detect cancerous areas

Chemical Imaging Using Fluorescent Sensor Layers

Visualization of Oxygen Distribution in Tumorous Hamster Skin Using an Oxygen-Responsive Polymer Layer in Close Contact with Skin

transmission **oxygen image** **images combined**



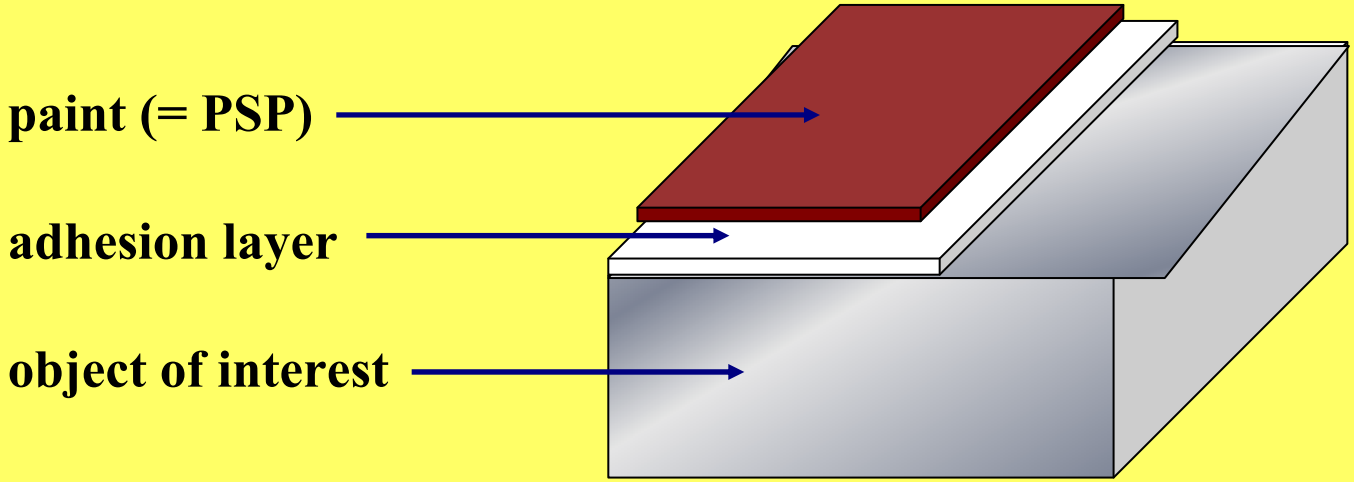
***p*O$_2$ [Torr]**

P. Babilas, V. Schacht, G. Liebsch, O. S. Wolfbeis, M. Landthaler, R. M. Szeimies, C. Abels, *Brit. J. Cancer* 88 (2008) 1462-1469.

Pressure-Sensitive Paints (PSPs)

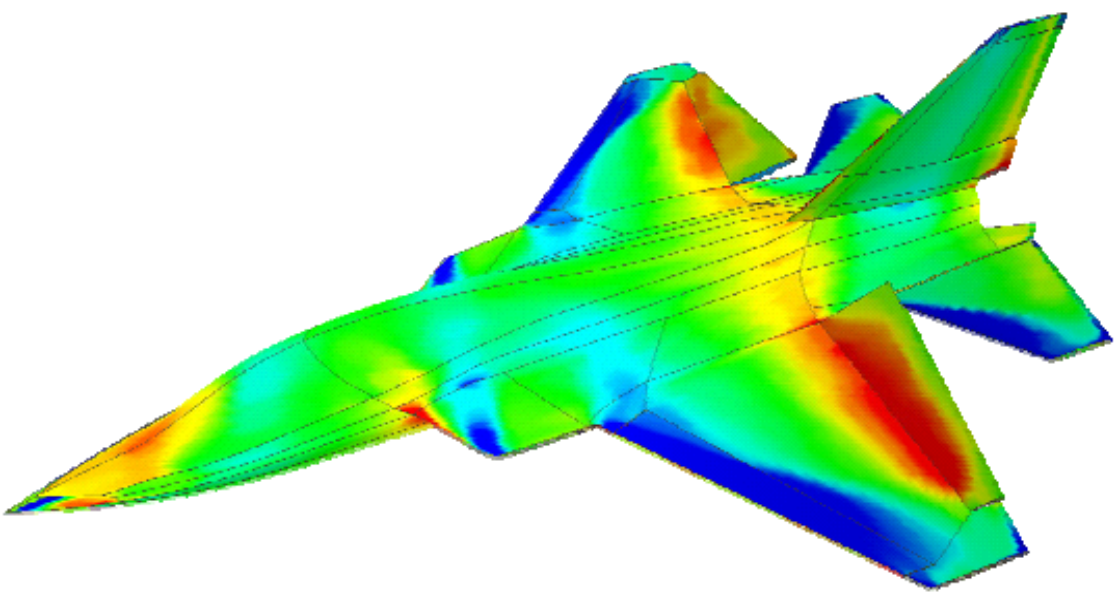
* Consists of an oxygen-sensitive luminescent material (wrongly termed "pressure-sensitive")

* Response to pressure depends on the quenching constant of the indicator used



Pressure-Sensitive Paints (PSPs)

* **Enables fast imaging of air pressure**



* **Free of turbulences by cables (as in former sensors)**

* **Response to pressure (= pressure range) depends on the Stern-Volmer quenching constant (K_{sv}) of the indicator**

* **Also used in the car industry (BMW, Audi, Daimler))**

Review: **Sensor Paints.** O. S. Wolfbeis; *Adv. Mat.* (**2008**), *20*, 3759–3763.

