Artificial nutrition monitoring through an optofluidic platform

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ABSTRACT: Parenteral artificial nutrition (PAN) is a lifesaving treatment for a large population of patients affected by different diseases, who are unable to feed themselves naturally. It consists of intravenous injection of nutritive fluids by means of infusion pumps. Wrong PAN solutions are, unfortunately, often administered, thus threatening the patients' well-being. Here, we report an optofluidic label-free sensor that can distinguish PAN solutions on the basis of their volumetric refractive index (RI) by measuring the laser beam displacement. Moreover, the sensing platform allows the detection of air bubbles that could generate along the fluidic path leading to embolism.

In the experimental configuration, the radiation provided by a red laser diode impinges obliquely the flat surface of a plastic cuvette containing the fluid under test. After being reflected by a mirror glued onto the back side of the cuvette, thus after crossing the channel of the cuvette twice, the radiation exits the cuvette in different positions when fluids with different refractive index fill its channel, according to Snell law, and it finally reaches the active surface of a position sensitive detector (PSD). We retrieved the position of the output light beam onto the PSD as $p_{PSD} = L/2 \times (V_1 - V_2)/(V_1 + V_2)$, where L is the length of the active surface, V_1 and V_2 are the voltage output signals, proportional to the photocurrents I_1 and I_2 generated at the extremities of the sensitive area. The output signals provided by the PSD are visualized in real-time and acquired with an oscilloscope. Data are elaborated in MATLAB environment. We developed a model based on ray optics in MATLAB environment: experimental results were found in good agreement with the simulations provided by the model. We successfully demonstrated the detection of artificial parenteral nutrition fluid with high sensitivity by exploiting a totally remote, non-invasive approach with the use of just a few low-cost optical elements and a biocompatible standard cuvette.

1. The Digital Smart Fluidics project

DSF goal: development of smart biomedical fluidic platforms for hospital and home infusion therapy in the areas

chemotherapy and palliative therapy

hospitalization

artificial nutrition

intensive care

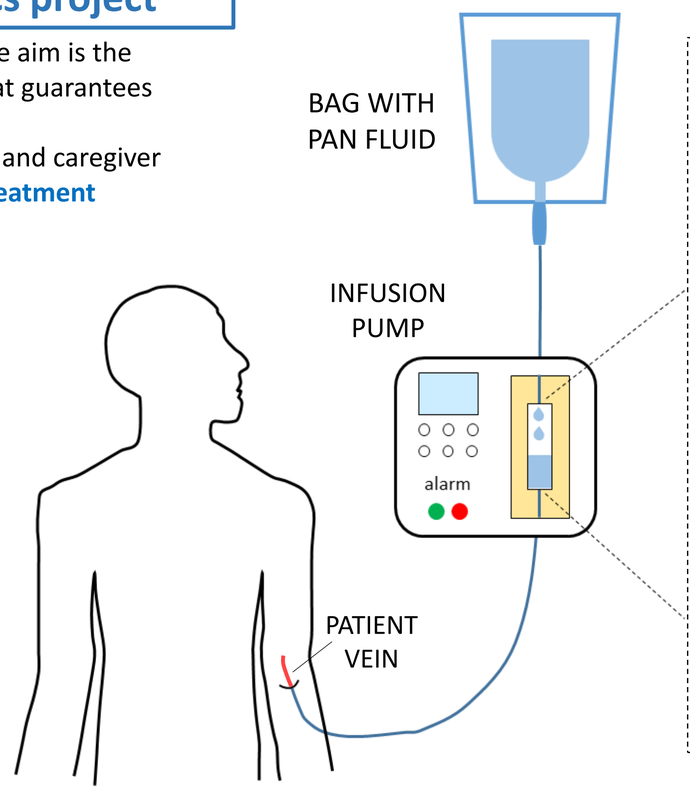
In the field of **artificial nutrition at home**, the aim is the realization of a smart miniaturized device that guarantees

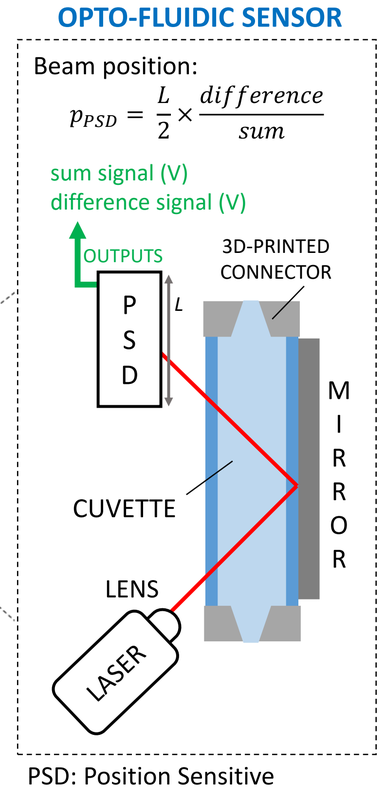
- customized therapies
- effective communication between patient and caregiver
- remote **monitoring of compliance with treatment**
- **safety** of the patient
- **portable** design and rechargeable battery

Hence, we have developed **an opto-fluidic sensing platform for identification** of commercial **mixtures for parenteral artificial nutrition** (PAN) and **detection of air bubbles** that could generate along the fluidic path leading to embolism.

