Piezoresistive membrane surface stress sensors for characterization of breath samples of head & neck cancer patients

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http://www.cantileversensors.unibas.ch

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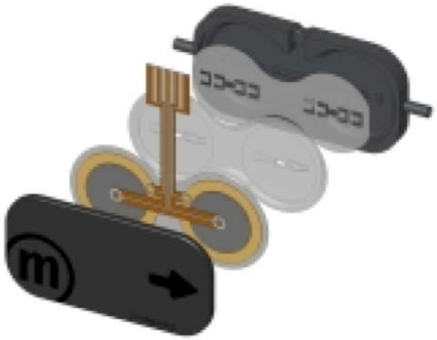
Breath sample test for detection of cancerous condition

- Long time ago, medical doctors tried to detect diseases by examining the breath of a patient

- Here we present a similar strategy based on polymer-coated sensors of an electronic nose.

After the patient has filled the breath sample bag, exhaled air is transported via a piezo actuated micropump to the sensor array.



D. Schmid et al, Eur. J. Nanomedicine **1**, 44 (2008)
H.P. Lang et al. J. Phys (Conf. Series) **61**, 663 (2007)

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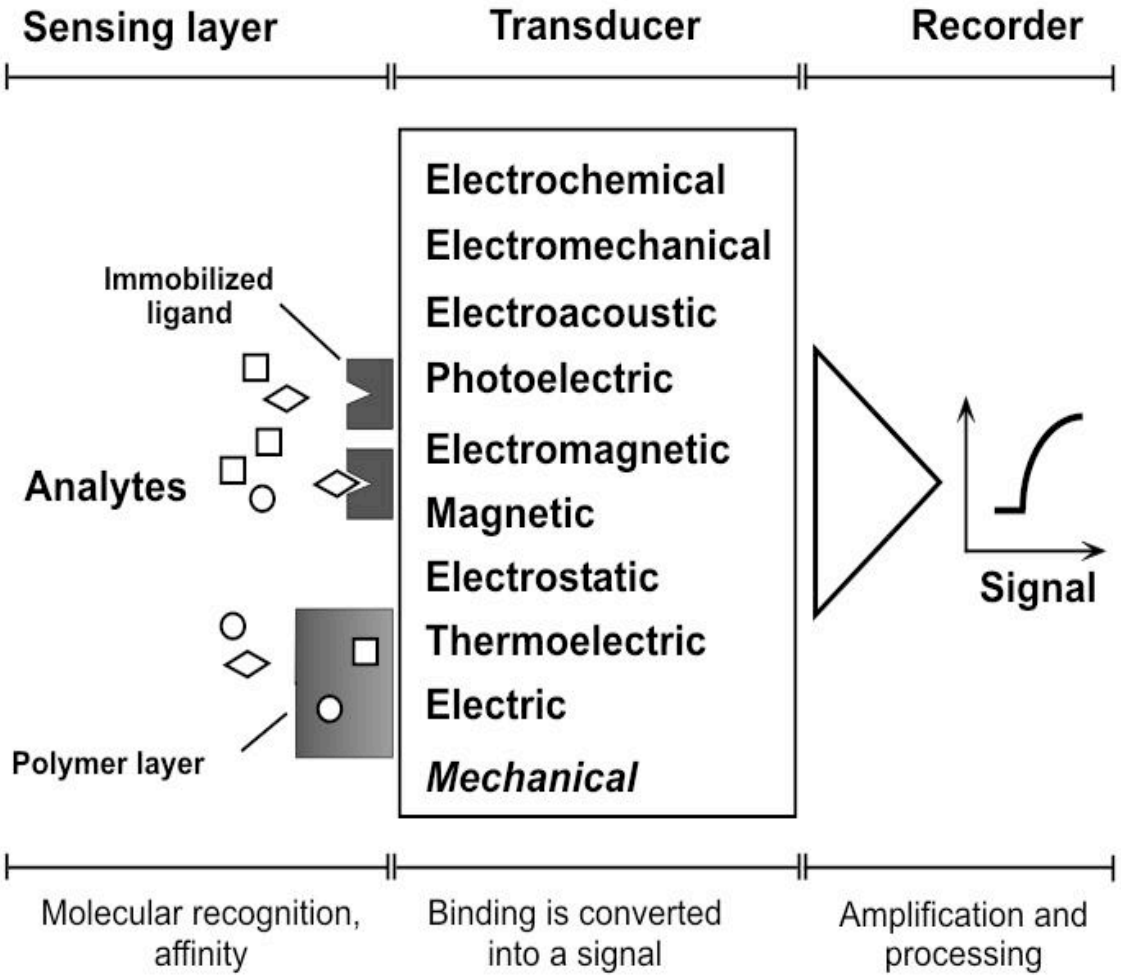
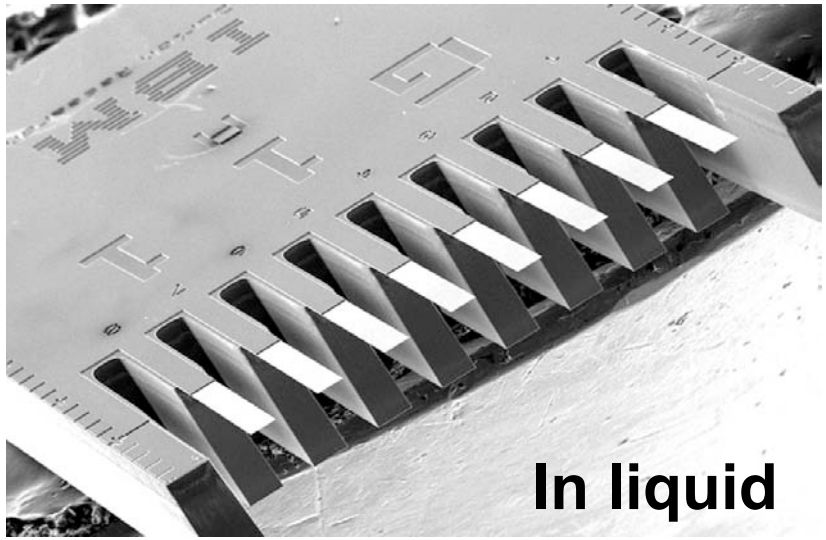
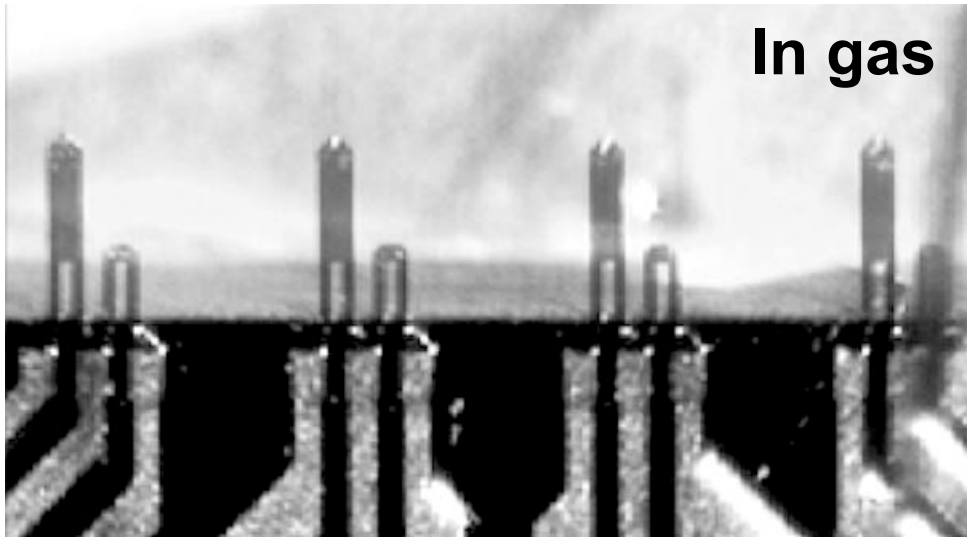
SENSING via MECHANICAL BENDING



