Introduction to Bioelectricity

Week 6: Numerical methods of solving differential equations
Lecture 6.4: Solving Hodgkin-Huxley

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Week 6: Numerical methods

- Lecture 6.4: Solving Hodgkin-Huxley

Outside the cell

\[ \begin{align*}
C_m & \quad \text{Outside the cell} \\
V_K & \quad \text{Inside the cell} \\
V_{Na} & \\
V_L & \\
G_K & \\
G_{Na} & \\
G_L & \\
\end{align*} \]

\[ V_{m(z,t)} \]

Time (ms)
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• Go back to the literature:
  • Over 16,000 citations
  • Nobel Prize
  • Actually very very well written
  • Go read it!
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• Two ways to solve HH equation:
  • Membrane action potential (26)

\[ J_m = \]

\[ C_m \frac{\partial V_m}{\partial t} + G_{K^+} n^4 (V_m - V_{K^+}) + G_{Na^+} m^3 h (V_m - V_{Na^+}) + G_L (V_m - V_L) \]

• Propagated action potential (30)

\[ \frac{1}{v^2 2\pi a (r_o + r_i)} \frac{d^2 V_m(z, t)}{dt^2} = \]

\[ C_m \frac{dV_m}{dt} + G_{K^+} n^4 (V_m - V_{K^+}) + G_{Na^+} m^3 h (V_m - V_{Na^+}) + G_L (V_m - V_L) \]

• What is the velocity \( v \)?

• Which to solve?
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• Recall:
  • Electrically large cells (propagating potentials)
  • Vs. electrically small cells (membrane potentials)
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- Solving the membrane action potential (26)

\[ J_m = \]

\[ C_m \frac{\partial V_m}{\partial t} + G_{K^+} n^4 \left( V_m - V_{K^+} \right) + G_{Na^+} m^3 h \left( V_m - V_{Na^+} \right) + G_L \left( V_m - V_L \right) \]

- Rearranging (26)

\[ \frac{\partial V_m}{\partial t} = \]

\[ \frac{1}{C_m} \left( J_m - G_{K^+} n^4 \left( V_m - V_{K^+} \right) + G_{Na^+} m^3 h \left( V_m - V_{Na^+} \right) + G_L \left( V_m - V_L \right) \right) \]

- (26) is a 1\textsuperscript{st} order ODE

- Four unknowns: J\textsubscript{m}, m, n, & h
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- First equation \( U_1 \) (26)

\[
\frac{\partial V_m}{\partial t} = \frac{1}{C_m} \left( J_m - G_{K^+} n^4 (V_m - V_{K^+}) + G_{Na^+} m^3 h (V_m - V_{Na^+}) + G_L (V_m - V_L) \right)
\]

- Second equation \( U_2 \) (7)

\[
\frac{\partial n}{\partial t} = \alpha_n (1 - n) - \beta_n n
\]

- Third equation \( U_3 \) (15)

\[
\frac{\partial m}{\partial t} = \alpha_m (1 - m) - \beta_m m
\]

- Fourth equation \( U_4 \) (16)

\[
\frac{\partial h}{\partial t} = \alpha_h (1 - h) - \beta_h h
\]
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- **Alphas and betas**
  
  - For $n$ (12, 13)
    
    \[
    \alpha_n = \frac{0.01(V_m + 10)}{e^{\frac{V_m + 10}{10} - 1}}
    \]
    \[
    \beta_n = 0.125e^{\frac{V_m}{80}}
    \]
  
  - For $m$ (20, 21)
    
    \[
    \alpha_m = \frac{0.1(V_m + 25)}{e^{\frac{V_m + 25}{10} - 1}}
    \]
    \[
    \beta_m = 4e^{\frac{V_m}{18}}
    \]
  
  - For $h$ (23, 24)
    
    \[
    \alpha_h = 0.07e^{\frac{V_m}{20}}
    \]
    \[
    \beta_h = \frac{1}{e^{\frac{V_m + 30}{10} + 1}}
    \]
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- Constants from page 520

\[
\begin{align*}
\overline{G}_{K^+} & = 36 \text{ ms/cm}^2 \\
\overline{G}_{Na^+} & = 120 \text{ ms/cm}^2 \\
G_L & = 0.3 \text{ ms/cm}^2 \\
V_{K^+} & = 12 \text{ mV} \\
V_{Na^+} & = -115 \text{ mV} \\
V_L & = -10.613 \text{ mV} \\
C_m & = 1 \text{ mF/cm}^2 
\end{align*}
\]

- Note \( V_m = -V_m \)
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- Four equations

\[
U'_1 = \frac{1}{C_m} \left( J_m - G_{K^+} u_2^4 (u_1 - V_{K^+}) + G_{Na^+} u_3^3 u_4 (u_1 - V_{Na^+}) + G_L (u_1 - V_L) \right)
\]

\[
U'_2 = \alpha_n (1 - u_2) - \beta_n u_2
\]

\[
U'_3 = \alpha_m (1 - u_3) - \beta_m u_3
\]

\[
U'_4 = \alpha_h (1 - u_4) - \beta_h u_4
\]

