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Institute of Bioelectromagnetism

Bioelectromagnetism

Exercise #2 – Answers

Q1: Characteristic Length and Time Constant

- The intracellular resistance of a nerve cell is $8.2 \cdot 10^6$ Ω/cm (r_i). Resistance of the cell membrane is $1.5 \cdot 10^4$ Ωcm and capacitance 12 nF/cm (c_m). Calculate the characteristic length and time constant of the axon. (start from the general cable equation to see how the time constant is derived)

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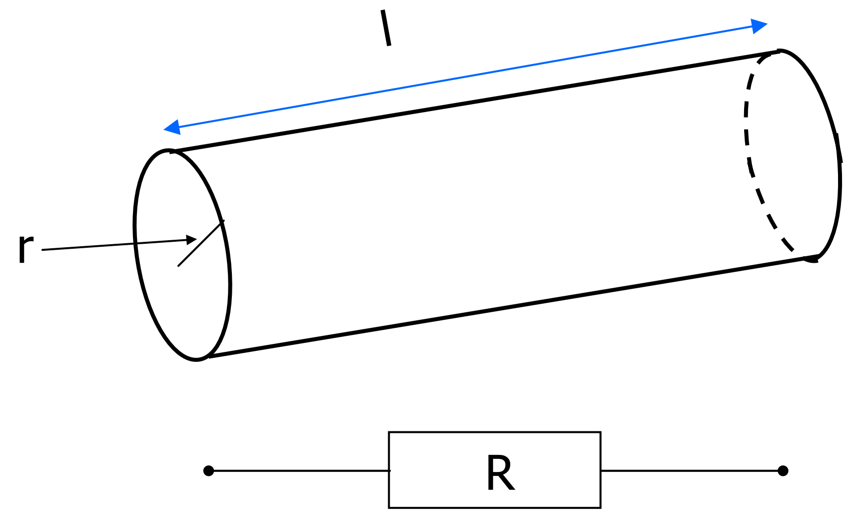
Q1: Characteristic Length and Time Constant - terminology

- Review of terminology

- **Intracellular resistance & resistivity**
  - Let R be the total resistance in *axial* direction [Ω]
  - > resistance per length
    - $r_i = R / l$ [Ω/m]
  - > resistivity
    - $R = \rho l / A$
      $\rightarrow \rho = RA / l = r_i * A$ [Ω m]

r_i



- **Extracellular resistance & resistivity**
    - $r_o = R / l$ [Ω/m]
    - $\rho = RA / l = r_o * A$ [Ω m]

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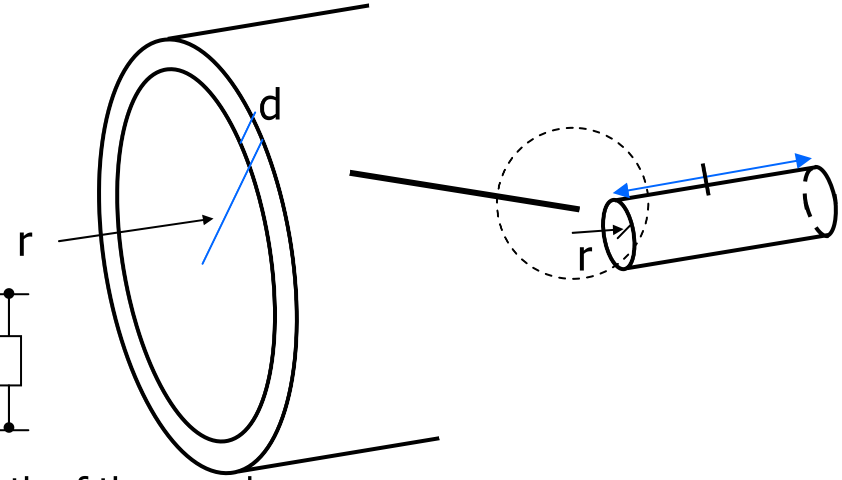
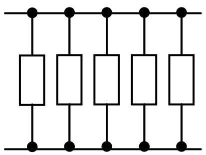
Q1: Characteristic Length and Time Constant - terminology

- **Cell membrane resistance & resistivity**
  - Let R be the total *radial* resistance [Ω]
  - > resistance in axial direction (as a function of the length of the membrane)