Optical sensor readout vs. Piezoresistive readout
SENSING via MECHANICAL BENDING





Beam deflection readout requires
- Laser alignment
- Comparatively large readout device due to optical components
- Non-opaque medium (gas/liquid)

Advantage: Bending in the nm range routinely detected

Piezoresistive readout requires
- NO alignment
- LESS space for readout electronics due to electrical deflection sensing
- Passivation layer in liquids

Disadvantage: lower sensitivity than optical beam deflection

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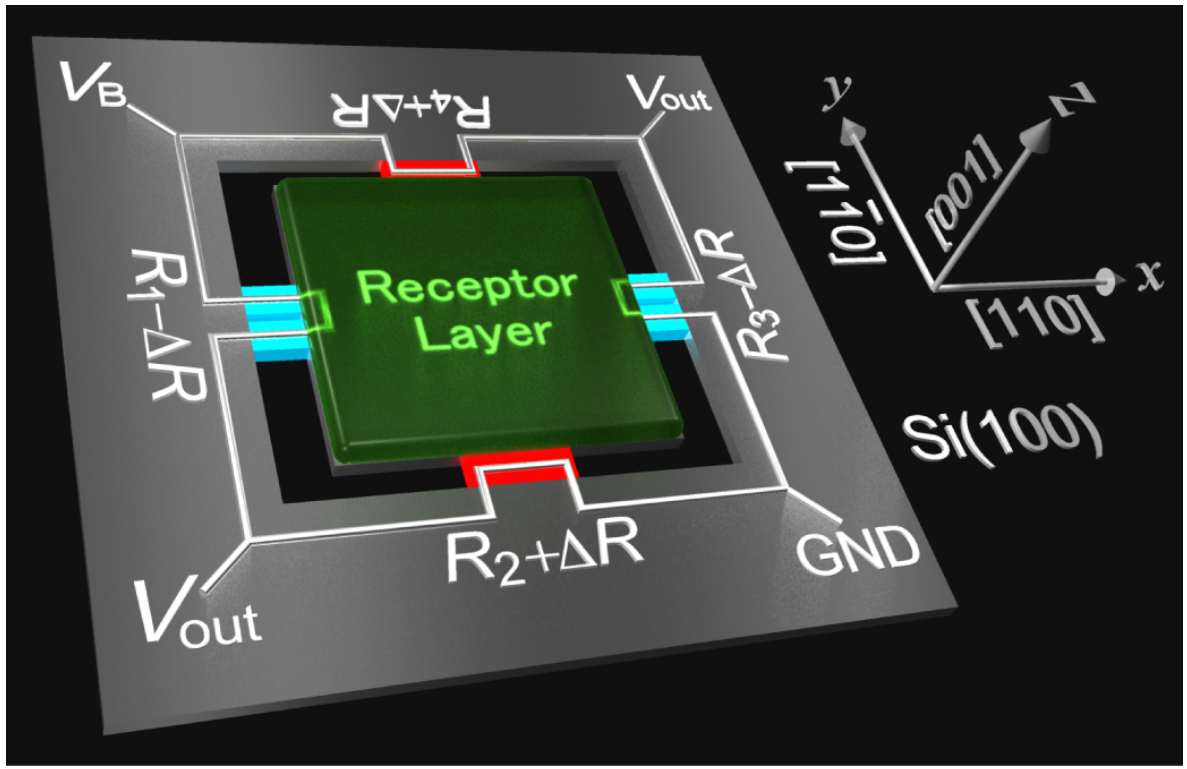
New Concept: M S S
Nanomechanical Membrane Surface-Stress Sensors



FOUR piezoresistive bridges:

4x higher sensitivity than piezoresistive cantilevers

Readout in Full Wheatstone Bridge Circuit

(NIMS-MANA-EPFL-IMT-SAMLAB)

