Dr Katharine Dibb

Lecture 1 - Membrane Excitability

Lecture 2 - Cardiac Electrophysiology

Case studies 4 and 5

Animations from Wikipedia
Learning objectives

• How is the heart beat generated?
• How does excitation propagate through the heart?
• What are the regional differences in the cardiac action potential?
• Effects of the autonomic nervous system
How membrane excitation links to other lectures

Membrane excitation → Cardiac Action Potential → L-type Ca current → Spread of excitation through the heart → Initiation of Excitation Contraction Coupling → Cardiac ECG
The sino-atrial node and the origin of the heart beat

Monfredi et al. Pacing and Clinical Electrophysiology 33; 1392-1406
How do sino-atrial node cells beat spontaneously?

- **Resting** membrane potential
- **Threshold potential**
- **Ca^{2+} influx**
- **K^{+} efflux**
- **Pacemaker potential**
What ion channels are responsible for the pacemaker potential?

 Ion channels responsible for the pacemaker potential:

- $\text{K}^+$ efflux
- $\text{Ca}^{2+}$ influx

Decay of the pacemaker potential:

- Opening of inward currents: $I_f$ - ‘funny’ current - Na influx (slow)
- Ca channels open (T-type and L-type)
- Closing of outward currents: K channels slowly close
Properties of the sino-atrial node (SAN) action potential

In comparison to the ventricular action potential

Slow to rise

Small amplitude

Slow conduction

fast Na channels, slower Ca channels
How does excitation spread through the heart? - Structure

Cardiac muscle cells form a syncytium
How does excitation spread through the heart? - Structure

Human ventricle

Intercalated disc

ID: intercalated disc

Structural and electrical coupling between cells


Professor Giorgio Gabella, Wellcome Images
The electrical coupling: Gap Junctions

Gap between two cells

Gap Junction

Connexin subunit
Six subunits form an ion channel

Channel formed by the gap junction

Closure limits cell death after MI
How does excitation spread through the heart? - Currents

Cell-to-cell spread of the cardiac action potential

Gap junction

Local circuit currents
Cell-to-cell spread of the cardiac action potential

Gap junction

Refractory

Local circuit currents
The cardiac conduction system

The conduction system delivers electrical excitation to the heart

Images from wikimedia

SAN

Left & right atria (atria contract) → AVN (delay) → Bundle of HIS → Left & right bundle branches → Purkinje system → ventricular myocardium (ventricles contract)
Factors controlling conduction rate

The speed of conduction is fastest when:-

Cells are wider - lower axial electrical resistance
(purkinje fibre vs SAN)

Action potentials are large and rapid to rise -
generate large propagating currents
(rate of ion influx)
The action potential of the sino-atrial node

Ca^{2+} influx

Small diameter cells
Action potential: slow and small

Conduction velocity
0.05 m/s
The action potential of the atrial myocardium

- True resting membrane potential
- Depolarization by rapid Na entry
- Brief plateau (phase 2)
- The APD in the atria is shorter than the ventricle
The action potential of the atrioventricular node (AVN)

Ca\(^{2+}\) influx

K\(^+\) efflux

Threshold potential

Pacemaker potential

Conduction velocity 0.05 m/s

Why does the action potential arise before threshold is reached?

Only conducting path between the atria and ventricles - slow (delay)
small diameter
action potential slow to rise
complex pathway
The action potential of the purkinje fibres

- **Threshold potential**
- **Pacemaker potential (weak)**
  - **Ca\(^{2+}\) influx**
  - **Na\(^{+}\) influx**
  - **K\(^{+}\) efflux**

```
0 mV
```

- **“Resting” membrane potential**
- **Conduction velocity** 4 m/s

- **-80 mV**
  - **Pacemaker potential (weak)**

- **Conduction velocity**
  - Largest cells in the heart
  - Rapid depolarization
  - Refractory
The action potential of the ventricular myocyte