    - $r_m = R * l$ [Ω m]



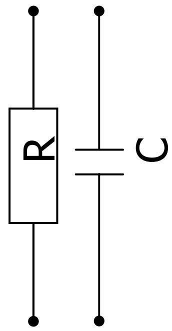
  - resistance is inversely proportional to the length of the membrane
  - > resistivity
    - $\rho_m = RA_m / l_m = R (2\pi\ r\ l) / d$ [Ω m]
      - d = thickness of the membrane
      - l = length of the cell

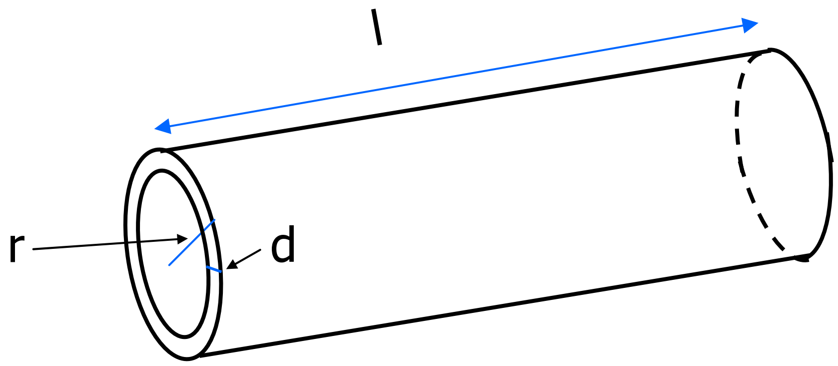
r_m/l

  - resistance per area
    - $R_m = R * A = R (2\pi\ r\ l) = r_m * 2\pi\ r$ [Ω m^2]

Q1: Characteristic Length and Time Constant - terminology

- Membrane capacitance
  - C total capacitance [F] (radial)





  - > Capacitance per length
    - $c_m = C / l$ [F/cm]
  - > Capacitance per area
    - $C_m = C / A = C / (2\pi r * l) = c_m / (2\pi r)$ [F/cm^2]

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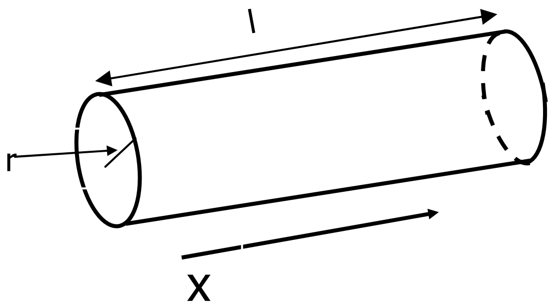
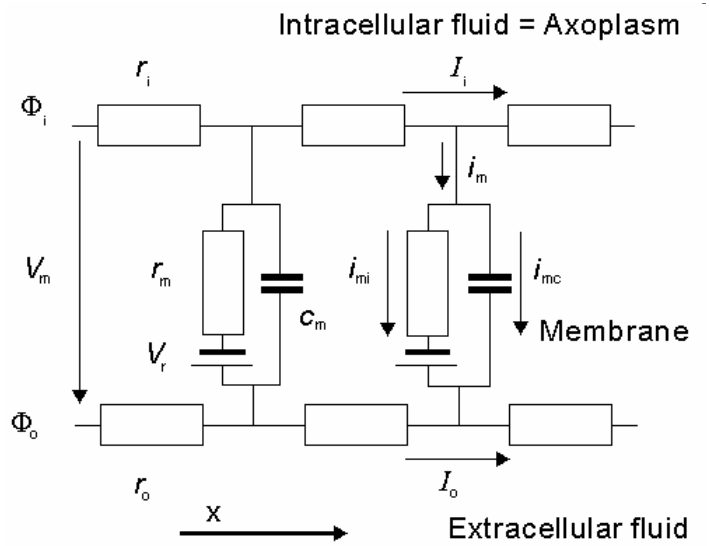
Q1: Characteristic Length and Time Constant