G. Yoshikawa et al, Nano Lett. 11, 1044 (2011)

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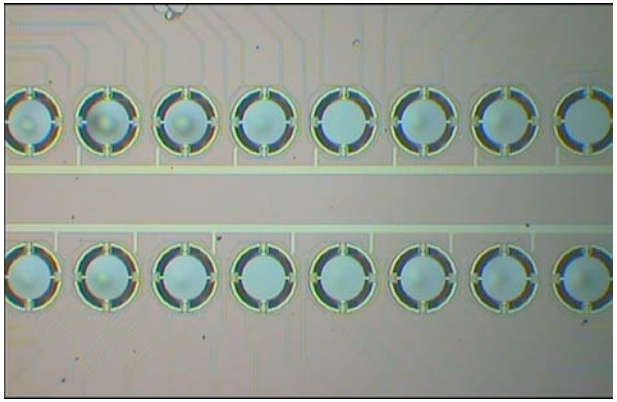
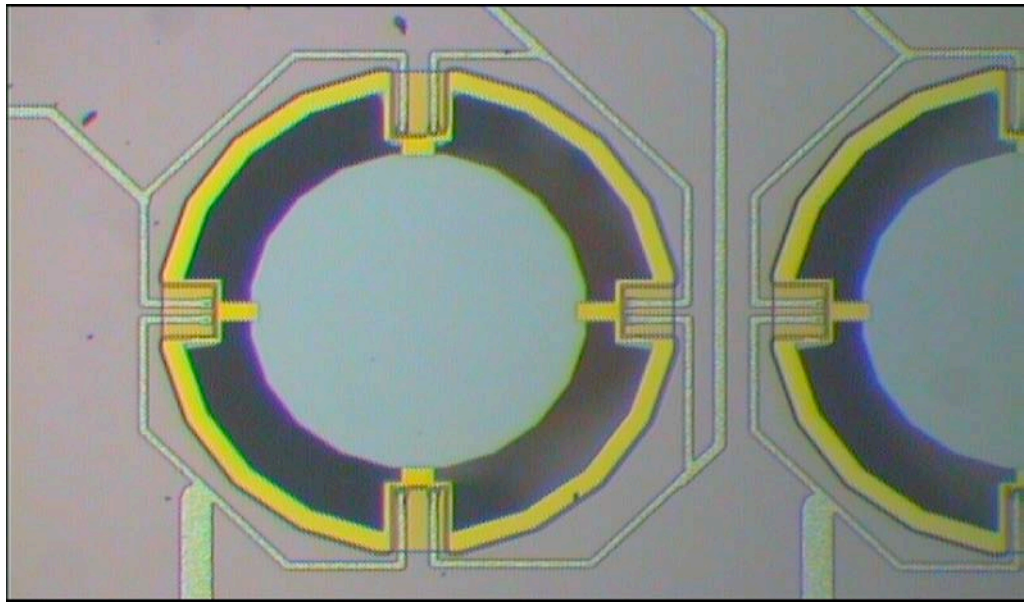
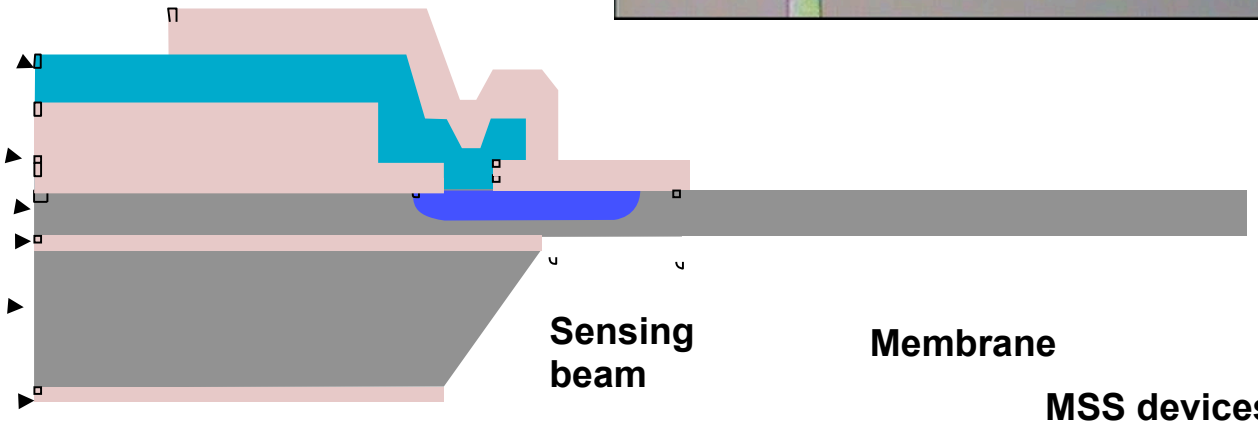
Piezoresistive Membrane Surface-stress Sensors MSS (NIMS-MANA-EPFL-IMT-SAMLAB)

Parallel readout of 8 membranes







MSS devices:
G. Yoshikawa (NIMS-MANA)
S. Gautsch (EPFL-IMT-SAMLAB)

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Coating of Membrane Surface-stress Sensors with polymers by inkjet spotting

Sensitization

Total dispensed amount per MSS: 6 nL polymer solution in water (1mg/mL)

Polymers: CMC, PEO, PEGMEMA, HPC, PAA-AA, PVPy, PIB, PEI

Measurement

Polymer-coated membrane sensor

Swelling of the Polymer layer

Expose to volatile vapor

Forces on piezoresistors

- On exposure to volatile organic compounds (VOCs), the polymer layer swells, producing surface stress and bulging of the membrane
- Presence of VOCs detected in piezoresistive response.

