

How does the choice of the baseline affect the meaning of the concentration change

Continuous wave NIRS system can measure only relative concentration changes. This note tries to answer the question: "relative to what?"

For a single wavelength the light attenuation in tissue is described with an exponential law. Adding detector noise one can write:

$$I(t) = I_0 \exp\left(-\sum_i^p \epsilon_i c_i(t)L - s\right) + n(t), \quad (1)$$

where $I(t)$ denotes the measured light intensity at the detector at time t , I_0 denotes the constant light intensity emitted into the tissue at the source and ϵ_i is the extinction coefficient of absorber i . The time-dependent concentration of this absorber is given by $c_i(t)$. The index i enumerates p different absorbing substances, e.g. Hb, HbO etc. The path length of the photons is given by L . Furthermore, there are time-independent intensity losses due to scattering, a poor optode-skin coupling etc. which are denoted by s . The noise contribution $n(t)$ accounts for electronic noise and is assumed to be a random number with zero mean.

In this equation both I_0 and s are not accessible through measurements and hence unknown. However, since they are time-independent they can be removed from the problem by considering only intensity changes relative to a reference (or baseline) intensity:

$$I(t)/I_{\text{ref.}}$$

This intensity change corresponds to concentration changes:

$$\Delta c_i(t) = c_i(t) - c_{i,\text{ref}}$$

relative to reference concentrations $c_{i,\text{ref}}$. The concentration changes can be calculated from intensity changes recorded at p different wavelengths by applying the modified Beer-Lambert law. However, this note is concerned with the interpretation of the reference concentration and how it depends on the choice of the reference intensity. For this purpose studying a single wavelength is enough.

1 IDEAL CASE, NO NOISE

In this scenario no detector noise is present ($n(t) = 0$) and the intensity at time t_{ref} is chosen as a reference.

$$I_{\text{ref}} = I(t_{\text{ref}}) \quad (2)$$

$$I(t) = I_0 \exp\left(-\sum_i^p \epsilon_i c_i(t)L - s\right) \quad (3)$$

$$\log I(t) = \log I_0 - s - \sum_i^p \epsilon_i c_i(t)L \quad (4)$$

$$\log\left(\frac{I(t)}{I(t_{\text{ref}})}\right) = \left(\log I_0 - s - \sum_i^p \epsilon_i c_i(t)L\right) - \left(\log I_0 - s - \sum_i^p \epsilon_i c_i(t_{\text{ref}})L\right) \quad (5)$$

$$= -\sum_i^p \epsilon_i (c_i(t) - c_i(t_{\text{ref}}))L \quad (6)$$

$$= -\sum_i^p \epsilon_i \Delta c_i(t)L \quad (7)$$

In this scenario the concentration change of each component is measured relative to the concentration at time t_{ref} , i.e.:

$$\Delta c_i(t) = c_i(t) - c_i(t_{\text{ref}}) \quad (8)$$

$$c_{i,\text{ref}} = c_i(t_{\text{ref}}) \quad (9)$$

2 ADDING NOISE

In this scenario detector noise is present and again the intensity at time t_{ref} is chosen as a reference.

$$I_{\text{ref}} = I(t_{\text{ref}}) \quad (10)$$

$$I(t) = I_0 \exp\left(-\sum_i^p \epsilon_i c_i(t)L - s\right) + n(t) \quad (11)$$

$$= I_0 \exp\left(-\sum_i^p \epsilon_i c_i(t)L - s\right) \left(1 + \frac{n(t)}{I_0 \exp(\dots)}\right) \quad (12)$$

$$\log I(t) = \log I_0 - s - \sum_i^p \epsilon_i c_i(t)L + \underbrace{\log\left(1 + \frac{n(t)}{I_0 \exp(\dots)}\right)}_{\tilde{n}(t)} \quad (13)$$

$$= \log I_0 - s - \sum_i^p \epsilon_i \left(c_i(t) - \frac{\tilde{n}(t)}{\epsilon_i L p}\right)L \quad (14)$$

The presence of noise modifies the measured intensities. This change in intensity can be attributed to changes in the concentrations as is shown in Eq. 14. Changing the intensity by $n(t)$ can be explained by changing each concentration by $\tilde{n}(t)/\epsilon_i L p$.