- General cable equation describes *passive function* of a cell (subtreshold i_m)
  - 1-D propagation (along x-axis)
  - $V' = V_m - V_r$ - deviation from RMP
  - equivalent circuit

$$\frac{\partial^2 V'}{\partial x^2} = (r_i + r_o) i_m = V' \frac{r_i + r_o}{r_m} \qquad (3.41 \ldots 3.45)$$





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Q1: Characteristic Length and Time Constant

- …

$$\frac{\partial^2 V'}{\partial x^2} = V' \frac{r_i + r_o}{r_m} \qquad (3.41 \ldots 3.45)$$

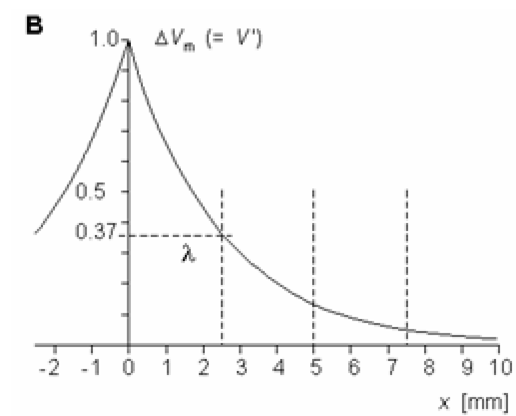
- General solution of this equation is

$$V' = Ae^{\frac{-x}{\lambda}} + Be^{\frac{x}{\lambda}}$$

boundary conditions: V′(x=0)=V′, V′(x=∞)=0

$$\lambda = \sqrt{\frac{r_m}{r_0 + r_i}}$$

- λ = characteristic length/length constant
  - describes spreading along the cell axis
  - think: r_m up -> λ up



Q1: Characteristic Length and Time Constant

$$\lambda = \sqrt{\frac{r_m}{r_0 + r_i}}$$

- since $r_i >> r_o$ =>

$$\lambda \approx \sqrt{\frac{r_m}{r_i}} \qquad (eq\ 3.48)$$

$$= \sqrt{\frac{1.5*10^4 \Omega cm}{8.2*10^6 \Omega / cm}} = 0.04277 cm \approx 428 \mu m$$

- Time constant $\tau = r_m * c_m$
  – measure to reach steady-state

$$= 1.5*10^4 \Omega cm * 12*10^{-9} F/cm = 180 \mu s$$

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Q2: Strength-Duration Curve

- The rheobasic current of the nerve cell in the previous exercise is 2 mA.

  a) What is the strength-duration equation of the cell. How long will it take to reach the stimulus threshold with a 2.5 mA stimulus current. What is the chronaxy of the cell?
  b) Determine the propagation speed of an action pulse if the cell diameter is 100 µm and coefficient K = 10.47 1/ms in propagation equation

$$\Theta = \sqrt{\frac{\mathrm{K}r}{2\rho C_m}}$$

  ρ is the intracellular resistivity.

- Definitions
  - Rheobase: smallest *current*, that generates an action impulse
  - Chronaxy: *time*, that is needed to generate action impulse with $2*I_{rh}$

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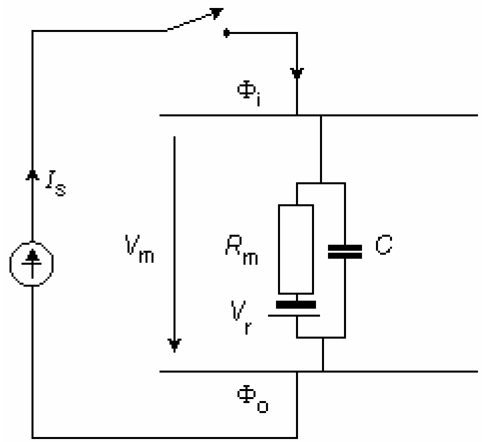
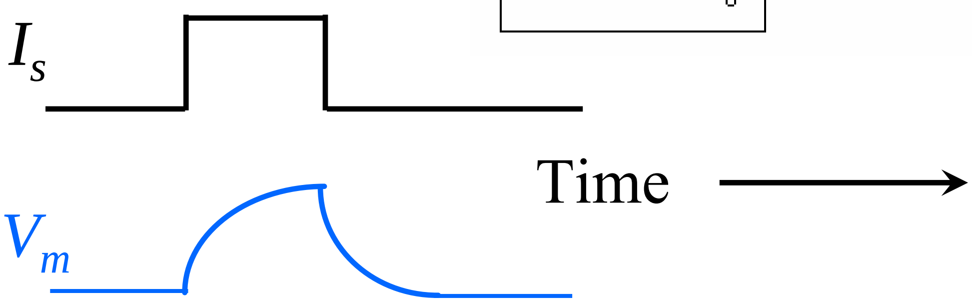
Q2: Strength-Duration Curve