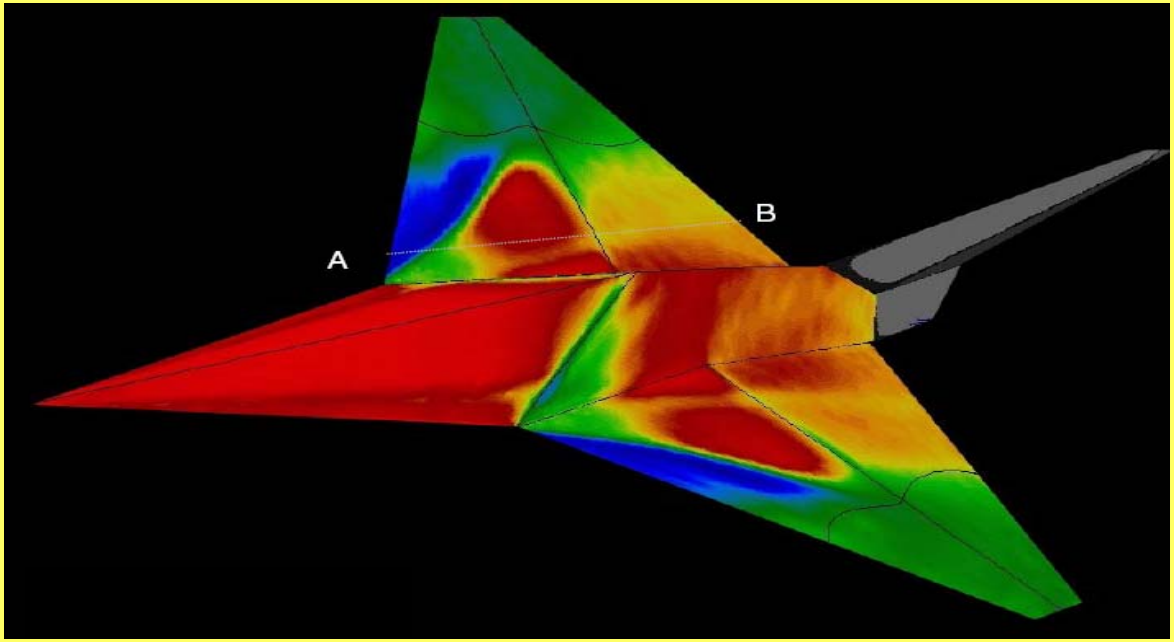
Temperature-Sensitive Paints (TSPs)

*** a luminescent paint composed of a metal-ligand dye and a polymer binder**

*** deposited on the object of interest (skin, metal, spacecraft)**

Refs.: (a) **Luminescent Europium(III) Nanoparticles for Sensing and Imaging of Temperature.** H. Peng et al.; *Adv. Mat.* (**2010**), *22*, 716.

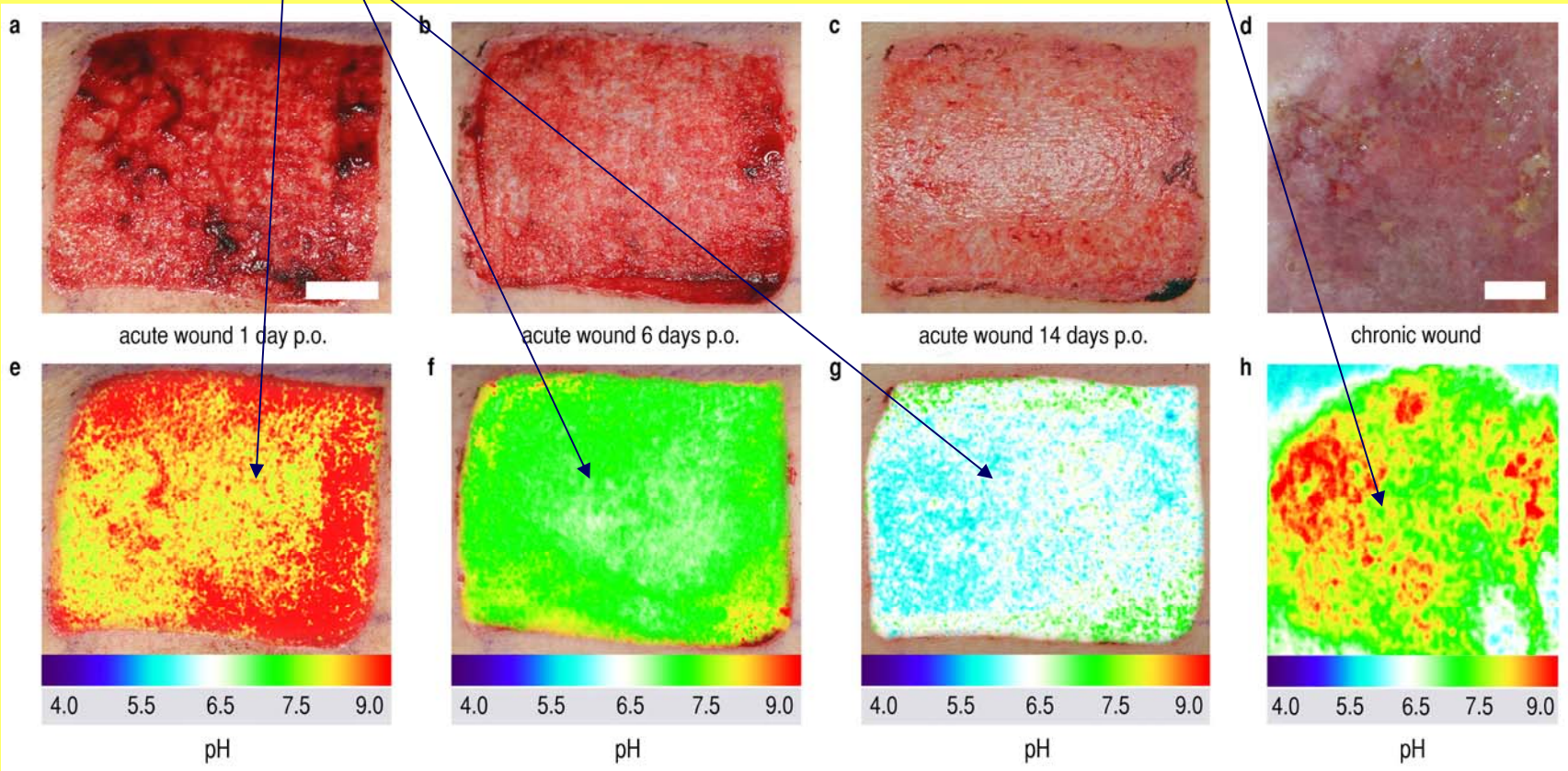
(b) **Temperature-Sensitive Luminescent Nanoparticles and Sensor Films Based on a Terbium(III) Complex Probe**. L. Sun et al.; *J. Phys. Chem. C* (**2010**), *114*, 12642;