MSS devices: G. Yoshikawa (NIMS-MANA), S. Gautsch (EPFL-IMT-SAMLAB)

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MSS-8
MEMBRANE
SURFACE STRESS
8 - SENSOR SYSTEM
UNI
BASEL
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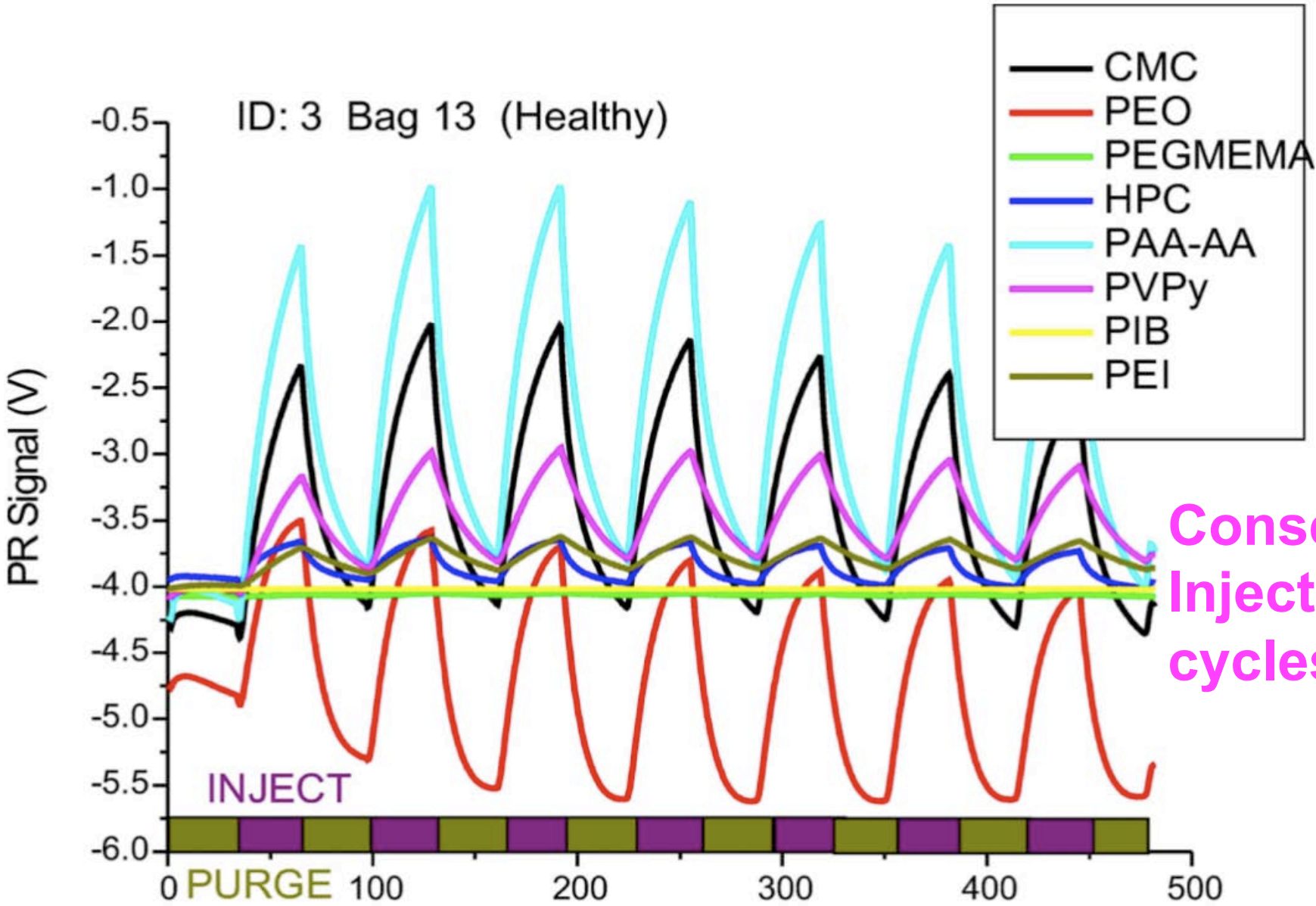
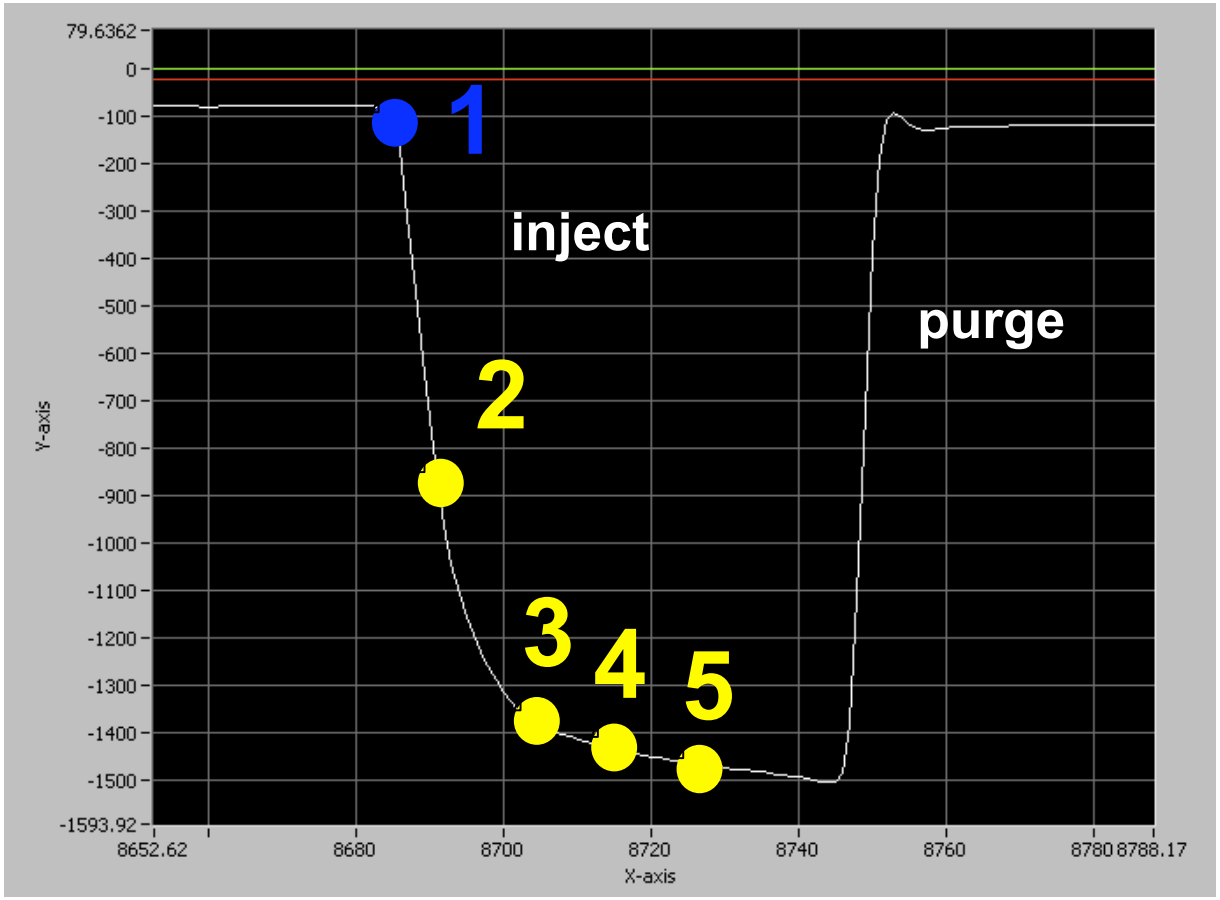
PURGING
INJECTING
PUMP
+5V USB
OFF
ON
40
80
120
160
200
240
PURGE
TIME [s]
INJECT
TIME [s]
:2
x1
x2
:4
x4
TIME FACTOR
USB