- **Ca\(^{2+}\) influx**
- **K\(^{+}\) efflux**
- **Na\(^{+}\) influx**

Resting membrane potential

Conduction velocity 1 m/s
### Summary of the characteristics of cells in various regions

<table>
<thead>
<tr>
<th>Area of heart</th>
<th>Cell diameter (microns)</th>
<th>Fast Na+ channels</th>
<th>Gap junction proteins</th>
<th>Speed of impulse conduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA Node</td>
<td>&lt; 10</td>
<td>(+)</td>
<td>+</td>
<td>0.05 m/s</td>
</tr>
<tr>
<td>Atrial muscle</td>
<td>15</td>
<td>+++</td>
<td>++</td>
<td>1 m/s</td>
</tr>
<tr>
<td>AV Node</td>
<td>&lt; 10</td>
<td>(+)</td>
<td>+</td>
<td>0.05 m/s</td>
</tr>
<tr>
<td>Purkinje fibres</td>
<td>40</td>
<td>+++++</td>
<td>++</td>
<td>4 m/s</td>
</tr>
<tr>
<td>Ventricular muscle</td>
<td>20</td>
<td>++</td>
<td>++</td>
<td>1 m/s</td>
</tr>
</tbody>
</table>
How does electrical activity relate to the ECG?

ECG electrodes only pick up current if voltage difference points towards them.

Depolarization wave travelling toward a positive electrode = positive deflection
Depolarization wave travelling away from a positive electrode = negative deflection.
Repolarization wave travelling toward a positive electrode = negative deflection.
Repolarization wave travelling away from a positive electrode = positive deflection.
Perpendicular to an electrode = no deflection.
Amplitude (V) is directly related to the mass of tissue.
How does the action potential relate to the ECG?
Effects of the autonomic nervous system on the heart

Autonomic nervous system
- Sympathetic
- Parasympathetic (vagal nerves)

Heart rate
- ↑ Sympathetic
- ↓ Parasympathetic

AVN conduction speed
- ↑ Sympathetic
- ↓ Parasympathetic

AP duration
- ↓ Sympathetic
- ↑ Parasympathetic

Sympathetic chains
- Vagus nerve (ACh)
- Purkinje fibres
The **sympathetic nervous system**

**Sinoatrial node**

Noradrenaline $\rightarrow$ $\beta$-receptors $\rightarrow$ ↑cAMP

↑ depolarizing currents e.g. Funny & Ca current

Deactivated repolarising (K) currents more quickly

**Tachycardia**

Stimulation of sympathetic nerve supply
The **sympathetic** nervous system

**Atrioventricular node**

Activates $\beta$-receptors in the AVN $\Rightarrow$ increased conduction speed

**Atria and ventricle**

Atrial and ventricular action potential is shortened due to increased repolarising (K) current
Effects of the autonomic nervous system on the heart

Autonomic nervous system

- Sympathetic
  - Heart rate
  - AVN conduction speed
  - AP duration

- Parasympathetic (vagal nerves)
  - Heart rate
  - AVN conduction speed

N.B. The ventricular myocardium does not receive parasympathetic innervation

Vagus nerve (ACh)

Sympathetic chains

Purkinje fibres
The parasympathetic nervous system

Sinoatrial node

ACh acts on muscarinic receptors $K^+$-channel opening - causes hyperpolarization and a pacemaker potential of reduced slope.

Bradycardia

Threshold potential

Pacemaker potential

Stimulation of vagus nerve
The parasympathetic nervous system

Atrioventricular node
Reduces conduction through the AVN $\Rightarrow$ strong enough heart block

Autonomic nerves and the normal heart rate

Nerve fibres are always active $\Rightarrow$ pacemaker firing continuously modified

Parasympathetic predominates at rest

atropine + propranolol = intrinsic rate (≈105 beats per minute)
Learning objectives

• How is the heart beat generated?
• How does excitation propagate through the heart?
• What are the regional differences in the cardiac action potential?
• Effects of the autonomic nervous system