(c) **Red and Green Emitting Iridium(III) Complexes for a Dual Barometric and Temperature Sensitive Paint.** L. H. Fischer et al.; *Chemistry – Eur. J.* (**2009**), *15*, 10857

Fluorescent Sensor Layers for Imaging of pH Values

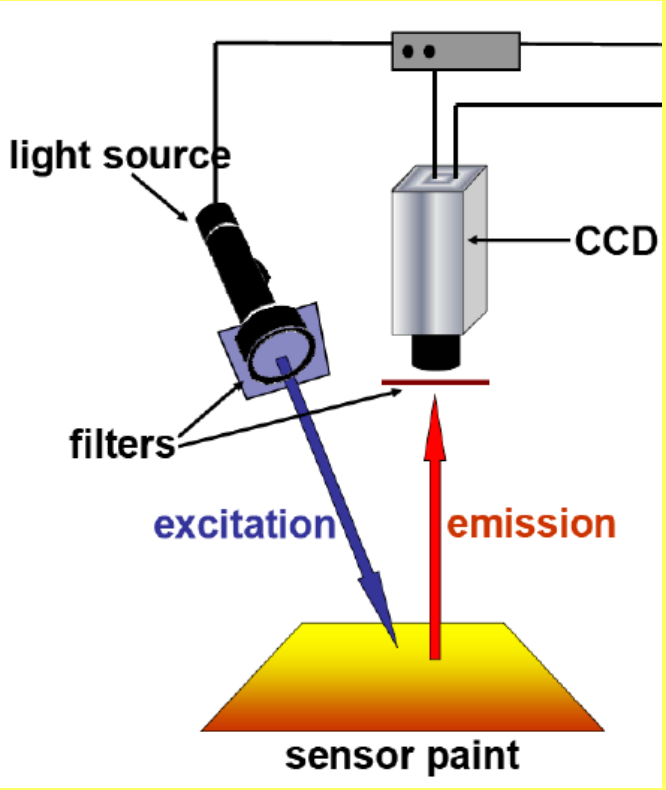
Visualization of pH in Wounds of Patients Using a pH-Responsive Sensor Layer: Recovery of Wound pH (and comparison to chronic wound pH)



Two-Dimensional Luminescence Imaging of pH In Vivo. S. Schreml et al., *Proc. Natl. Acad. Sci* (2011) *108*, 2432

Making Imaging More and More Simple

Small is beautiful and – usually – more intelligent!



2005: CCD based imager (36 k€)