Consecutive Inject – purge cycles

Difference response extraction



Diff.

2 – 1

3 – 1

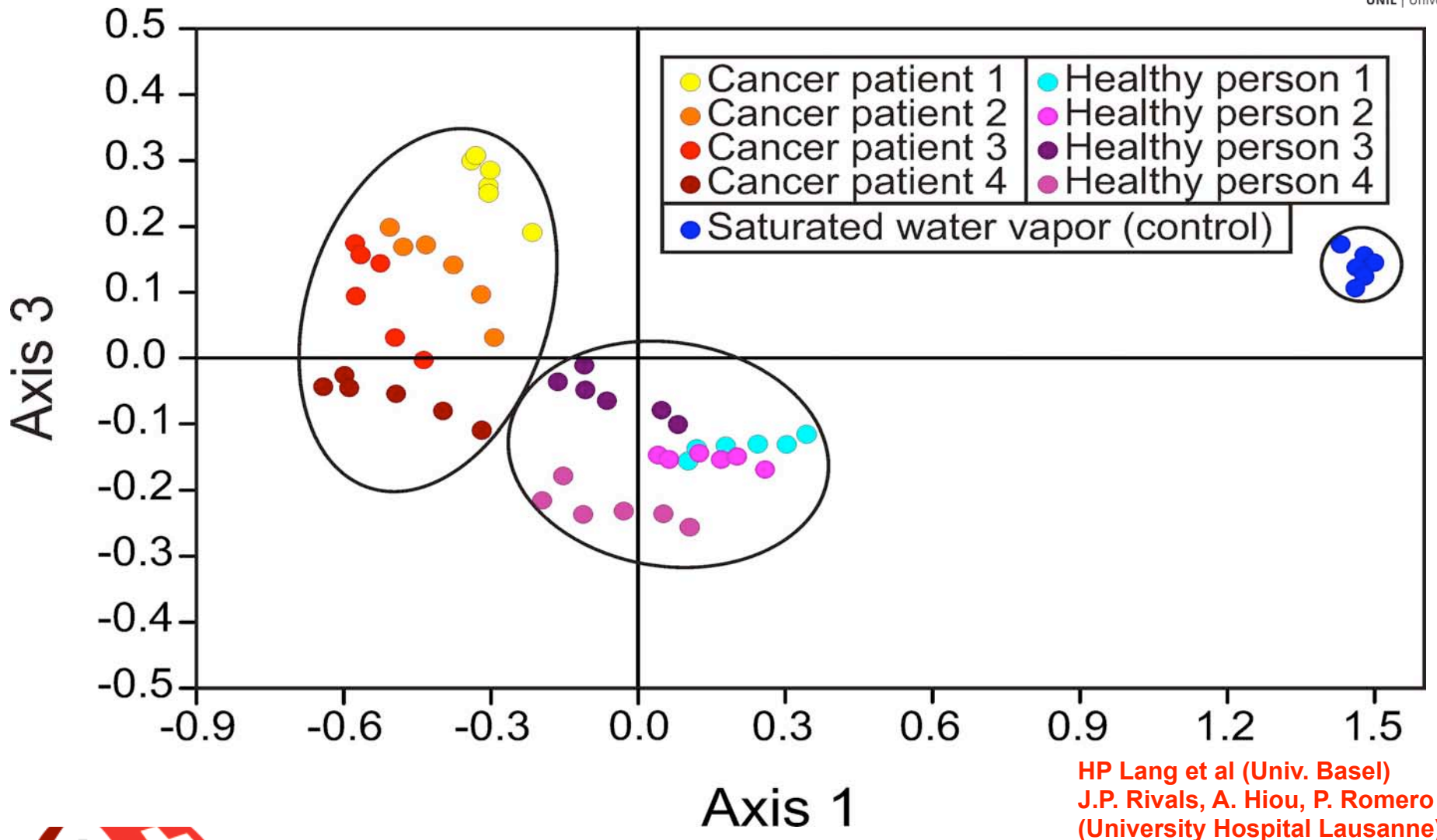
4 – 1

5 – 1

Drift compen-sation

Feed response differences for 8 sensors to Principal Component Analysis Software (PCA) for projection from higher-dim. data space into 2 dimensions