How does this affect the reference concentration?

$$\log I(t_{\text{ref}}) = \log I_0 - s - \sum_i^p \epsilon_i \left(c_i(t_{\text{ref}}) - \frac{\tilde{n}(t_{\text{ref}})}{\epsilon_i L p} \right) L \quad (15)$$

$$\log \left(\frac{I(t)}{I(t_{\text{ref}})} \right) = - \sum_i^p \epsilon_i \left(\left(c_i(t) - \frac{\tilde{n}(t)}{\epsilon_i L p} \right) - \left(c_i(t_{\text{ref}}) - \frac{\tilde{n}(t_{\text{ref}})}{\epsilon_i L p} \right) \right) L \quad (16)$$

$$(17)$$

Therefore, in this scenario the concentration change of each component is measured relative to the concentration at time t_{ref} plus a random shift that depends on the unknown noise contribution $n(t_{\text{ref}})$ at that timepoint:

$$\Delta c_i(t) = \left(c_i(t) - \frac{\tilde{n}(t)}{\epsilon_i L p} \right) - \left(c_i(t_{\text{ref}}) - \frac{\tilde{n}(t_{\text{ref}})}{\epsilon_i L p} \right) \quad (18)$$

$$c_{i,\text{ref}} = c_i(t_{\text{ref}}) - \frac{\tilde{n}(t_{\text{ref}})}{\epsilon_i L p} \quad (19)$$

$$\tilde{n}(t_{\text{ref}}) = \log \left(1 + \frac{n(t_{\text{ref}})}{I_0 \exp(-\sum_i^p \epsilon_i c_i(t_{\text{ref}}) L - s)} \right) \quad (20)$$

The random offset makes this an uncertain reference. ¹

3 USING THE AVERAGE INTENSITY (WHAT WE NORMALLY DO)

The contribution due to detector noise is a random number with zero mean. Hence, by averaging the intensities over several time points one can remove the noise contribution. In this scenario the reference intensity is obtained by averaging the intensity over a baseline of N consecutive time points t_k :

$$I_{\text{ref}} = \frac{1}{N} \sum_k^N I(t_k) \quad (21)$$

$$= I_0 \exp(-s) \left(\frac{1}{N} \sum_k^N \exp \left(- \sum_i^p \epsilon_i c_i(t_k) L \right) \right) + \underbrace{\frac{1}{N} \sum_k^N n(t)}_{-0} \quad (22)$$

Please note that the first summand is not an average over concentrations. It is an average over exponentials of concentrations. In order to transform the equations further the concentrations are now taken apart into the average concentration in the baseline interval and and

¹Furthermore, the presence of noise adds random shifts $\tilde{n}(t)/\epsilon_i L p$ to the concentration at each time point. So one does not measure $c_i(t)$ but always $c_i(t) - \tilde{n}(t)/\epsilon_i L p$. Averaging the concentrations that one get out of the modified Beer-Lambert-law over short time-scales should remove this noise contribution.

their variation around this mean:

$$c_i(t) = \hat{c}_i + \delta_i(t) \quad (23)$$

$$\hat{c}_i = \frac{1}{N} \sum_k^N c_i(t_k) \quad (24)$$

Then one can write Eq. 22 as:

$$I_{\text{ref}} = I_0 \exp(-s) \left(\frac{1}{N} \sum_k^N \exp \left(- \sum_i^p \epsilon_i (\hat{c}_i + \delta_i(t_k)) L \right) \right) \quad (25)$$

$$= I_0 \exp(-s) \exp \left(- \sum_i^p \epsilon_i \hat{c}_i L \right) \left(\frac{1}{N} \exp \left(- \sum_i^p \epsilon_i \delta_i(t_k) L \right) \right) \quad (26)$$

$$\log I_{\text{ref}} = \log I_0 - s - \sum_i^p \epsilon_i \hat{c}_i L + \underbrace{\log \left(\frac{1}{N} \exp \left(- \sum_i^p \epsilon_i \delta_i(t_k) L \right) \right)}_{c_{\text{avg}}} \quad (27)$$

$$= \log I_0 - s - \sum_i^p \epsilon_i \left(\hat{c}_i - \frac{c_{\text{avg}}}{\epsilon_i L p} \right) L \quad (28)$$

