**Reply to Reviewer 1**

The authors would like to thank the reviewer for the positive feedback and for the constructive questions and suggestions.

The reviewer commented that “the manuscript failed in explaining how the sensor is interesting for the user.” The authors are strongly convinced that the sensor is extremely interesting because it measures oxygen and temperature without a separate sensor (or an additional indicator) to measure the temperature. The measurement of the temperature it is a perhaps trivial problem from the point of view of the physics or technology, but it remains a practical challenge. Any sensor mounted on the housing of any sensor will always measure the temperature of the housing, which is never the temperature of the indicator. The determination of the temperature is a well-known source of error for luminescence quenching based sensors.

The question of the calibration is a legitimate one. Since the parameters of the neural network model are specific of the spot, when substituting it with a new unknown one, an adjustment to the network is most certainly needed. TRANSFER LEARNING

* Modify text?

The method can most certainly used for real-time sensing. Once the network has been trained, the output (in our case the oxygen concentration and the temperature from the phase shift) is instantaneous.

The reviewer asks about the performance at low oxygen concentration. The most relevant limiting factors for low concentrations are the sensitivity of the indicator, the experimental error on the measurement of the concentration during the acquisition of the data for the training. The spot used in this work (Pt-TFPP) is specified from the manufacturer to have a limit of detection of 0.03%. However, for concentrations below 0.5-1% air (saturation) or equivalently 0.1-0.2% O2 we would recommend another indicator with higher sensitivity in the lower range (for example Pd-TFPP). The method described here is however independent of the sensor used. Similarly, the limiting range of the method is mainly due to the dynamical range of the indicator or spot itself.

The reviewer mentions the paper <https://doi.org/10.1021/acssensors.9b02512>. A reference to the paper was added in an introduction as an example on how, by measuring multiple quantities (specifically the apparent lifetime and an intensity ratio) it is possible to perform dual sensing with one indicator. The approach is similar to what discussed by O.S. Wolfbeis, SPIE, Vol 1368 (1990), also added as a reference. The paper, although very interesting since proposing an ingenious material, clearly shows 1) you need two measure two physical quantities instead of just one as proposed by our approach; 2) the parametrization of the sensor response scales correspondently in complexity (a nonlinear fit of the two equations 3 and 4 is required, with a plethora of temperature dependent coefficients). Our sensor 1) and 2)

Add two references

Please find below the answer to the specific points:

Line 15-16: Within the manuscript, the method is applied to a single indicator and not to a multi-indicator system. Multi-indicator systems are more complex as inherent parameter interactions might occur that are not predicable leading to an error propagation throughout the evaluation procedure. As the method proposed here bases on a single indicator, I doubt whether the method can directly be transferred to a multi-indicator system without any adjustments.

It would be extremely interesting to apply the method to a multi-indicator system. Particularly for complex system, with inherent parameter interaction an approach based on neural networks may solve the difficulties of the parametrization. The author would be thrilled to try the method on a multi-indicator system.

Line 25-27: unclear

Boh

Line 43: Stern-Volmer is not an empirical model and T-dependencies neither.

The Stern-Volmer is not an empirical model but there are other models proposed for oxygen luminescence quenching which are justified only by their ability to fit well the Ster-Volmer non-liner curves. Even the two-site model, according to the fundamental papers proposing (Carraway, E. *et al.* Analytical chemistry 1991, 63, 337–342 and Demas, J.N. *et al.* Analytical Chemistry 1995, 67, 1377–1380) finds part of its justification in its ability to fit experimental observations: “Even though the two-site model may be chemically incorrect, it is excellent for fitting intensity-quenching curves”.

The temperature dependence of the sensor response depends not only on the properties of the indicator (which may be described by an Arrenius-type dependence) but also on how it is immobilized and on the chemical matrix used. Therefore, in practice the sensor-specific temperature dependence needs a parametrization (frequently with exponential functions) which is determined empirically.

Linear 51: the manuscript describes a new approach on data evaluation not a new sensor.

Line 66-68: Are all parameter-dependencies and especially all sensor-specific response characteristics learnable? What about the photo-degradation over time? Is it something the method might be able to compensate?

This work shows that all parameter-dependencies and especially all sensor-specific response characteristics are learnable.

The photo-degradation affects the phase shift and with time it is to be expected, that the photo-degradation will reduce the accuracy of this sensor just as every other sensor. It could be taken into account for by a specific training. BOH? E’ una buona domanda.