The sensing patform we have developed is:

- based on **contactless**, label-free, **non-invasive** and safe **optical** readout
- **low-cost**
- user-friendly and **easy-to-use**
- **integrable in** drug delivery **pumps** for liquid infusion





PSD: Position Sensitive Detector

2. Fluids for parenteral nutrition

Fluids for Parenteral Artificial Nutrition (PAN fluids) are **transparent mixtures** containing water, glucose, amino acids and electrolytes in variable concentration.

Theoretical predictions of their **refractive index (RI) value** of their refractive index through the formula:

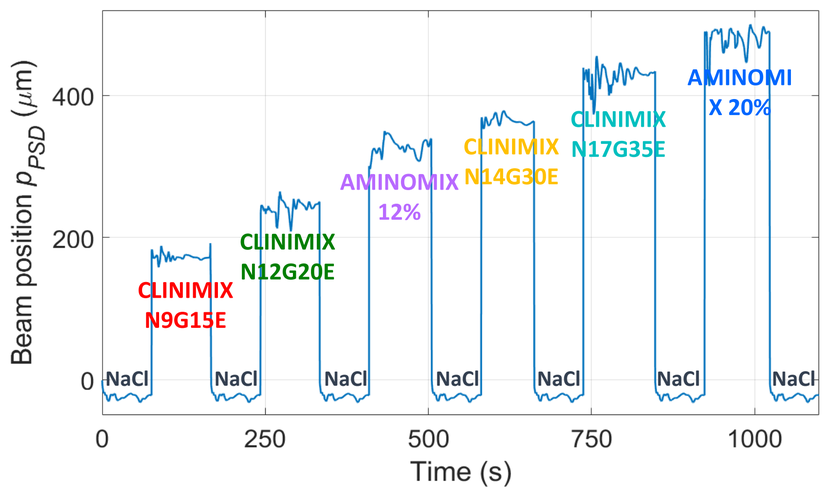
$$n_{PAN\ fluid} = \underbrace{n_{H2O}}_{\text{water contribution}} + \underbrace{\frac{\partial n}{\partial C_{glu}} \cdot C_{glu}}_{\text{glucose contribution}} + \underbrace{\left(\sum_{j=1}^{N_{amino\ tot}} \frac{\partial n}{\partial C_{amino}(j)} \cdot C_{amino}(j) \right)}_{\text{amino acids contribution}} + \underbrace{\left(\sum_{k=1}^{N_{el\ tot}} \frac{\partial n}{\partial C_{el}(k)} \cdot C_{el}(k) \right)}_{\text{electrolytes contribution}}$$

PAN fluid	Theoretical $n_{PAN\ fluid}$ (RIU) @670 nm	Theoretical $n_{PAN\ fluid}$ (RIU) @589 nm	Measured $n_{PAN\ fluid}$ (RIU) @589 nm
CLINIMIX N9G15E	1.3488	1.3503	1.3497
CLINIMIX N12G20E	1.3538	1.3624	1.3608
AMINOMIX 12%	1.3593	1.3689	1.3681
CLINIMIX N14G30E	1.3623	1.3640	1.3633
CLINIMIX N17G35E	1.3673	1.3554	1.3548
AMINOMIX 20%	1.3707	1.3738	1.3720

Examples of commercial bags containing PAN mixtures

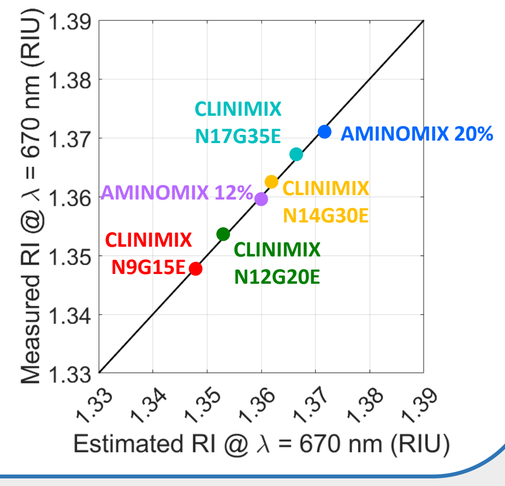
PAN fluids can be distinguished on the basis of their refractive index

3. Identification of PAN fluids



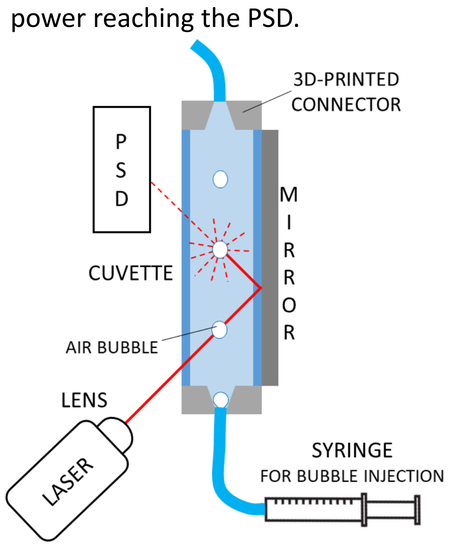
To simulate a realistic situation where the sensing platform is initially calibrated using a reference fluid, **experimental measurements** were carried out by first flowing in the cuvette physiological solution and then the PAN fluids.

