Some very basic electrophysiology

Intracellular fluid:
10 mM Na\(^+\), 140 mM K\(^+\), etc.

Extracellular fluid:
140 mM Na\(^+\), 4 mM K\(^+\), etc.
Ion gradient plus selective permeability generates electrical potential difference

Concentration gradient pushes $K^+$ out.

$K^+$

Inside cell

Outside cell

Ion gradient plus selective permeability generates electrical potential difference

Concentration pushes $K^+$ out → charge imbalance → electric field. This is the membrane potential, in all cells, negative on the inside.

$K^+$

Inside cell

Outside cell
Ion gradient plus selective permeability generates electrical potential difference

Concentration pushes $K^+$ out → charge imbalance → electric field which pulls $K^+$ back. Equilibrium occurs when chemical and electrical forces balance, so membrane potential is predictable.

The Nernst Equation:-

1. $V = -(RT/ZF) \log_e ([\text{ion}]_{\text{in}}/ [\text{ion}]_{\text{out}})$
2. $V = -61 \log \text{(ion ratio)}$ millivolts
3. Predicts the membrane potential for an ideal situation with a membrane permeable to a single ion species.
4. Ten fold ratio $\rightarrow$ -60 mV approx.
5. Thirty fold ratio $\rightarrow$ -90 mV approx.
6. Resting muscle cells are mainly permeable to $K^+$ ions, so resting membrane potential is close to the Nernst potential for $K^+$. 

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Inside cell

$K^+$

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Resting Membrane Potentials

- Skeletal muscle: $V_m = -90 \text{ mV}$
- Cardiac muscle: $V_m = -90 \text{ mV}$
- Spinal motor neurons: $V_m = -70 \text{ mV}$
- Gland epithelia: $V_m = -50 \text{ mV}$
- If these numbers seem small (millivolts), remember that membranes are thin (7 nm), so the electric field pulling ions through channels in the membrane is about 10 million volts per meter. Air flashes over at about one tenth that field strength.

Action Potentials

- The basic unit of activity in excitable tissues (nerve, muscle) is the action potential.
- The action potential consists of a swift change in membrane potential, going from negative through zero briefly to a positive value and back again.
- This is achieved by switching the membrane permeability from being predominantly $K^+$ permeable to being briefly $Na^+$ permeable, without altering the concentrations of ions inside or outside the membrane.
Action Potential of Nerve Axons

- **Depolarization**: Voltage-gated Na⁺ channels turn on for about a millisecond, letting + charge into the cell and pushing the membrane potential +ve.
- **Repolarization**: The Na⁺ channels turn off (time) and K⁺ channels turn on, allowing more + charge out, and pushing the membrane potential back -ve.
- **After-hyperpolarization**: in many neurons, the K⁺ conductance persists for some time after the completion of the spike.
- **Na⁺-K⁺ pump restores the tiny reduction in ionic gradients caused by the flux of ions**
My Favourite Howler

Seen over and over in first year biology exams is this picture of an action potential:-
“The sodium rushes in and the potassium rushes out, reversing the ion gradients, so the membrane potential reverses. Then the sodium pump gets going and fixes the gradients so the membrane potential returns.”

Sorry, that would take an hour!.. And many action potentials take a millisecond. Of course, the concentrations don’t change, the ion permeabilities do, by opening channels.

Cardiac versus Skeletal Muscle APs

![Cardiac versus Skeletal Muscle APs](chart_image)
Why that funny action potential?

Skeletal muscle:-
• one action potential gives a brief twitch
• repeated action potentials give contraction
• increasing frequency of action potentials gives increasing force of contraction (up to a maximum)

Cardiac muscle:-
• must give a full contraction on each action potential

Ventricular Muscle Action Potential
Features of Cardiac Action Potential

- Phase 0: the spike current carried by voltage-sensitive Na+ channels (as nerve, skeletal muscle)
- Phase 1: partial repolarization is inactivation of the voltage-sensitive Na+ channels
- Phase 2: plateau held near zero by current through Ca channels (drug actions here...).
- Phase 3: repolarization as Ca channels inactivate
- Phase 4: slow ramp up to threshold - prominent in pacemaker and atrial muscle: suppressed by overdrive normally in ventricles...

The Electrocardiogram (ECG)

0.2 sec
Recording from Cells

Action Potential
Intracellular & Extracellular Recording

**Intracellular recordings:**
- Show a negative resting membrane potential, and
- a positive going action potential

**Extracellular recordings:**
- Don’t show resting membrane potential at all, and
- show negative pulse as depolarization passes, and
- positive pulse as repolarization passes the recording electrode...

The Electrocardiogram (ECG)

- The ECG is a DISTANT extracellular recording, as it is recorded from electrodes on the body surface
- The electrodes are so far away that the heart looks like a compact electric dipole (e.g. an Eveready D cell sitting there in the body)
- The dipole (the D cell) rotates around and turns on and off as events take place in the cardiac cycle.
The Electrocardiogram (ECG)

- **P wave**: Atrial depolarization
- **QRS complex**: Ventricular depolarization
- **T wave**: Ventricular repolarization

0.2 sec
The Electrocardiogram (ECG)

Ventricular Action Potential & ECG
At rest in diastole, the heart appears electrically neutral.
The Electrocardiogram (ECG)

Depolarization approaching gives upward deflection.

Depolarized in systole, the heart appears electrically neutral.
The Electrocardiogram (ECG)

Repolarization retreating gives upward deflection.

At rest in diastole, the heart appears electrically neutral.
The Electrocardiogram (ECG)

- Notice that the wave of depolarization looks, to a distant recording system, like an electric dipole: -

- How does the wave of depolarization impact on a particular recording lead?