Line 72: Even though decay time-based approaches are more robust, might it be possible to use also an intensity-based approach?

Yes, this would be possible. The neural network model would have as input normalized intensities.

Line 76: The Temperature dependency depends on the chosen indicator and range. There are multiple systems known where the T-dependency can be described as a linear correlation with a negligible error propagation.

Line 85: What is the expected dynamic (in terms of decay time) of the indicators regarding the oxygen and the temperature dependency?

The dynamic depends entirely on the indicator chosen for the oxygen sensing. A review of indicators for oxygen can be found in Wang, X.d.; Wolfbeis, O.S. Chemical Society Reviews 2014, 43, 3666–3761.

Line 87: Even though the setup was already described somewhere else, it would be great to include it in the SI. Please, add also the reference sensors that are needed to ensure that the target parameters are matched.

The setup was removed after the specific request of the editor. ….

Line 91: Have you experienced any background effects at low modulation frequencies (200Hz)?

We did not experience any background effects at low modulation frequencies.

Line 100: The section 2.3 requires elaboration. It might be nice to get a better understanding on how the data are analyzed. How are the (unknown) sample data analyzed after the training? Maybe you could use one sample as explanation and attach it to the SI. What about the visualization? Can you show how the final matrix pattern, identified by the algorithm, looks like?

Line 104-105: You submit your paper in a sensor journal who might be not familiar with the network architecture. Please, revise this sentence for a reader-oriented outreach and include more information on how the network architecture is supposed to work.

Line 113: Elaborate in more detail, why 32 is the optimal number. How did you optimize the batch size?

According to your literature, a special tuning is needed here.

Line 123: What is the CPU and how many cores are needed? Please, provide concrete information focusing on the facts required here and avoid woolly formulations.

Line 130: Why did you use the mean of the absolute error instead of the residuals?

Line 141: Why did you choose accuracy as the only performance parameter? To my knowledge, the accuracy can be biased and shouldn’t be the only figure of merit, when it comes to describe the performance of an algorithm (http://eecs.wsu.edu/~holder/courses/cse6363/spr04/pubs/Provost98.pdf)

Line 180: Have you thought about reproducibility / calibration-transfer? How is the sensor intended to be used by the user? Does the user have to make the whole calibration by themselves again?

Line 198: Single indicator sensors are unusual for optical chemical sensors? How would the approach perform in multi-layer systems and deal with their inherent indicator-interaction that possibly occur?

The author would be thrilled to try the method on a multi-indicator system. We do not have currently any sensing element with multi elements but would be glad to measure one.

Line 199: A calibration curve of the final matrix would help to understand how the user can then analyze its unknown samples.

Line 200: Please, provide more (concrete) information on the comparison. What is the typical error of commercial sensors? Which sensors did you use for comparison?

A comparison of several commercial fluorescence-based sensors for O2 is reported in the paper Wolfbeis O.S. Bioessays 2015 37: 921–928. The reference was added to the text.

Add reference Wolfbeis 2015

**Reviewer 1**

In principle, the manuscript provides an interesting approach of how to evaluate data and how to deal with interfering parameters. It is definitely worth to follow the concept although there are few sections that need to be elaborated further.

The proposed method sounds like a supervised pattern-recognition algorithm to me, where the underlying correlation between the analyte and the measurement parameter / indicator response is unknown. Scanning over the whole frequency range either the oxygen concentration or the temperature is changed continuously to establish a calibration matrix of the sensor.

First of all, it must be noted that the correlation between the two parameters and the indicator response is one of the best characterized. However, the approach is interesting for other parameter interdependencies and indicator correlations that are still unknown.

Unfortunately, the manuscript failed in explaining how the sensor is interesting for the user. Is the calibration reproducible / transferable or must the user calibrate the sensor each time investing 65 hours for the calibration? How is the procedure to evaluate an unknown sample? Is it possible to apply the method online for real-time sensing? How well would the algorithm perform at low oxygen concentrations and high temperatures or vice versa, meaning on the extrema? What is the dynamic range of the method and the maximal error then?

A similar procedure has already been published using an indicator based on thermally activated delayed fluorescence and should be addressed here (https://doi.org/10.1021/acssensors.9b02512).

Despite all the comments, the approach is an interesting one that has a high potential for other optical sensors, where the correlation is not as well known as it is the case for oxygen and temperature.

Specific comments:

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