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## Chapter 1

- 1.1. How can weak photocurrent of an Si photodiode be converted to a voltage signal on continuous-wave NIRS or spatially resolved NIRS?

**Answer**

A current-to-voltage converter using an operational amplifier is generally used to convert a weak current signal  $I$ . A photodiode is connected to the input of an operational amplifier. When a feedback resistor of the circuit is  $R_f$ , the output voltage is simply  $R_f I$ . The design of the converter requires a lot of trial and error in order to reduce noise and bias. For the details, refer to the articles listed under Further Reading.

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## Chapter 2

- 2.1. A random number used on Monte Carlo simulation should be long period and of almost uniform distribution. How can this random number be generated?

**Answer**

A Mersenne Twister (MT) is a pseudorandom number-generating algorithm developed by Matsumoto and Nishimura in 1997. It has the following features: (1) a far longer period and a far higher order of equidistribution than any other implemented generator, (2) fast generation, and (3) efficient use of memory. For example, the implemented C-code `mt19937.c` consumes only 624 words of working area and provides a random number that has a period of  $2^{19937} - 1$  and a 623-dimensional equidistribution property. Please refer to the papers cited in Further Reading for details.

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## Chapter 3

- 3.1. Assume that the concentration of hemoglobin is changed from 0.1 to 0.11 mM and the oxygen saturation of the blood is changed from 65% to 70% in the activated region of the brain. The extinction coefficients of oxygenated hemoglobin and deoxygenated hemoglobin at 780-nm

wavelength are  $0.16$  and  $0.25 \text{ mM}^{-1} \text{ mm}^{-1}$ , respectively. The partial optical pathlength in the activated region for a probe pair is  $5 \text{ mm}$ .

(a) Find the change in absorption coefficient at  $780\text{-nm}$  wavelength in the activated region.

**Answer**

The concentration change in the oxygenated hemoglobin  $\Delta c_{\text{oxy-Hb}}$  and deoxygenated hemoglobin  $\Delta c_{\text{deoxy-Hb}}$  can be calculated as follows:

$$\Delta c_{\text{oxy-Hb}} = 0.11 \text{ [mM]} \times 70 \% - 0.1 \text{ [mM]} \times 65 \% = 0.012 \text{ [mM]},$$

$$\Delta c_{\text{deoxy-Hb}} = 0.11 \text{ [mM]} \times 30 \% - 0.1 \text{ [mM]} \times 35 \% = -0.002 \text{ [mM]}.$$

The change in absorption coefficient is

$$\begin{aligned} \Delta \mu_a &= \epsilon_{\text{oxy-Hb}} \cdot \Delta c_{\text{oxy-Hb}} + \epsilon_{\text{deoxy-Hb}} \cdot \Delta c_{\text{deoxy-Hb}} \\ &= 0.16 \text{ [mM}^{-1} \text{ mm}^{-1}] \times 0.012 \text{ [mM]} + 0.25 \text{ [mM}^{-1} \text{ mm}^{-1}] \times -0.002 \text{ [mM]} \\ &= 1.42 \times 10^{-3} \text{ [mm}^{-1}]. \end{aligned}$$

(b) Find the change in the optical density (NIRS signal) at  $780\text{-nm}$  wavelength caused by the absorption change in the activated region:

$$\Delta \text{OD} = \Delta \mu_a \cdot \langle L_{\text{act}} \rangle = 1.42 \times 10^{-3} \text{ [mm}^{-1}] \times 5 \text{ [mm]} = 7.1 \times 10^{-3}.$$

3.2. Derive the equations that calculate the concentration change in oxygenated and deoxygenated hemoglobins from change in optical density (NIRS signal) at two wavelengths,  $\lambda_1$  and  $\lambda_2$ . The extinction coefficient of oxygenated hemoglobin and deoxygenated hemoglobin is  $\epsilon_{\text{oxy-Hb}}$  and  $\epsilon_{\text{deoxy-Hb}}$ , respectively. (Assume that the wavelength dependence of the partial optical pathlength in the activated region  $\langle L_{\text{act}} \rangle$  can be ignored.)