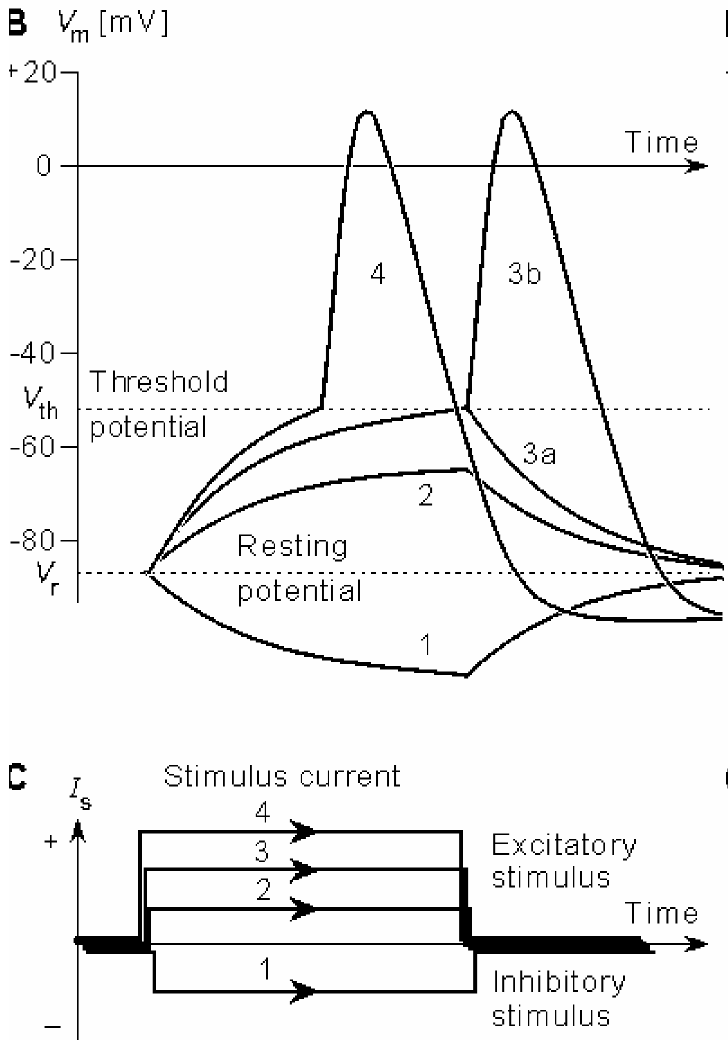
- Definitions
  - impulse response of the membrane (radial direction only)





$$V' = I_s R_m (1 - e^{-t/\tau}) \qquad (3.56)$$

Q2: Strength-Duration Curve



Q2: Strength-Duration Curve

- Rheobase

  V_{th} = membrane potential, that can generate action impulse

$$I_s = \frac{V'}{R_m (1 - e^{-t/\tau})}$$

when t=∞:

$$I_s = I_{rh} = \frac{V_{th}}{R_m \underbrace{(1 - e^{-t/\tau})}_{\rightarrow 0}} = \frac{V_{th}}{R_m}$$ == Rheobase

->

$$I_s = \frac{I_{rh}}{(1 - e^{-t/\tau})} \Leftrightarrow 1 - e^{-t/\tau} = \frac{I_{rh}}{I_s} \Leftrightarrow t = \tau * \ln \frac{1}{1 - \frac{I_{rh}}{I_s}}$$