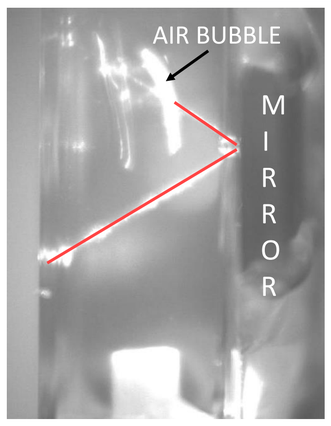
The opto-fluidic sensor can distinguish every PAN mixture from all the others. Moreover, the value of their RI can be successfully retrieved.



4. Detection of air bubbles

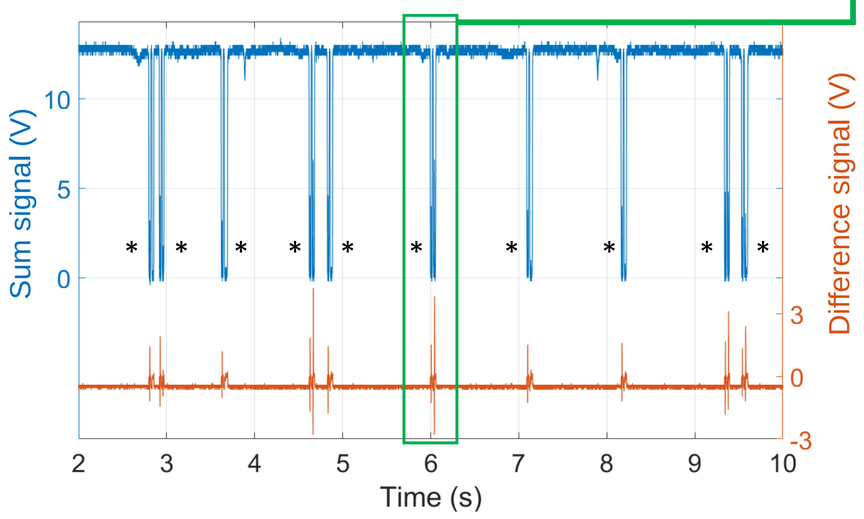
Detection of **air bubbles** is based on the fact that each bubble crossing the cuvette interrupts the laser beam twice, causing **light scattering** and hence a strong reduction of the optical power reaching the PSD.

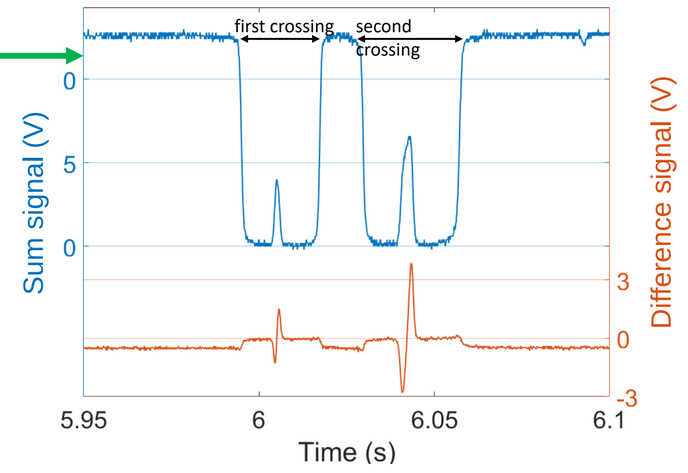




Picture of a bubble crossing the cuvette acquired with a CMOS camera.
It is clearly recognizable the air bubble intercepting and interrupting the reflected laser beam.

During experiments, air bubbles were generated in a controlled manner. The graph below clearly shows the **identification and counting** of 10 air bubbles. Each bubble generate a well-defined and highly repeatable shape in the signal detected by the PSD.





By looking at the signals generated by the passage of single bubble, it is possible to identify a **characteristics double-spike fingerprint** due to the double crossing of the laser beam by the bubble.

References

[1] V. Bello, E. Bodo, R. Calvaruso, F. Nicollini, S. Merlo, "Refractive index sensing in microfluidic channels with integrated reflectors by measuring light spot displacement," *IEEE Transaction on Instrumentation and Measurements*, 2022.
[2] V. Bello, E. Bodo and S. Merlo, "Optical identification of parenteral nutrition exploiting refractive index sensing," *Sensors*, 2022.
[3] V. Bello, E. Bodo and S. Merlo, "Optical multi-parameter measuring system for and air bubble recognition," *Sensors*, 2023.