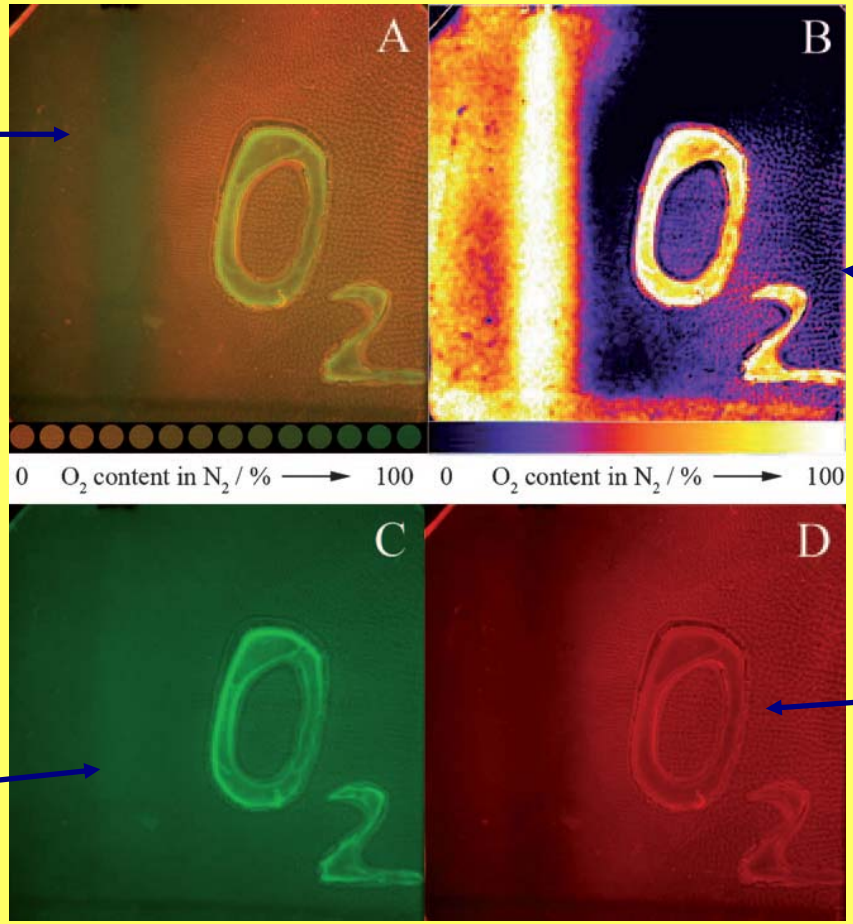
2009: First portable imager (12 k€)

2011: Camera with ring of purple LEDs (380 €)

Photographing Oxygen Using a Sensor Film

Uses two dyes; makes use of the fact that each digital camera is based on the RGB technique:

(A) Regular photo



(B) Pseudo color image of oxygen pressure

(signal R/G)

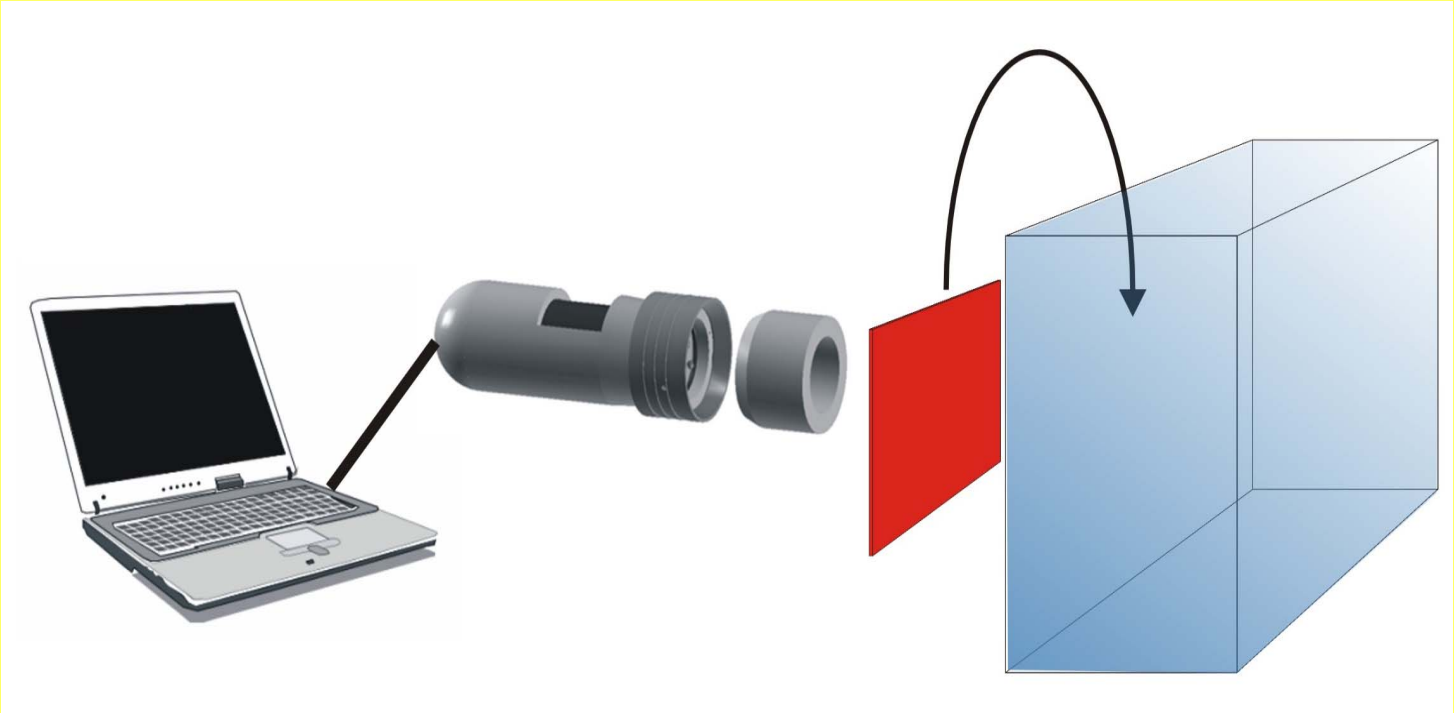
(C) green channel of camera

(D) red channel of camera

Photographing Oxygen. X. Wang et al.; *Angew. Chem. Intl. Ed.* (2010), *49*, 4907