Detection of Head & Neck Cancer in Patients‘ Breath



HP Lang et al (Univ. Basel)
J.P. Rivals, A. Hiou, P. Romero
(University Hospital Lausanne)

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Clinical Study: Head & Neck Cancer

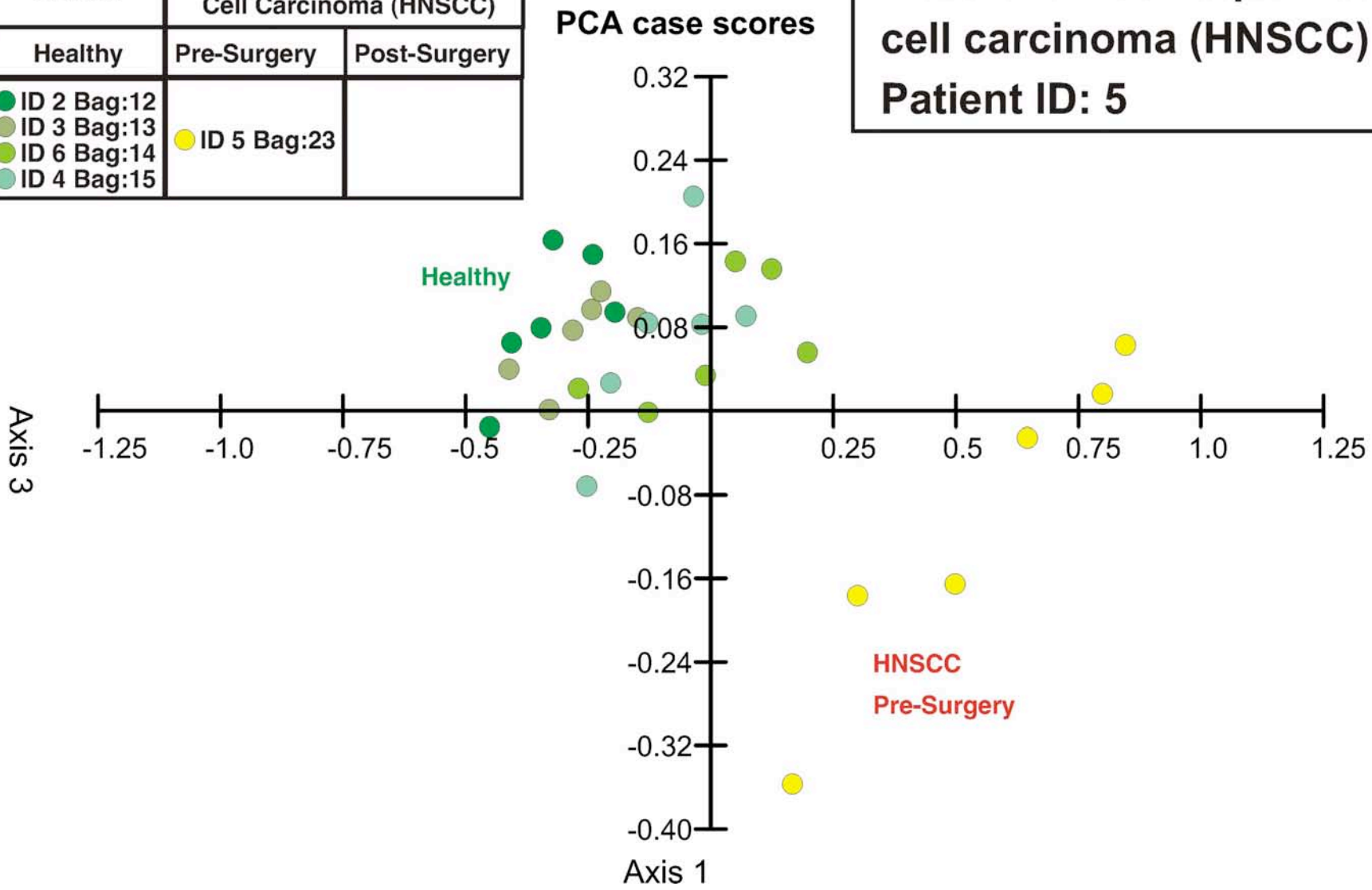
Head & Neck Cancer is a type of cancer that can be completely removed by surgery provided no metastases are present.

The study comprises:

- **patients before surgery treatment,**
- **patients 2 weeks after surgery treatment (cancerous tissue is removed)**
- **Healthy donors**