And finally:

$$\log \left(\frac{I(t)}{I_{\text{ref}}} \right) = - \sum_i^p \epsilon_i \left(\left(c_i(t) - \frac{\tilde{n}(t)}{\epsilon_i L p} \right) - \left(\hat{c}_i - \frac{c_{\text{avg}}}{\epsilon_i L p} \right) \right) L \quad (29)$$

$$\Delta c_i(t) = \left(c_i(t) - \frac{\tilde{n}(t)}{\epsilon_i L p} \right) - \left(\hat{c}_i - \frac{c_{\text{avg}}}{\epsilon_i L p} \right) \quad (30)$$

$$c_{i,\text{ref}} = \hat{c}_i - \frac{c_{\text{avg}}}{\epsilon_i L p} \quad (31)$$

$$c_{\text{avg}} = \log \left(\frac{1}{N} \exp \left(- \sum_i^p \epsilon_i \delta_i(t_k) L \right) \right) \quad (32)$$

In this scenario the concentration change of each component is basically measured relative to the average concentration in the baseline interval. However, also here is a shift $c_{\text{avg}}/\epsilon_i L p$ present. It depends on the variations of the concentration around this average. Mathematically it is caused by the difference between averaging x and $\exp(x)$ which is not the same. This somewhat speaks for choosing short baselines: then the deviations from the average δ_i are small and the shift becomes neglectable.

4 USING THE MEAN LOGARITHMIC AMPLITUDE

Finally, in order to really measure concentrations relative to the mean concentration in the baseline one can average the logarithms of the amplitude over a baseline:

$$I_{\text{ref}} = \frac{1}{N} \sum_k^N \log I(t_k) \quad (33)$$

$$= \frac{1}{N} \sum_k^N \log \left(I_0 \exp(-s) \exp \left(- \sum_i^p \epsilon_i c_i(t_k) L \right) \left(1 + \frac{n(t_k)}{I_0 \exp(\dots)} \right) \right) \quad (34)$$

$$= \frac{1}{N} \sum_k^N \left(\log I_0 - s - \sum_i^p \epsilon_i c_i(t_k) L + \log \left(1 + \frac{n(t_k)}{I_0 \exp(\dots)} \right) \right) \quad (35)$$

$$= \log I_0 - s - \sum_i^p \epsilon_i \hat{c}_i L + \underbrace{\frac{1}{N} \sum_k^N \log \left(1 + \frac{n(t_k)}{I_0 \exp(\dots)} \right)}_{=\hat{n}} \quad (36)$$

$$= \log I_0 - s - \sum_i^p \epsilon_i \left(\hat{c}_i(t) - \frac{\hat{n}}{\epsilon_i L p} \right) L \quad (37)$$

As in all previous cases the reference concentration contains an offset (here: \hat{n}). While the noise contribution $n(t)$ has zero expectation value, this is not necessarily mean that \hat{n} tends to zero. However, in channels with good signal to noise ration, i.e. $n(t) \ll I_0$, also \hat{n} becomes neglectable. For these channels, with this choice of reference intensity, one measures relative to the mean concentration in the baseline interval. For channels with larger noise contamination the previous choice of using the mean intensity as a reference deals better with the noise.

5 SUMMARY

- the concentration changes are measured relative to a reference concentration
- the interpretation of this reference depends on the reference intensity
- basically we measure changes relative to the mean concentration in the baseline interval, but there is a subtle shift that depends on how much the concentration changed in the baseline
- for channels with good signal to noise using the mean logarithmic amplitude might be a good alternative when one really needs concentrations relative to the mean.

Finally, one should point that independent on the choice of the reference concentration the following holds. If one measured two concentration changes at two time points, i.e. $c(t_1) - c_{\text{ref}}$ and $c(t_2) - c_{\text{ref}}$, their difference is independent on the reference concentration:

$$\Delta c = (c(t_2) - c_{\text{ref}}) - (c(t_1) - c_{\text{ref}}) = c(t_2) - c(t_1),$$

i.e. the concentration change during an activation compared to the time before the stimulus is independent on the choice of the reference concentration.