A Dedicated Handheld Imager

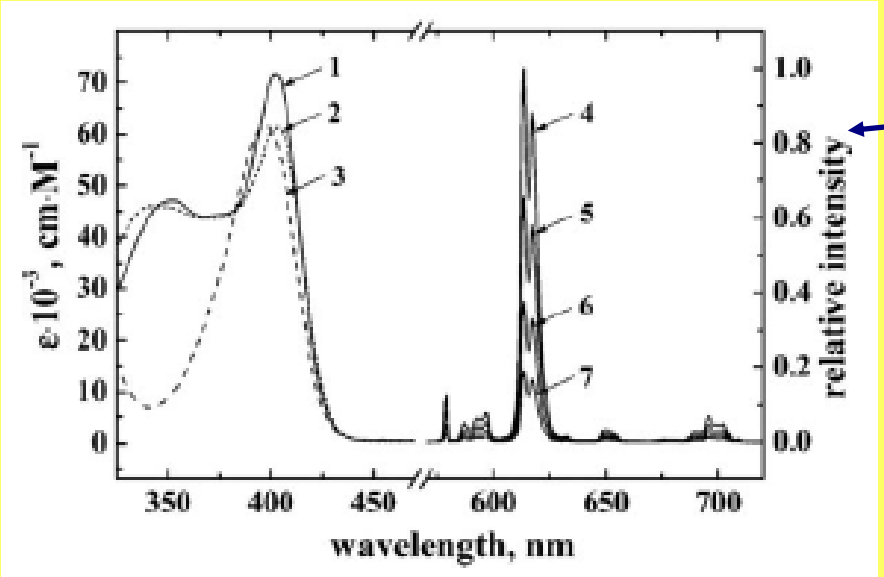
Let us make another experiment, Mr. Fischer!



Quantitative readout possible

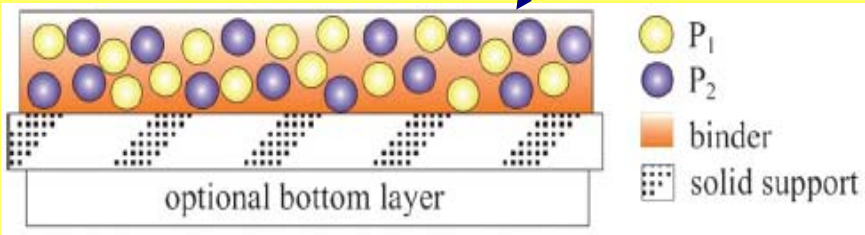
Further Extension: Multiple Sensing

Let us exploit the whole width of the spectrum
(as people do in high-speed data transfer on the internet)



Use 2 or 3 indicator probes with different emission bands

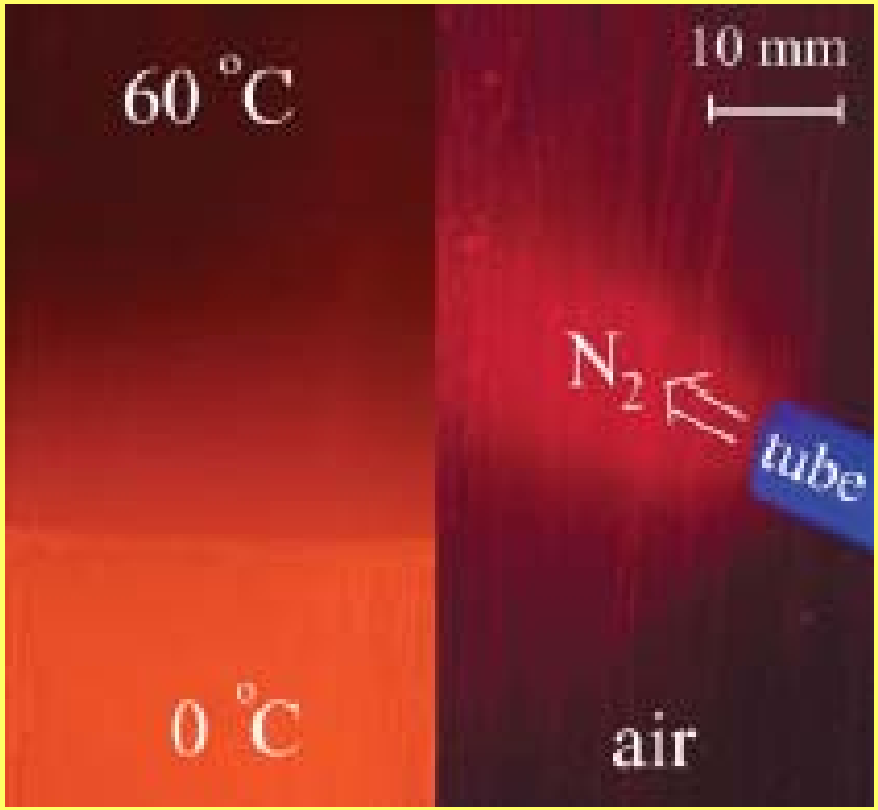
and contained in microbeads



Review: **Multiple Fluorescent Chemical Sensing and Imaging.** M. I. J. Stich, L. H. Fischer, O. S. Wolfbeis; *Chem. Soc. Rev.* (**2010**), *39*, 3102.