- Initial condition for current stimulus

\[
V_m = 0, \quad J_m = J_{m0}, \quad t_1 \leq t \leq t_2
\]

- Initial condition for PSP

\[
V_m = V_{m0}, \quad J_m = 0
\]
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- Four equations

\[
\begin{align*}
U'_1 &= \frac{1}{C_m} \left( J_m - G_{K^+} u_2^4 (u_1 - V_{K^+}) + G_{Na^+} u_3^3 u_4 (u_1 - V_{Na^+}) + G_L (u_1 - V_L) \right) \\
U'_2 &= \alpha_n (1 - u_2) - \beta_n u_2 \\
U'_3 &= \alpha_m (1 - u_3) - \beta_m u_3 \\
U'_4 &= \alpha_h (1 - u_4) - \beta_h u_4
\end{align*}
\]

- Initial values

\[
\begin{align*}
u_{0,1} &= V_{m_0} \\
u_{0,2} &= \frac{\alpha_n}{\alpha_n + \beta_n} \bigg|_{V_{m_0}} \\
u_{0,3} &= \frac{\alpha_m}{\alpha_m + \beta_m} \bigg|_{V_{m_0}} \\
u_{0,4} &= \frac{\alpha_h}{\alpha_h + \beta_h} \bigg|_{V_{m_0}}
\end{align*}
\]
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- 4th order Runge-Kutta solution of HH
- N points from 0 to N-1
- Four 1st order ODEs as functions \( U_1 \) to \( U_4 \)
- Step 1: first slope, first point, all equations

\[
\begin{align*}
k_{1,1,1} &= U_1(t_1, u_1, u_2, u_3, u_4) \\
& \quad \text{– Slope 1 at n=1 for } U_1 \\

k_{1,1,2} &= U_2(t_1, u_1, u_2, u_3, u_4) \\
& \quad \text{– Slope 1 at n=1 for } U_2 \\

k_{1,1,3} &= U_3(t_1, u_1, u_2, u_3, u_4) \\
& \quad \text{– Slope 1 at n=1 for } U_3 \\

k_{1,1,4} &= U_4(t_1, u_1, u_2, u_3, u_4) \\
& \quad \text{– Slope 1 at n=1 for } U_4 
\end{align*}
\]
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- 4\textsuperscript{th} order Runge-Kutta solution of HH
- N points from 0 to N-1
- Four 1\textsuperscript{st} order ODEs as functions $U_1$ to $U_4$
- Step 2: second slope, first point, all equations

\begin{align*}
k_{2,1,1} &= U_1 \left( t_1 + \frac{h}{2}, u_1 + \frac{h}{2} k_{1,1,1}, u_2 + \frac{h}{2} k_{1,1,2}, \ldots, u_4 + \frac{h}{2} k_{1,1,4} \right) \\
&\quad - \text{Slope 2 at } n=1 \text{ for } U_1 \\
k_{2,1,2} &= U_2 \left( t_1 + \frac{h}{2}, u_1 + \frac{h}{2} k_{1,1,1}, u_2 + \frac{h}{2} k_{1,1,2}, \ldots, u_4 + \frac{h}{2} k_{1,1,4} \right) \\
&\quad - \text{Slope 2 at } n=1 \text{ for } U_2 \\
k_{2,1,3} &= U_3 \left( t_1 + \frac{h}{2}, u_1 + \frac{h}{2} k_{1,1,1}, u_2 + \frac{h}{2} k_{1,1,2}, \ldots, u_4 + \frac{h}{2} k_{1,1,4} \right) \\
&\quad - \text{Slope 2 at } n=1 \text{ for } U_3 \\
k_{2,1,4} &= U_4 \left( t_1 + \frac{h}{2}, u_1 + \frac{h}{2} k_{1,1,1}, u_2 + \frac{h}{2} k_{1,1,2}, \ldots, u_4 + \frac{h}{2} k_{1,1,4} \right) \\
&\quad - \text{Slope 2 at } n=1 \text{ for } U_4
\end{align*}
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- 4th order Runge-Kutta solution of HH
  - N points from 0 to N-1
  - Four 1st order ODEs as functions U₁ to U₄
  - Step 3: third slope, first point, all equations
    \[ k_{3,1,1} = U₁\left( t₁ + \frac{h}{2}, u₁ + \frac{h}{2} k_{2,1,1}, u₂ + \frac{h}{2} k_{2,1,2}, \ldots, u₄ + \frac{h}{2} k_{2,1,4} \right) \]
    - Slope 3 at n=1 for U₁
    \[ k_{3,1,2} = U₂\left( t₁ + \frac{h}{2}, u₁ + \frac{h}{2} k_{2,1,1}, u₂ + \frac{h}{2} k_{2,1,2}, \ldots, u₄ + \frac{h}{2} k_{2,1,4} \right) \]
    - Slope 3 at n=1 for U₂
    \[ k_{3,1,3} = U₃\left( t₁ + \frac{h}{2}, u₁ + \frac{h}{2} k_{2,1,1}, u₂ + \frac{h}{2} k_{2,1,2}, \ldots, u₄ + \frac{h}{2} k_{2,1,4} \right) \]
    - Slope 3 at n=1 for U₃
    \[ k_{3,1,4} = U₄\left( t₁ + \frac{h}{2}, u₁ + \frac{h}{2} k_{2,1,1}, u₂ + \frac{h}{2} k_{2,1,2}, \ldots, u₄ + \frac{h}{2} k_{2,1,4} \right) \]
    - Slope 3 at n=1 for U₄
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• 4\textsuperscript{th} order Runge-Kutta solution of HH
  • N points from 0 to N-1
  • Four 1\textsuperscript{st} order ODEs as functions U_1 to U_4
  • Step 4: fourth slope, first point, all equations