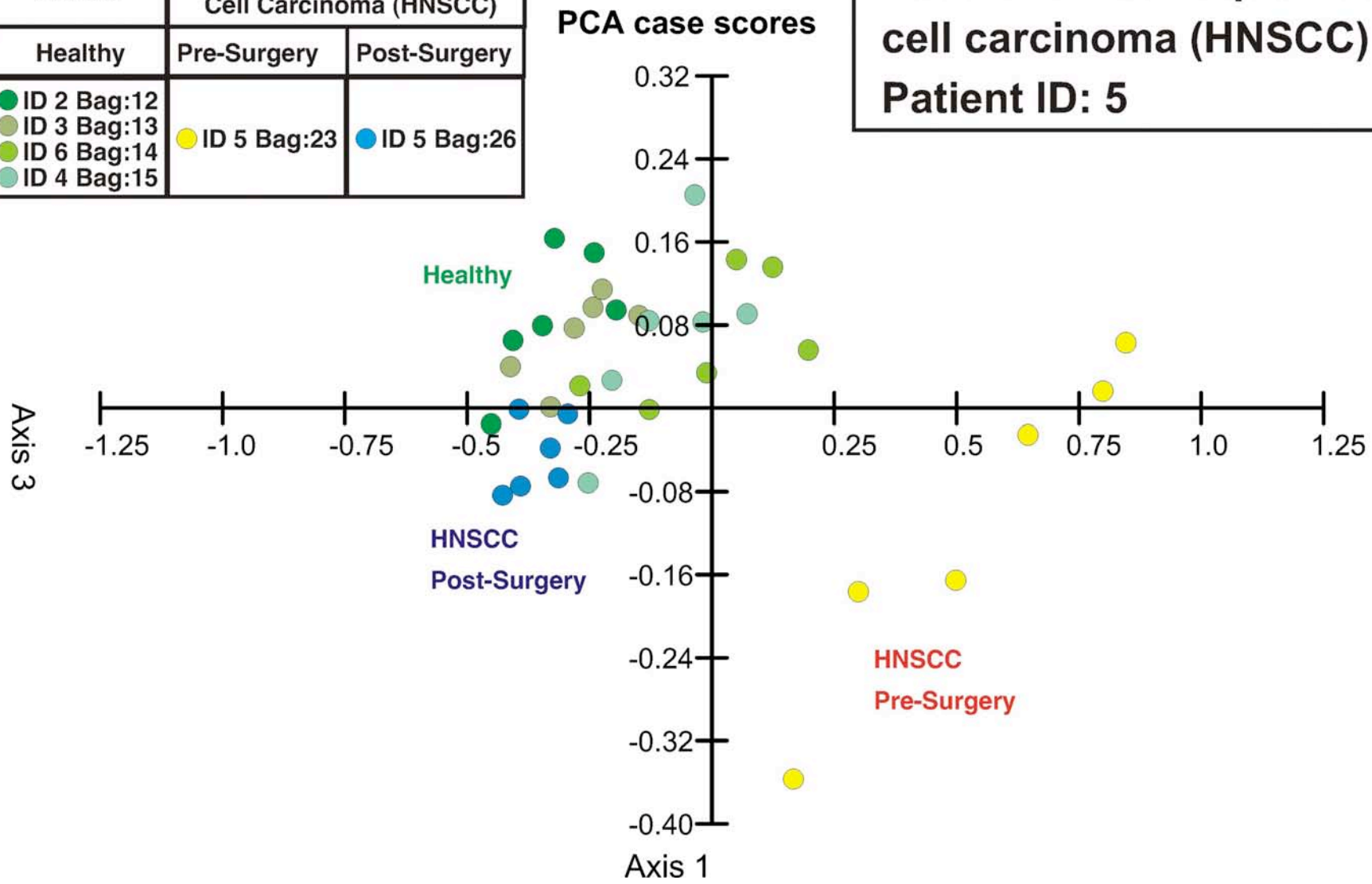
Control	Head and neck squamous Cell Carcinoma (HNSCC)	
Healthy	Pre-Surgery	Post-Surgery
ID 2 Bag:12 ID 3 Bag:13 ID 6 Bag:14 ID 4 Bag:15	ID 5 Bag:23	

Head and neck squamous cell carcinoma (HNSCC)
Patient ID: 5



Control	Head and neck squamous Cell Carcinoma (HNSCC)	
Healthy	Pre-Surgery	Post-Surgery
ID 2 Bag:12 ID 3 Bag:13 ID 6 Bag:14 ID 4 Bag:15	ID 5 Bag:23	ID 5 Bag:26