$$= 180 \mu s * \ln \frac{1}{(1 - \frac{2}{2.5})} = 290 \mu s$$

- Chronaxy

  $I_s = 2 * I_{rh}$ => $t = \tau * \ln 2 =$ **125 µs**

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Q2: Strength-Duration Curve

- Propagation speed

$$\Theta = \sqrt{\frac{\mathrm{K}r}{2\rho C_m}}$$

where

K = 10.47 1/ms

d = 100*10^{-6} m

ρ = intracellular resistivity

ρ = RA/l =Ri*A

Ri = R/l=8.2*10^{6} Ω/cm

ρ = Ri * π r^2 = 8.2*10^6 Ω/cm * π (5000*10^{-6}cm)^2 = 644 Ωcm

C_m = c_m/(2πr) = 12nF/cm / (2π*5000*10^{-6}cm) = 0.382 μF/cm^2

=> 327 cm/s

empirical (eq. 4.33):

$$\Theta \propto \sqrt{r} \propto \sqrt{d}$$

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Q3: Sodium Conductance

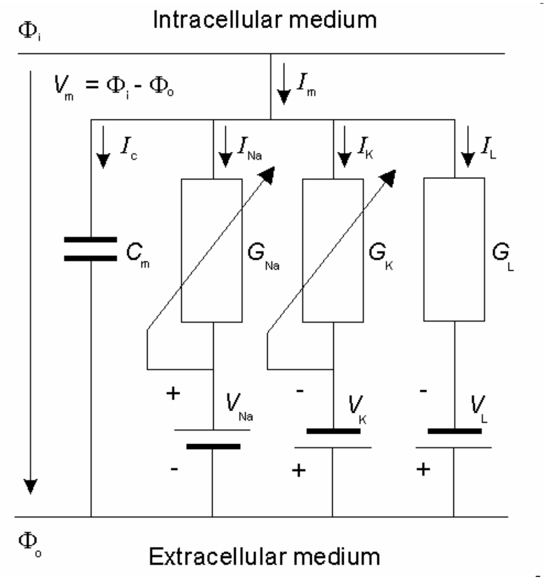
- Derive the equation of sodium conductance in voltage clamp measurements (with chemical clamping) using the Hodgkin-Huxley model.

- Hodgkin-Huxley model

  Transmembrane current equation

$$I_m = C_m \frac{dV_m}{dt} + (V_m - V_{Na})G_{Na} + (V_m - V_K)G_K + (V_m - V_L)G_L$$

This is eq. 4.10 in the Bioelectromagnetism book



Q3: Sodium Conductance

- Hodgkin-Huxley model equations…

$$I_{Na} = (V - V_{Na})g_{Na} = (V - V_{Na})\overline{g}_{Na} m^3 h$$
$$I_K = (V - V_K)g_K = (V - V_K)\overline{g}_K n^4$$
$$I_{leak} = (V - V_{leak})g_{leak}$$

$$dm / dt = \alpha_m (1 - m) - \beta_m m$$
$$dh / dt = \alpha_h (1 - h) - \beta_h h$$
$$dn / dt = \alpha_n (1 - n) - \beta_n n$$

$$\alpha_m = 0.1 \frac{v+37}{1-\exp(\frac{-v-37}{10})} \qquad \beta_m = 4\exp(\frac{v-62}{18})$$

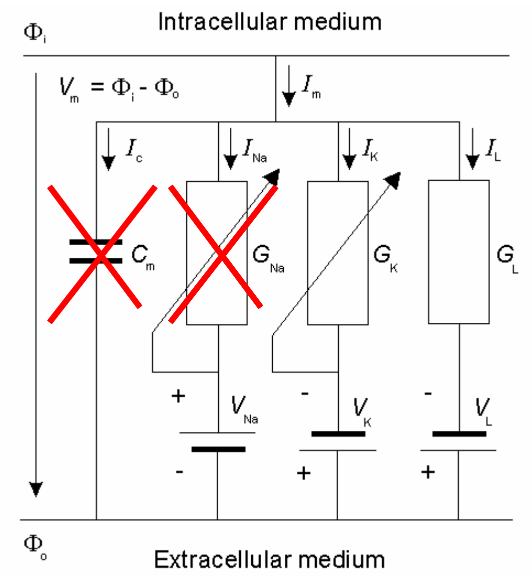
$$\alpha_h = 0.07\exp(\frac{v+62}{-20}) \qquad \beta_h = \frac{1}{1+\exp(\frac{v+32}{-10})}$$

$$\alpha_n = 0.01 \frac{v+52}{1-\exp(\frac{v+52}{-10})} \qquad \beta_n = 0.125\exp(\frac{v+62}{80})$$