Simultaneous Photographing of Oxygen and pH *in-vivo* Using Sensor Films. R. J. Meier et al.; *Angew. Chem.*(**2011**), *50*, 10893.

Simultaneous Sensing of O_2 and Temperature



← Nitrogen simulates low air pressure!

Left: **temperature gradient imaged through a Chroma 580 bandpass filter.**

Right: **oxygen partial pressure imaged through a longpass optical filter**

Dual Paint for PSP and TSP

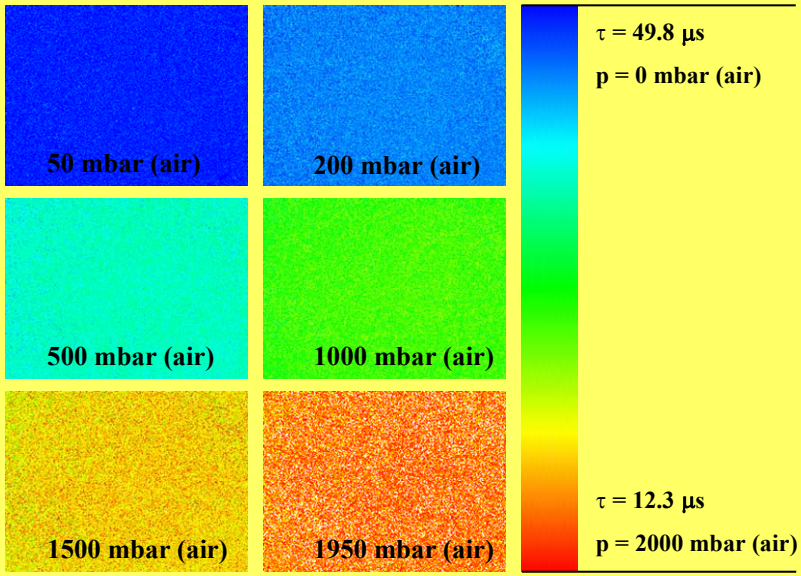
Dual Sensing of *p*O2 and Temperature Using a Water-Based and Sprayable Fluorescent Paint. L. H. Fischer et al.; *Analyst* (**2010**) *135*, 1224

New features:

*** Luminescence lifetime measured rather than intensity**

*** Ecological (water as a solvent)**

Pseudo-color mages of the PSP in the dual sensitive paint at 30 °C and at different air pressures.



Current Activities: Looking into Cells: Nanosensors for Oxygen

Fluorescence often is the only non-destructive means for "seeing" the metabolism of cells, for example to image oxgysen, pH, glucose, ions (Na, K, Ca, Cl) or temperature.

Fortunately, we do have respective fluorescent probes and sensors (after 15 years of research)

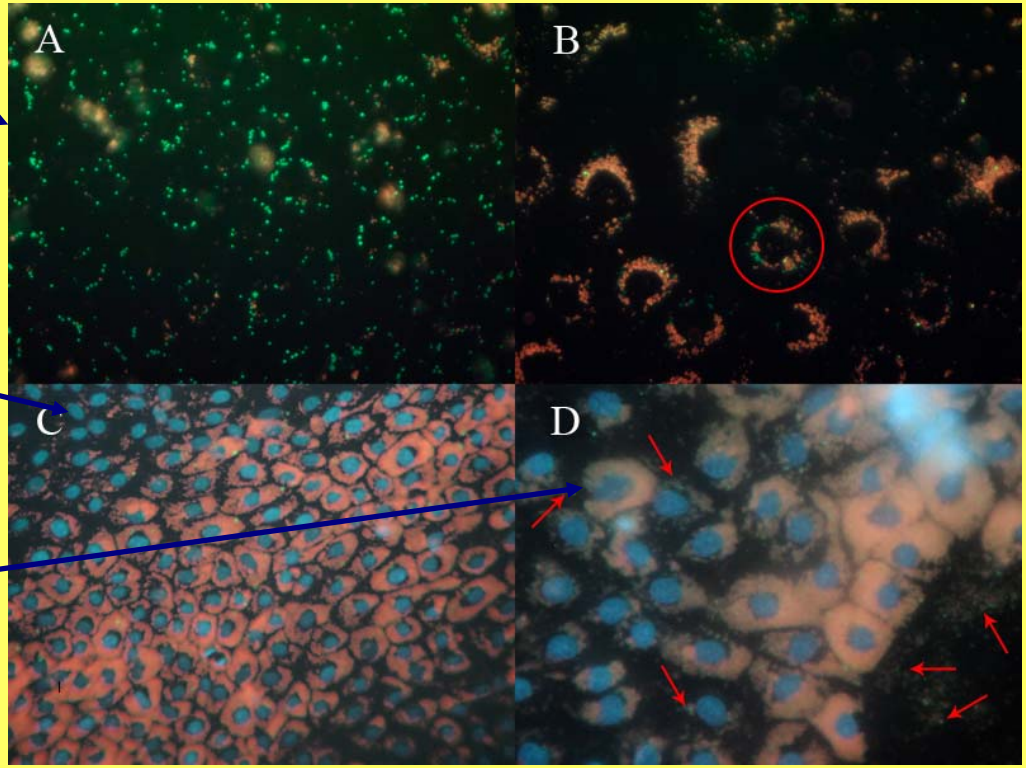
The Oxygenation of Cells

(A) Nanobeads outside the cells; green fluorescence at air saturation; red luminescence quenched by oxygen;