**Answer**

The relationship between the NIRS signal at two wavelengths and change in oxygenated and deoxygenated hemoglobins is

$$\begin{aligned} \Delta \text{OD}(\lambda_1) &= (\epsilon_{\text{oxy-Hb}}(\lambda_1) \cdot \Delta c_{\text{oxy-Hb}} + \epsilon_{\text{deoxy-Hb}}(\lambda_1) \cdot \Delta c_{\text{deoxy-Hb}}) \cdot \langle L_{\text{act}} \rangle, \\ \Delta \text{OD}(\lambda_2) &= (\epsilon_{\text{oxy-Hb}}(\lambda_2) \cdot \Delta c_{\text{oxy-Hb}} + \epsilon_{\text{deoxy-Hb}}(\lambda_2) \cdot \Delta c_{\text{deoxy-Hb}}) \cdot \langle L_{\text{act}} \rangle. \end{aligned}$$

The equations, which calculate the concentration change in oxygenated and deoxygenated hemoglobins, can be derived by solving the above simultaneous equations:

$$\begin{aligned} \Delta c_{\text{oxy-Hb}} &= \frac{\Delta \text{OD}(\lambda_2) \epsilon_{\text{deoxy-Hb}}(\lambda_1) - \Delta \text{OD}(\lambda_1) \epsilon_{\text{deoxy-Hb}}(\lambda_2)}{(\epsilon_{\text{oxy-Hb}}(\lambda_2) \epsilon_{\text{deoxy-Hb}}(\lambda_1) - \epsilon_{\text{oxy-Hb}}(\lambda_1) \epsilon_{\text{deoxy-Hb}}(\lambda_2)) \langle L_{\text{act}} \rangle}, \\ \Delta c_{\text{deoxy-Hb}} &= \frac{\Delta \text{OD}(\lambda_1) \epsilon_{\text{oxy-Hb}}(\lambda_2) - \Delta \text{OD}(\lambda_2) \epsilon_{\text{oxy-Hb}}(\lambda_1)}{(\epsilon_{\text{oxy-Hb}}(\lambda_2) \epsilon_{\text{deoxy-Hb}}(\lambda_1) - \epsilon_{\text{oxy-Hb}}(\lambda_1) \epsilon_{\text{deoxy-Hb}}(\lambda_2)) \langle L_{\text{act}} \rangle}. \end{aligned}$$

3.3. Draw polar plots of the probability distribution of deflection angle  $p(\theta)$  described by the Henyey-Greenstein phase function for  $g = 0.1$ ,  $g = 0.5$ , and  $g = 0.9$ .

**Answer**

The probability distribution of the deflection angle can be calculated by the following equation:

$$p(\theta) = \frac{1 - g^2}{4\pi(1 + g^2 - 2g \cos \theta)^{\frac{3}{2}}},$$

- 3.4. A pencil beam of a short pulse is incident onto tissues and diffusely reflected light is detected at 20 mm from the incident point. Analyze light propagation in the tissues by analytical solution of the diffusion equation described in [26]. The optical properties of the tissues: (1)  $\mu_s = 10 \text{ mm}^{-1}$ ,  $g = 0.9$ ,  $\mu_a = 0.01 \text{ mm}^{-1}$ . (2)  $\mu_s = 10 \text{ mm}^{-1}$ ,  $g = 0.85$ ,  $\mu_a = 0.01 \text{ mm}^{-1}$ . (3)  $\mu_s = 5 \text{ mm}^{-1}$ ,  $g = 0.8$ ,  $\mu_a = 0.02 \text{ mm}^{-1}$ . Although the diffusion coefficient is defined as  $\kappa = 1/3\{\mu'_s + \mu_a\}$  in [26],  $\kappa = 1/(3\mu'_s)$  can be used for the calculations. The speed of light in the medium is 0.2 mm/ps, and refractive index mismatch at the tissue boundary can be ignored.

(a) Determine the transport scattering coefficient of each tissue.

**Answer**

The transport scattering coefficient  $\mu'_a$  is calculated using the scattering coefficient  $\mu_s$  and anisotropic factor  $g$  by the following equation:

$$\mu'_a = (1 - g)\mu_s.$$

1.  $\mu'_s = (1 - 0.9) \times 10 [\text{mm}^{-1}] = 1.0 [\text{mm}^{-1}]$ ,
2.  $\mu'_s = (1 - 0.85) \times 10 [\text{mm}^{-1}] = 1.5 [\text{mm}^{-1}]$ ,
3.  $\mu'_s = (1 - 0.8) \times 5 [\text{mm}^{-1}] = 1.0 [\text{mm}^{-1}]$ .