Q3: Sodium Conductance

- Transmembrane current

$$I_m = C_m \frac{dV_m}{dt} + (V_m - V_{Na})G_{Na} + (V_m - V_K)G_K + (V_m - V_L)G_L$$



- Voltage Clamp
  - no I_C
- Chemical Clamp
  - no I_{Na}

=> $I'_m = (V_m - V_K)G_K + (V_m - V_L)G_L$

- Sodium current:

$$I'_{Na} = I_m - I'_m = (V_m - V_{Na})G_{Na}$$

$$G_{Na} = \frac{I_m - I'_m}{V_m - V_{Na}}$$

Q4:Value of G_{Na}

- Cell membrane was studied with the voltage clamp measurement with a 56 mV positive voltage step. 2.5 ms after the step the membrane current is 0.6 mA/cm^2. When the sodium current was blocked with pharmaceutical the current was 1 mA/cm^2 (again, t = 2.5 ms after the step). Also, it was observed that the flow of sodium ions could be stopped with 117 mV increase in resting membrane potential.

  What is the sodium ion conductance G_{Na} (stimulation 56 mV, 2.5 ms)?

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Q4:Value of G_{Na}

- Voltage Clamp = no I_C
- Two cases (56 mV voltage step)
  1. no chemical clamping (t=2.5 ms): $I_m = 0.6\ mA/cm^2$
  2. chemical clamping (t=2.5 ms): $I'_m = 1.0\ mA/cm^2$

$$I'_m = I_K\ (+I_{Cl})$$
$$I_m = I_K + I_{Na}\ (+I_{Cl})$$
$$\Rightarrow \quad I_{Na} = I_m - I'_m$$

- I_{Na} can be blocked with 117 mV voltage step
  $V_{Na} = V_r + 117\ mV$

- $V_m = V_r + 56mV$

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Q4:Value of G_{Na}

- G_{Na} (56 mV, 2.5 ms) =

$$G_{Na} = \frac{I_m - I'_m}{V_m - V_{Na}} \qquad = \frac{i_m - i'_m}{(V_r + 56\,\mathrm{mV}) - (V_r + 117\,\mathrm{mV})}$$

$$= \frac{0.6 - 1.0\,\mathrm{mA/cm^2}}{(56 - 117)\,\mathrm{mV}}$$

=> 65.6 S/m^2

Q5: BSM

- The body surface ECG is measured using 26 to 256 electrodes. Figure 1 represents voltages of a normal body surface ECG measured at the end of a QRS complex. What can you say about the nature of the source according to this map?

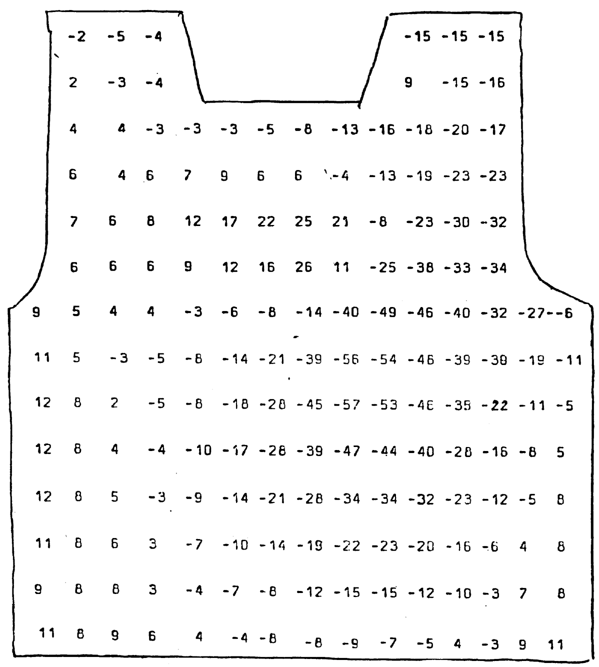

Figure 1. Anterior body surface map (BSM).

Q5: BSM

- Zero potential
- +
- -

⇒ dipolar field
⇒ eq. dipole I source
⇒ not normal BSM?
  - inverted?