\[ k_{4,1,1} = U_1 \left( t_1 + h, u_1 + hk_{3,1,1}, u_2 + hk_{3,1,2}, \ldots, u_4 + hk_{3,1,4} \right) \]
  \hspace{1cm} – Slope 4 at n=1 for U_1

\[ k_{4,1,2} = U_2 \left( t_1 + h, u_1 + hk_{3,1,1}, u_2 + hk_{3,1,2}, \ldots, u_4 + hk_{3,1,4} \right) \]
  \hspace{1cm} – Slope 4 at n=1 for U_2

\[ k_{4,1,3} = U_3 \left( t_1 + h, u_1 + hk_{3,1,1}, u_2 + hk_{3,1,2}, \ldots, u_4 + hk_{3,1,4} \right) \]
  \hspace{1cm} – Slope 4 at n=1 for U_3

\[ k_{4,1,4} = U_4 \left( t_1 + h, u_1 + hk_{3,1,1}, u_2 + hk_{3,1,2}, \ldots, u_4 + hk_{3,1,4} \right) \]
  \hspace{1cm} – Slope 4 at n=1 for U_4
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- 4th order Runge-Kutta solution of HH
  - N points from 0 to N-1
  - Four 1st order ODEs as functions $U_1$ to $U_4$
  - Step 5: average slope, first point, all equations
    \[
    \bar{k}_{1,1} = \frac{1}{6} \left( k_{1,1,1} + 2k_{2,1,1} + 2k_{3,1,1} + k_{4,1,1} \right)
    \]
    - Average slope at n=1 for $U_1$
    \[
    \bar{k}_{1,2} = \frac{1}{6} \left( k_{1,1,2} + 2k_{2,1,2} + 2k_{3,1,2} + k_{4,1,2} \right)
    \]
    - Average slope at n=1 for $U_2$
    \[
    \bar{k}_{1,3} = \frac{1}{6} \left( k_{1,1,3} + 2k_{2,1,3} + 2k_{3,1,3} + k_{4,1,3} \right)
    \]
    - Average slope at n=1 for $U_3$
    \[
    \bar{k}_{1,4} = \frac{1}{6} \left( k_{1,1,4} + 2k_{2,1,4} + 2k_{3,1,4} + k_{4,1,4} \right)
    \]
    - Average slope at n=1 for $U_4$
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- 4th order Runge-Kutta solution of HH
  - N points from 0 to N-1
  - Four 1st order ODEs as functions U_1 to U_4
  - Step 6: calculate $u_{n+1,m}$

  $u_{2,1} = u_{1,1} + h\bar{k}_{1,1}$
  - Next point for $U_1$

  $u_{2,2} = u_{1,2} + h\bar{k}_{1,2}$
  - Next point for $U_2$

  $u_{2,3} = u_{1,3} + h\bar{k}_{1,3}$
  - Next point for $U_3$

  $u_{2,4} = u_{1,4} + h\bar{k}_{1,4}$
  - Next point for $U_4$
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- 4\textsuperscript{th} order Runge-Kutta solution of HH
  - N points from 0 to N-1
  - Four 1\textsuperscript{st} order ODEs as functions $U_1$ to $U_4$
  - Step 7: repeat for $u_{n+2,m}$ through $u_{N-1,m}$
  - Extract the membrane voltage
    \[
    V_m = -u_{n,1}\bigg|_{n=0}^{N-1}
    \]
  - Extract the potassium current
    \[
    I_{K^+} = \bar{G}_{K^+} u_{n,2}^4\bigg|_{n=0}^{N-1}
    \]
  - Extract the sodium current
    \[
    I_{Na^+} = \bar{G}_{Na^+} u_{n,3}\bigg|_{n=0}^{N-1} u_{n,4}\bigg|_{n=0}^{N-1}
    \]
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- 4th order RK solution of HH ($V_{\text{stim}}$)
Lecture 6.4: Solving Hodgkin-Huxley

- 4\textsuperscript{th} order RK solution of HH ($I_{\text{stim}}$)