(b) Determine the depth of the isotropic point source created by the incident beam.

**Answer**

The depth of the isotropic point source  $z_0$  is the reciprocal of the transport scattering coefficient:

$$z_0 = 1/\mu'_s.$$

1.  $z_0 = 1/\mu'_s = 1/1.0 [\text{mm}^{-1}] = 1.0 [\text{mm}]$ ,
2.  $z_0 = 1/\mu'_s = 1/1.5 [\text{mm}^{-1}] = 0.667 [\text{mm}]$ ,
3.  $z_0 = 1/\mu'_s = 1/1.0 [\text{mm}^{-1}] = 1.0 [\text{mm}]$ .

(c) Draw the temporal distribution of the reflectance.

**Answer**

The temporal distribution of the reflectance is given by

$$R(\rho, t) = (4\pi\kappa c)^{-3/2} z_0 t^{-5/2} \exp(\mu_a c t) \exp\left(-\frac{\rho^2 + z_0^2}{4\kappa c t}\right),$$

where  $\rho$  is the distance between the detection and incident points,  $c$  is the speed of light in the tissue, and  $t$  is time.

## Chapter 4

4.1. How does NIRS help us better understand the relationship between vasculature and tissue function?

**Answer**

See Further Reading.

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## Chapter 5

5.1. How would you quantify muscle NIR signals?

5.2. List the various muscle NIR indicators. Which indicator reflects muscle oxidative function? How?

**Answer**

See Further Reading.

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## Chapter 6

6.1. NIRS measurement of Mb saturation ( $S_{MbO_2}$ ) at different tensions during muscle contraction shows the following:

Tension (%)	$S_{MbO_2}$ (%)
50	70
75	59
10	49

What is the corresponding change in  $PO_2$ , given an Mb P50 of 2.37 at 37°C? What is the change in  $O_2$  gradient, given a resting  $PO_2$  of 10 mmHg? Plot out the curves. Does the change in  $S_{MbO_2}$ ,  $PO_2$ , and  $O_2$  gradient show a linear relationship? What is the physiological implication in interpreting the  $S_{MbO_2}$  data with respect to  $O_2$  gradient?

**Answer**

See Takakura H, Masuda K, Hashimoto T, Iwase S, Jue T (2010) Quantification of myoglobin deoxygenation and intracellular partial pressure of  $O_2$  during muscle contraction during haemoglobin-free medium perfusion. *Exp Physiol* 95:630–640

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## Chapter 7

7.1. What is the ratio of Mb to Hb in a gram of the locomotory muscle of a seal versus that of a dog? (see [41–45]).

**Answers**

1. To solve this problem, we need to first determine the  $\mu\text{mol}$  content of Mb in 1 g of locomotory muscle in the seal and the dog:

(a) Using seal Mb concentration and its molecular weight, the micromole content is easily calculated.

Seal [Mb] is 37 mg/g of the epaxial muscle (from [44]).

**Note:** Different [Mb] or [Hb] concentrations or capillary characteristics may be found in different studies or for different muscles. However, although the calculations may change, the trends demonstrated in this problem will be the same.

The gram content of Mb in 1 g of muscle is converted to micromoles as follows:

$$\begin{aligned} \text{Mb} &= 37 \text{ mg} = 0.037 \text{ g}, \\ \text{Mb molecular weight} &= 17,000 \text{ g/mol}, \\ \text{Mb} &= 0.037\text{g}/17,000 \text{ g/mol} = 2.18 \times 10^{-6}\text{mol}, \\ 2.18 \times 10^{-6}\text{mol} &= 2.18 \mu\text{mol}, \\ \text{Seal Mb} &= 2.18 \mu\text{mol}. \end{aligned}$$

(b) The same calculation is done for the dog Mb:

Dog [Mb] is 1.5 mg/g in the gastrocnemius (provided from [44]).  
Again Mb is converted to micromoles:

$$\begin{aligned} \text{Mb} &= 1.5 \text{ mg} = 0.0015 \text{ g}, \\ \text{Mb molecular weight} &= 17,000 \text{ g/mol}, \\ \text{Mb} &= 0.0015 \text{ g}/17,000 \text{ g/mol} = 8.82 \times 10^{-8}\text{mol}, \\ \text{Mb} &= 8.82 \times 10^{-8}\text{mol} = 0.0882 \mu\text{mol}. \\ \text{Dog Mb} &= 0.0882 \mu\text{mol}. \end{aligned}$$

2. Next, the  $\mu\text{mol}$  content of Hb in 1 g of locomotory muscle must be determined. To do this, the muscle capillary volume ( $V_c$ ) must first be determined in a gram of muscle and then the content of Hb in that volume can be calculated. The values for both the seal and dog are provided in [41, 42] and the formula for  $V_c$  is in [43].

(a) Using the formula and capillary data for harbor seals, the  $V_c$  in 1 g of locomotory muscle (longissimus dorsi) is calculated, which is then multiplied by the [Hb]:

$$V_c = (\text{capillary density in \# capillaries/mm}^2) (\text{capillary anisotropy coefficient})$$

$$(\pi/4) (\text{diameter mm}^2)/(\text{muscle density g/ml}),$$

$$\text{capillary density} = 1138/\text{mm}^2(\text{mean of several muscles}),$$

$$\text{capillary anisotropy coefficient} = 1.2,$$

$$\text{diameter} = 0.00449 \text{ mm},$$

$$\text{muscle density} = 1.06 \text{ g/ml},$$

$$\text{Seal } V_c = (1138/\text{mm}^2) (1.2) (0.785) (0.00449 \text{ mm}) (0.00449 \text{ mm})/(1.06 \text{ g/ml}),$$

$$\text{Seal } V_c = 0.0204 \text{ ml}$$

Taking the concentration of [Hb] in a seal (provided from [42]), Hb content in the  $V_c$  per 1 g of muscle can be determined:

$$\begin{aligned} \text{Seal [Hb]} &= 0.222 \text{ g/ml,} \\ \text{Hb in } V_c &= (0.0204 \text{ ml}) (0.222 \text{ g/ml}), \\ \text{Hb in } V_c &= 0.0045 \text{ g,} \\ \text{Hb molecular weight} &= 64,500 \text{ g/mol,} \\ \text{Hb in } V_c &= 0.0045 \text{ g}/64,500 \text{ g/mol,} \\ \text{Hb in } V_c &= 6.97 \times 10^{-8} \text{ mol,} \\ \text{Seal Hb in 1 gm muscle} &= 0.070 \text{ } \mu\text{mol.} \end{aligned}$$

(b) Using the formula and capillary data for dogs, the  $V_c$  in 1 g of locomotory muscle is calculated, which is then multiplied by the dog [Hb].

The calculation can be done for the dog using data from [41, 42]:

$$\begin{aligned} V_c &= (\text{capillary density in } \# \text{ capillaries/mm}^2)(\text{capillary anisotropy coefficient}) \\ &\quad (\pi/4) (\text{diameter mm}^2)/(\text{muscle density g/ml}), \\ \text{capillary density} &= 1,617/\text{mm}^2(\text{mean of several muscles}), \\ \text{capillary anisotropy coefficient} &= 1.23, \\ \text{diameter} &= 0.00416 \text{ mm,} \\ \text{muscle density} &= 1.06 \text{ g/ml.} \\ \text{Dog } V_c &= (1,617/\text{mm}^2) (1.23) (0.785)(0.00416 \text{ mm}) (0.00416 \text{ mm})/ (1.06 \text{ g/ml}), \\ \text{Dog } V_c &= 0.0255 \text{ mL.} \end{aligned}$$

Taking the concentration of [Hb] in a dog, provided from the citation below, Hb content in the  $V_c$  in 1 g of muscle can be determined (see [42]):

$$\begin{aligned} \text{Dog [Hb]} &= 0.188 \text{ g/ml,} \\ \text{Hb in } V_c &= (0.0255 \text{ ml}) (0.188 \text{ g/ml}), \\ \text{Hb in } V_c &= 0.0048 \text{ g,} \\ \text{Hb molecular weight} &= 64,500 \text{ g/mol,} \\ \text{Hb in } V_c &= 0.0048 \text{ g} / (64,500 \text{ g/mol}), \\ \text{Hb in } V_c &= 7.43 \times 10^{-8} \text{ mol.} \\ \text{Dog Hb in 1 gm muscle} &= 0.074 \mu\text{mol.} \end{aligned}$$