- Depends on:-
  - Angle between recording axis and dipole
  - Magnitude of the electrical dipole
  - Physics of the intervening medium (ignore!!!)
Visualizing vector resolution...

QRS events seen in 3 recording axes...
Labelling bits of wire...

What do those + and - signs mean?
• The + electrode is always electrically +ve?
• If you make it negative the equipment, or the universe, explodes?

No! If you:-
• make the + go +ve, the recording goes up
• make the + go -ve, the recording goes down

QRS events seen in 3 recording axes...
QRS events seen in 3 recording axes...

Einthoven’s Triangle: Bipolar Limb Leads

R. arm - Lead I + L. arm

L. leg

Lead II

Lead III
(augmented) Unipolar Limb Leads

- aVR +
- Lead I +
- Lead II
- Lead III
- aVL +
- aVF +

II, III and aVF look at the inferior surface

Coronal vs Horizontal Plane

- The 6 limb leads are in the coronal plane: -
  - bipolar limb leads I, II and III
  - unipolar limb leads aVR, aVL and aVF

- In the horizontal plane are 6 precordial (chest) leads: -
  - V1, V2, V3, V4, V5, V6
  - these are also unipolar, hence the V in the label...
The shape of the QRS complex?

The vector of depolarization sweeps around during depolarization, but it is convenient to think in terms of three phases, or snapshots (and interpolate when you really need to): -

- early: septum running towards right and up (odd!)
- mid: apex running left, down and back
- late: base running up and often R
Generation of the QRS complex

Diastole

Generation of the QRS complex

Early QRS
Generation of the QRS complex

Mid QRS

Generation of the QRS complex

Late QRS
Why?

- Above has been some elementary background to help with seeing how the wave shapes in the QRS vary between leads, and between subjects…

- But what is it all for…?
Uses of the EGC in medicine...

There are many, but let us look at the ECG in the diagnosis of myocardial infarction...

ECG Pathology

Important changes in the ECG associated with myocardial infarction are:

- ST segment elevations and depressions (current of injury)
- Q waves (vector changes from loss of part of the myocardium)
- T wave inversion (timing changes in repolarization)
Currents of Injury

- Injured cardiac muscle cells will have different membrane potential from their healthy neighbours.
- This potential difference drives electric currents: through the heart and through the patient’s body.
- These electrical effects show up as ST segment elevations and depressions in the ECG.
- The current of injury is an important and early sign of myocardial injury.

Current of injury: ST segment shifts

- ST segment *elevation* is seen on leads facing an injury (e.g. chest leads V1-V4 for an antero-septal infarct; II, III and aVF for an inferior infarct).
- ST segment *depression* is seen in leads opposite to the injury.
Action Potential of **Injured** Muscle

**Membrane Potential (mV)**

- **Usually fully depolarizes**
- **May have slower depolarization**
- **May start repolarizing early**
- **Does not fully repolarize**

**Injured** Muscle not fully Repolarized

**Injury looks relatively -ve**

Time
**Injured** Muscle Depolarizes O.K.

Injury looks neutral

**Injury** Repolarizes Incompletely

Injury looks relatively -ve
ST segment Elevation

- The injured muscle fails to fully repolarize.
- Therefore its surface is negative, displacing the trace downwards (during diastole).
- But it will depolarize essentially completely, so the heart looks neutral in the ST segment, which comes out on the (real) zero line of the recording.
- By contrast with the surrounding depressed trace, the ST segment looks “elevated”
- And vice versa: in leads facing away from the injury, the ST segment is “depressed”

Q waves

- Q waves are initial downgoing deflections in the QRS complex.
- Small Q waves occur in many leads
- They are mostly due to the early septal phase of depolarization

Large (or prolonged) Q waves in leads which should not have them are a serious sign:
- an electrical window in the heart, which means
- dead/dying muscle of a myocardial infarct.
Q waves in Full Thickness Infarct

- Infarcts render a region of muscle non-functional, both electrically and mechanically.
- This destroys the symmetry of spread of depolarization, revealing the dipole of the opposite portions of the ventricle.
- These vector effects are conveniently recognised as the appearance of Q waves in leads related to the anatomy of the injury.
- Since small Q waves are normal, there are criteria for significant Q waves (depth, time, leads...).
T waves

- T waves are a puzzle
- Notice in the lab that T waves are usually upright, whereas you would predict (after a little thought) that they should be opposite in direction to the main deflection of the QRS...

Ventricular Repolarization - T wave

Depolarization moves inside → out.
Repolarization moves outside → in.
Note AP durations.

Remember the conducting system! Depol. starts inside.
The Puzzle of T waves

• Commonsense suggests T waves should be of opposite polarity to the QRS (depol. vs. repol.).
• However the direction of movement of the repolarization event is basically opposite to depol.
• This is caused by timing differences in layers of myocardium.
• The T vector will depend on the subtle gradation of action potential durations.
• This is often disturbed in myocardial ischaemia and infarction, leading to inverted T waves.

What is the ECG useful for?

• Detection of myocardial ischaemia/infarction - very diagnostic when signs present, but occasionally misses serious pathology {high specificity, low-ish sensitivity}.
• Detection and analysis of arrhythmias, both acutely and for monitoring in CCU.
• Many different incidental findings like drug effects, electrolyte and metabolic abnormalities...
• It’s quick, it’s cheap, it’s often helpful, and it kills no patients...
The good news...

You do not have to be ECG experts till 2003

Cheers,
Simon.