Head and neck squamous cell carcinoma (HNSCC)
Patient ID: 5



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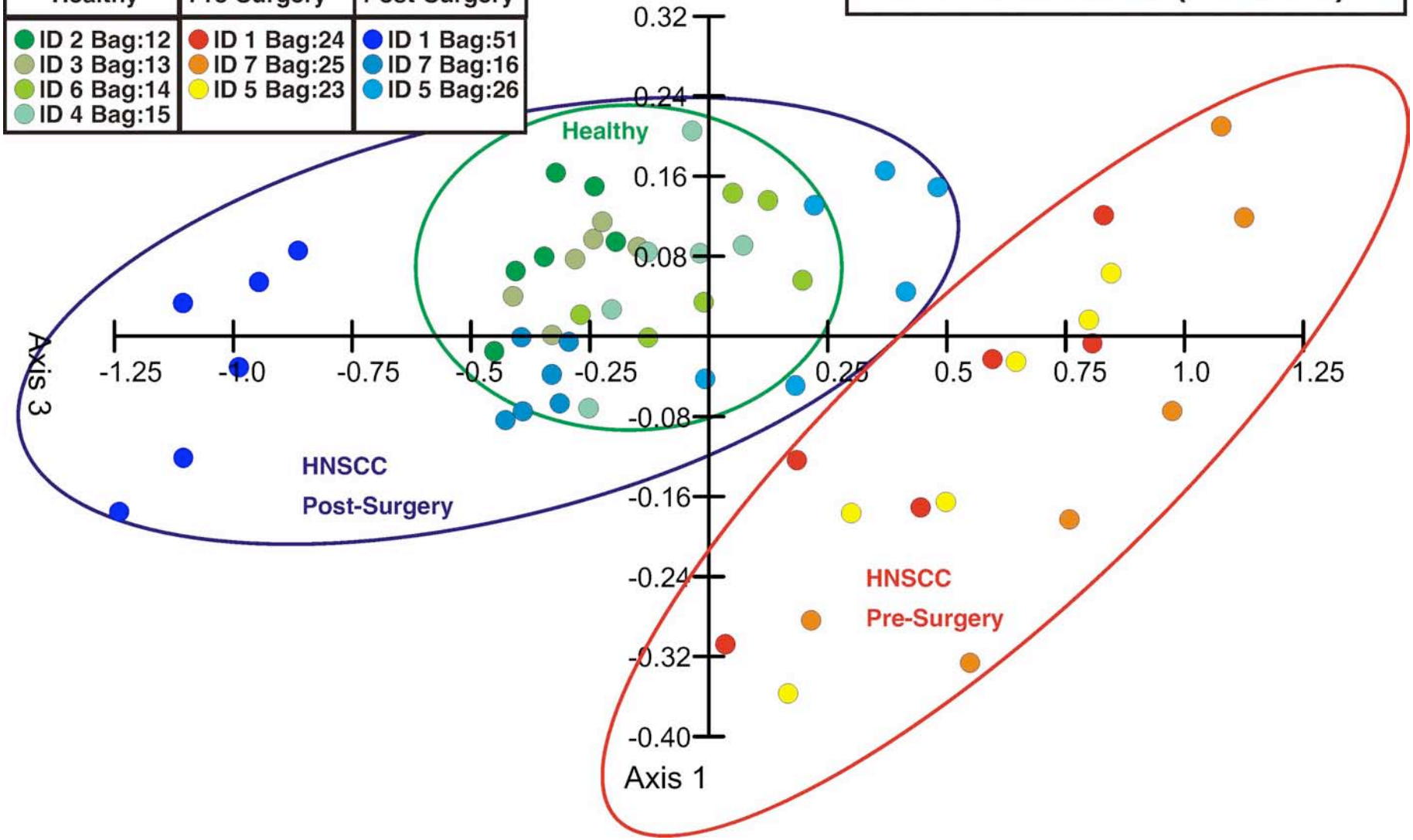
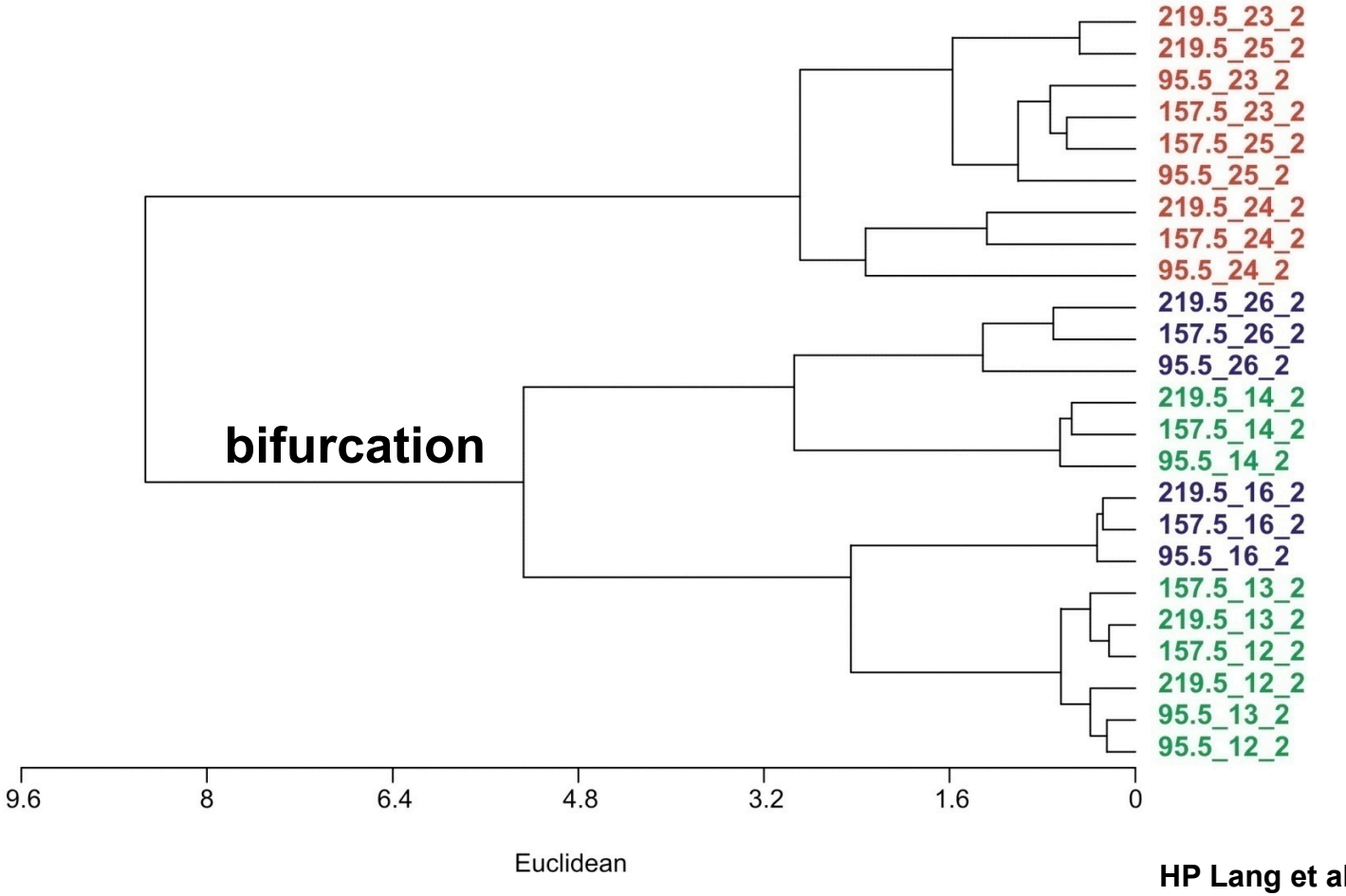
Control	Head and neck squamous Cell Carcinoma (HNSCC)	
Healthy	Pre-Surgery	Post-Surgery
ID 2 Bag:12 ID 3 Bag:13 ID 6 Bag:14 ID 4 Bag:15	ID 1 Bag:24 ID 7 Bag:25 ID 5 Bag:23	ID 1 Bag:51 ID 7 Bag:16 ID 5 Bag:26



Cluster Analysis

Unweighted Pair Group Method with Arithmetic Mean (UPGMA)



cancer

cured

healthy

cured

healthy

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Conclusion

→ By investigating patients‘ breath samples, head & neck cancer patients can be identified using an electronic nose in a non-invasive way.

→ The success of surgery treatment can be monitored

→ Extension to other diseases of the respiratory tract possible