

1. Show that the form of the equation that Krogh and his mathematician colleague, K Erlang (who did all the work and got none of the credit), derived in 1919 to describe the difference in oxygen tension of nutrient radially (at some location radially that he—inexplicably—calls,  $x$ ) is compatible (if simpler) than the expression for  $C_t(z,r)$  that we derived (in part) in class, given below. Our derivation includes variation axially (in the  $z$  direction) as well. Show that our expression simplifies to their expression for a fixed  $z$ . Show me a list of what parameters in our nomenclature are equivalent to theirs. What simplifications to our equation are necessary?

ours: 
$$\bar{C}(z,r) = C_0 - \frac{R_0}{V r_c^2} (r_T^2 - (r_c + t_m)^2) z - \frac{R_0}{r_c z P_m} (r_T^2 - (r_c + t_m)^2) + \frac{R_0}{4D} (r^2 - (r_c + t_m)^2) - \frac{r_T^2 R_0}{2D} \ln \left( \frac{r}{r_c + t_m} \right)$$

2. Show that the equation relating Permeability to Extraction fraction given by Crone (1963) is compatible with what we derived in class by simplifying the expression for the derivative of the concentration axially in the blood in the Krogh cylinder, given below.

$$-V \frac{dC(z)}{dz} = \frac{2}{r_c} P_m (C(z) - \bar{C}(z)) \Big|_{r=r_c+t_m}$$

3. Crone (1963) provides estimates of the permeability of capillary membranes from various different organs (in what species?) to various solutes.
  - a. There are some limitations to what he did. One serious limitation is that his estimates for  $P$  were dependent on knowing surface area,  $S$ , for each capillary type. Why?
  - b. How well did Crone do? Find modern estimates for Permeability for at least one solute and various capillary membranes. Make a table of Crone's numbers and the numbers you find. What method was used to make the estimates you cite. Give the reference and explain the newer technique briefly.

4. Use Crone's multiple indicator diffusion method and the data, below, for a reference substance and 3 test substances to calculate the permeability of each test substance if the surface area of the capillary membrane is estimated to be  $300 \text{ cm}^2/\text{g}$  of tissue. What key assumption(s) are you making by using this technique?

time (sec)	reference	test1	test2	test3
1	0.0	0.0	0.0	0.0
2	0.0	0.0	0.0	0.0
3	0.0	0.0	0.0	0.0
4	40.7	41.1	38.4	24.6
5	76.0	73.7	59.6	40.2
6	75.3	72.4	60.1	49.4
7	57.7	55.5	50.8	53.9
8	38.3	37.1	39.0	55.2
9	23.3	22.8	28.1	54.2
10	13.3	13.2	19.4	51.8
11	7.2	7.3	13.0	48.5
12	3.8	3.9	8.5	44.6
13	2.0	2.1	5.5	40.6
14	1.0	1.1	3.5	36.6
15	0.5	0.5	2.2	32.7
16	0.2	0.3	1.3	29.0
17	0.1	0.1	0.8	25.5
18	0.1	0.1	0.5	22.4
19	0.0	0.0	0.3	19.6

5. Some treatments for cancer involve a pre-treatment with a drug that disrupts the blood-brain-barrier for long enough to increase the permeability of brain capillaries to chemotherapeutic agents in order to increase delivery of these agents to brain tumors. We want to monitor the effectiveness of the BBB disrupters through serial PET imaging. Briefly outline the design for an imaging experiment to calculate the change in permeability of brain capillaries with disrupter treatment. What tracer do you propose to use? What characteristic(s) of the tracer must you consider?

Please find me a paper that treats people (or animals) with brain tumors with such a permeability enhancing agent.