**Ratio of Mb:Hb for the seal:**

$$\begin{aligned} \text{Seal Mb:Hb} &= 2.18 \text{ } \mu\text{mol}/0.070 \text{ } \mu\text{mol,} \\ \text{Seal Mb:Hb} &= 31.1:1. \end{aligned}$$

**Ratio of Mb:Hb for the dog:**

$$\begin{aligned} \text{Dog Mb:Hb} &= 0.0882 \text{ } \mu\text{mol}/0.074 \text{ } \mu\text{mol,} \\ \text{Dog Mb:Hb} &= 1.19:1. \end{aligned}$$

**Ratios of Mb: Hb in Muscle:**

$$\begin{aligned} \text{Seal:} & 31.1:1, \\ \text{Dog:} & 1.19:1. \end{aligned}$$

**Seal Mb: Dog Mb:**

26.1:1.

These calculations, based on Mb concentration, Hb concentration, and muscle capillary density, reveal that the ratio of Mb to Hb in seal muscle is 26 times greater than in dog muscle. This is primarily a reflection of the 25-fold greater Mb concentration in seal muscle. Although Hb concentration is lower in the dog, capillary density is slightly greater in the dog than in the seal. These ratios are representative of the resting state. During exercise in dogs, increased muscle blood flow and muscle capillary recruitment would make the dog's Mb-to-Hb ratio even lower. In contrast, in the diving seal, even if muscle blood flow is only partially reduced, the Mb-to-Hb ratio will be increased. Thus, although it is difficult to quantify the contribution of Hb to the NIRS signal in muscle, the high Mb concentration and the cardiovascular responses in the diving seal minimize the potential contribution of Hb to the NIRS signal in muscle.

**Chapter 8**

- 8.1. Marine mammals have a much higher of Mb in their skeletal muscle than terrestrial mammals. What is the typical Mb concentration range in marine and terrestrial mammals? Why would an increase in Mb concentration confer a more prominent role for Mb facilitated O<sub>2</sub> diffusion? Discuss the role of Mb-facilitated O<sub>2</sub> diffusion in terms of O<sub>2</sub> diffusivity, Mb diffusivity, O<sub>2</sub> concentration, and Mb concentration in marine and terrestrial mammal myocytes. Assume identical O<sub>2</sub> and Mb diffusivity in all muscle cells.

**Answer**

See Ponganis PJ, Kreutzer U, Sailasuta N, Knowler T, Hurd R, Jue T (2002) Detection of myoglobin desaturation in *Mirounga angustirostris* during apnea. *Am J Physiol Regul Integr Comp Physiol* 282:R267–R272

- 8.2 A <sup>1</sup>H NMR experimental measurement of the deoxy-Mb signals in human gastrocnemius muscle shows no deoxy-Mb at rest. When the subject starts plantar flexion exercise at the rate of 70 contractions per minute, the deoxy-Mb signal appears and rises exponentially, consistent with the monoexponential relationship,  $y = c - c^* \exp(-x/\tau)$  ( $y = \text{Mb concentration (mM)}$ ,  $x = \text{time (s)}$ ,  $\tau = \text{time constant (s)}$ , and  $c = \text{arbitrary constant (mM)}$ ). During the first 2 min of exercise, venous pO<sub>2</sub> does not change, suggesting that almost all of the initial increase in muscle O<sub>2</sub> consumption arises from O<sub>2</sub> released from intracellular Mb. If  $\tau = 30$  s, what is the mitochondrial respiration rate at the onset of plantar flexion exercise? What does the mitochondrial respiration at the onset of muscle contraction imply about the contribution of oxidative phosphorylation? Use a gastrocnemius Mb concentration estimate of 0.4 mM.

**Answer**

See Ponganis PJ, Kreutzer U, Stockard TK, Lin PC, Sailasuta N, Tran TK, Hurd R, Jue T (2008) Blood flow and metabolic regulation in seal muscle during apnea. *J Exp Biol* 211 (Pt 20): 3323–3332