BIOELECTRIC/BIOMAGNETIC PHENOMENA: ION CHANNELS TO ORGAN FUNCTION

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Ion channels; neurophysiology applications; general applications to other organs

Topics

- Scales in space and time for the bioelectric forward and inverse problems
- Interdisciplinary instrumentation development

The Electrocardiograph, the magnetocardiograph, ETC

Examples of the Inverse Problem

- Determination of an effective source for the electrical activity of the heart from the ECG or MCG; estimation of the epicardial potentials from the thoracic potential or magnetic field maps.
- Determination of an effective source for the electrical activity of the brain from the EEG or MEG; sharpening of cortical potentials/fields from scalp measurements.
- Understanding the complexities of the electrical activity of the human gastrointestinal system from measurements of the magnetoenterogram (MENG).

The Einthoven triangle, dipoles in the brain

Examples of the Forward Problem

- Prediction of the ECG or MCG from a description of the cardiac sources.
- Estimation of the effects of the CSF, the skull, and scalp on the EEG or MEG.
- Coupled-oscillator models of the fields produced by intestinal electrical activity .

The Ultimate Inverse Problem

- Identification of cellular mechanisms and channel-specific targets from global behavior for therapeutic intervention.
- Identify channel-level effects from the ECG for arrhythmiagenesis and control.

The Ultimate Forward Problem

- Prediction of global functional consequences of channel-level defects and interventions.
- Predict the ECG from knowledge of channel protein structure.

The Problems of Scale in Space and Time

Fibrillation involves the entire heart and has spatial and temporal scales of 10 cm and seconds, but is also governed by the nanosecond conformational changes of molecules with sizes of several nanometers. Rational cardiac drug therapy requires an understanding of the spatial and temporal breadth of the arrhythmia process, including insights as to how the binding of a drug on a specific conformation of a particular channel affects the properties of a macroscopic event.

We need to span experimentally and theoretically a scale of 10^{24} in volume and 10^{9} in time!

The Ultimate Problem of Cardiac Modeling

Development of new instruments and techniques can require long-term, multi-disciplinary efforts

- PET. SPECT, MRI, fMRi
- MEG, MCG, MENG
- Cardiac fibrillation and defibrillation
- Laser surgery and the free-electron laser
- Tunneling microscope, proximity probes...
- Protein folding and dynamics

Recommendations

- Researchers and the NIH both should be aware of the computational and experimental challenges posed by the large ranges in space and time in biological systems.
- The NIH should be sensitive to the special needs of multi-disciplinary research programs.
- NIH should support development and evaluation of new instrumentation whose applicability to biomedicine needs to be determined.

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