(B) Beads in cells; red luminescence because oxygen is low due to metabolism

(C) Nanobeads taken up by cells; red fluorescence

(D) Membrane disrupted with detergent



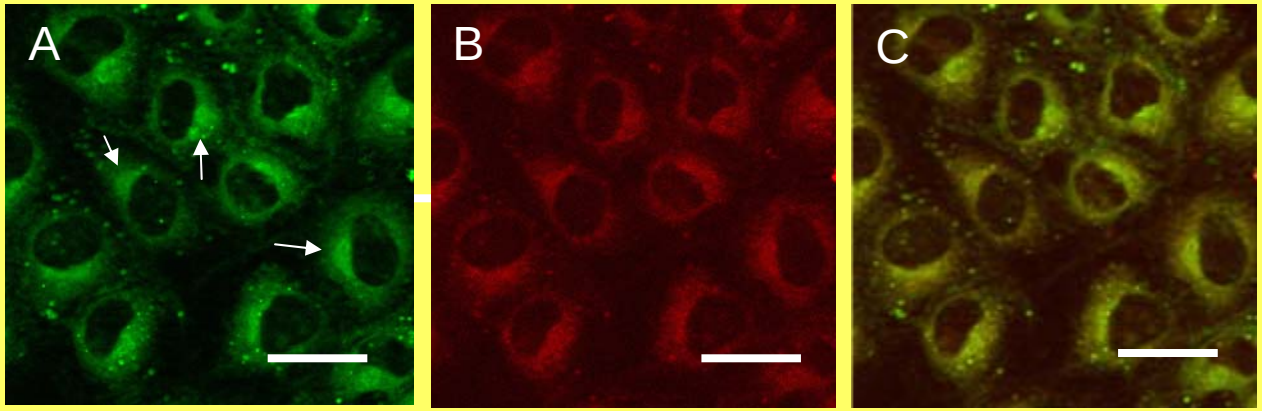
Ref.: **Self-Referenced RGB Colour Imaging of Intracellular Oxygen.**
X. D. Wang et al. ; *Chem. Sci (Cambridge)* (**2011**), *2*, 901

Intracellular Sensing of pH: A look inside a cell

<u>Fluorescent</u> probes and nanosensors are the <u>only</u> means at present to reveal intracellular concentration gradients of (bio)chemical species

Pioneers: R. Kopelman, J. Slavik, and others

A recent example from our group:
Soft nanogel (50 nm) for 2-color sensing of intracellular pH:



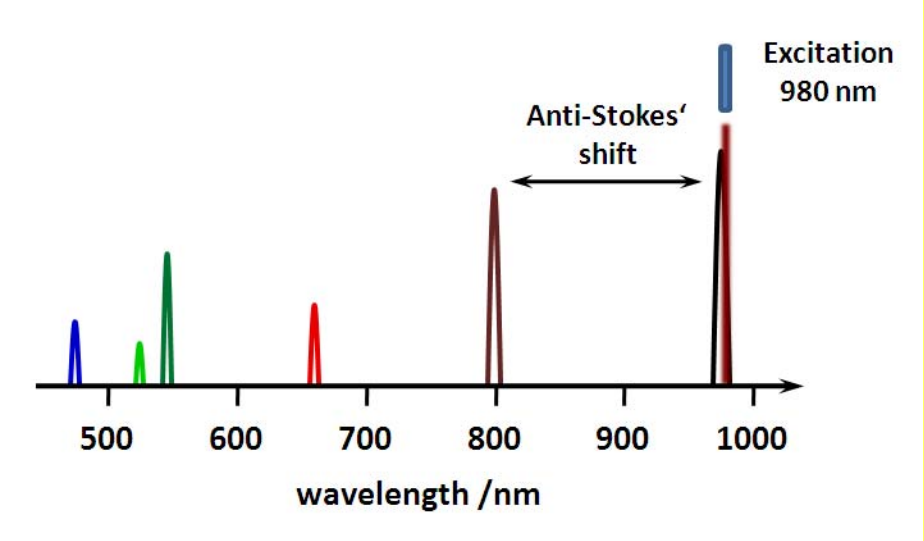
H. Peng et al.; *Angew. Chem.* (2010) *49*, 4246

Upconversion Nanoparticles: Excitation at 980 nm, emission in the visible

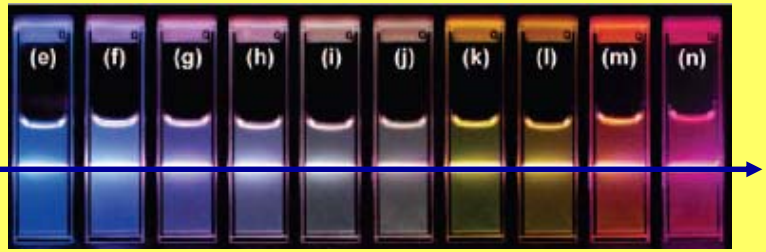
* **Materials:** mostly NaYF4 doped with rare earth ions (Er, Tb, Eu, Yt, Ho)

* **Size:** 15 – 100 nm

* **Surface:** partially oxidic; can be modified or coated with silica



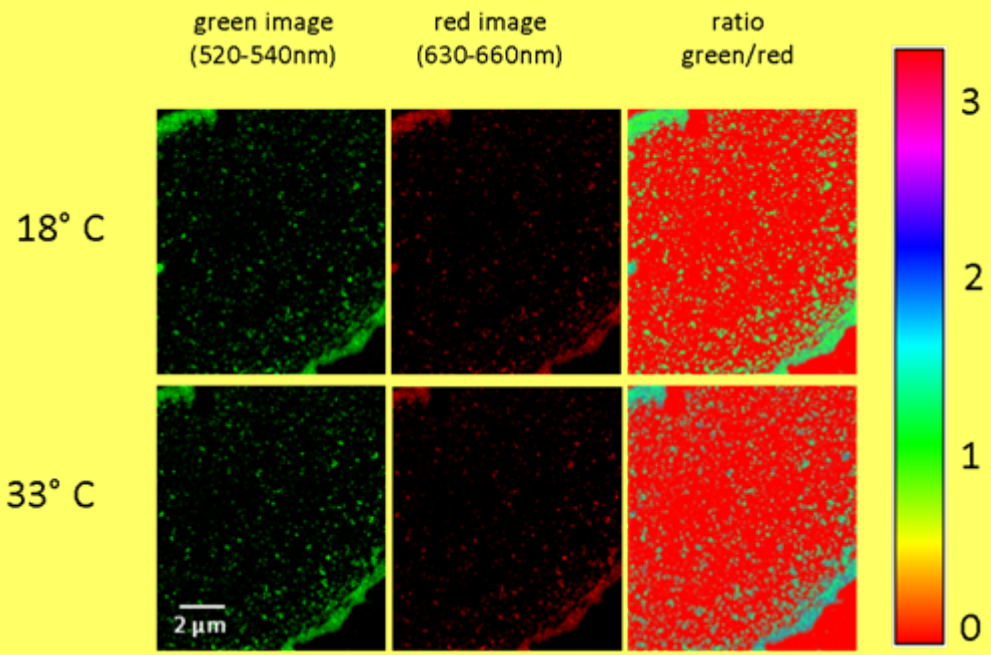
980-nm diode laser

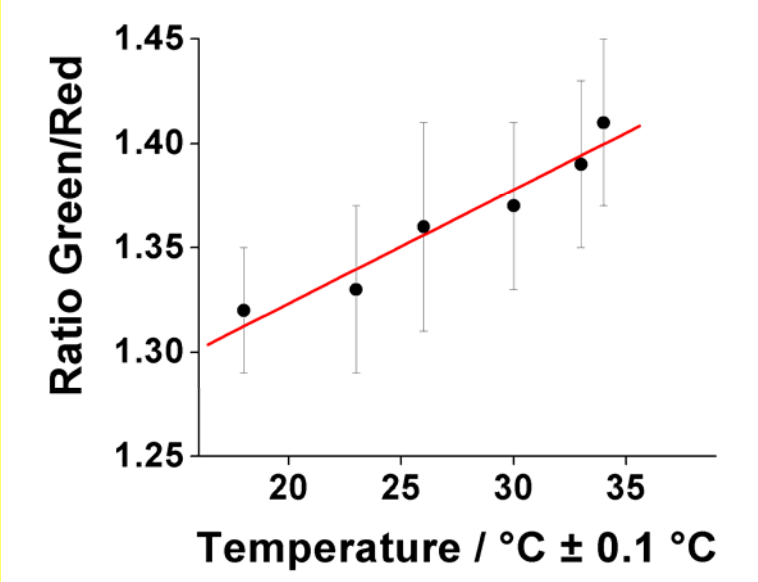


(a) F. Auzel, *Chem. Rev.* 2004, *104*, 139; (b) Upconverting Luminescent Nanoparticles for Use in Bioconjugation and Bioimaging. H. S. Mader, P. Kele, S. M. Saleh, O. S. Wolfbeis; *Curr. Opin.. Chem. Biol.* (**2010**), *14*, 582

Upconversion Nanoparticles: Imaging of Cell "Fever"

Temperature mages of human embryo kidney cells transfected with UCNPs.
Panel gives the green/red ratio in pseudo colors.
The far-right bar reflects the green-to-red ratio, also in pseudo colors.





Upconversion Nanoparticles for Nanoscale Thermometry. L. H. Fischer et al. ; *Angew. Chem. Intl. Ed.* (2011), *50*, 4546 DOI: 10.1002/anie.201006835.

Optical (and Organoleptic) Sensing

can be fun →

but requires

*** smart materials (==> materials chemistry);**
*** smart structures (often on a micro- or nano level);**
*** smart spectroscopies;**
*** smart people (see the picture); and**
*** smart partners (outside the "chemistry fence")**

Enjoy life
(science included)!

and then will lead to results one may not have anticipated when entering the field.