

Capacitance, Membrane

Definition

The membrane capacitance results from the fact that the plasma membrane acts as a capacitor: the phospholipid bilayer is a thin insulator separating two electrolytic media, the extracellular space and the cytoplasm. The membrane capacitance is proportional to the cell surface area and, together with the membrane resistance, determines the membrane time constant which dictates how fast the cell membrane potential responds to the flow of ion channel currents.

Detailed Description

Membrane capacitance is the electrical capacitance associated with a biological membrane, expressed in units of Farads (F). The electrical capacitance of a biological membrane results from the membrane composition of a bilayer of mostly phospholipids that form an insulating matrix to which proteins are attached or embedded. The total membrane capacitance c_m of a cell is a quantity directly proportional to the membrane surface area and the dielectric properties of the membrane, provided that the thickness of the membrane is constant. Thus, the total membrane capacitance is $c_m = C_m A$, where C_m is the specific membrane capacitance (typically expressed in units of $\mu\text{F}/\text{cm}^2$) and A is the area.

Because of its linear relationship with cell surface area, capacitance is often measured experimentally as a way of determining cell area and thus cell size if the cell geometry is simple, for example, spherical or cylindrical (Streit and Lux 1987), or changes in membrane surface area (Neher and Marty 1982). These changes can be global or local, for example, when cells grow dendritic branches or add or remove membrane due to endocytosis or exocytosis at a synapse. Cell capacitance may also change due to local membrane thickness variations at lipid rafts, which are ~10 % thicker than non-raft membranes (Alberts et al. 2008).

Because membrane capacitance determines the time constant of a neuron ($\tau_m = r_m c_m$), it plays an important role in the integration of the electrical inputs a neuron receives. It also determines the propagation velocity of action potentials which is inversely proportional to c_m (Matsumoto and Tasaki 1977). Finally, cell capacitance is a crucial parameter in detailed conductance-based computational models, which are widely used to understand the activity and output of complex neuronal systems (Koch 1999).

To determine the exact surface area of a cell, a precise value of the specific membrane capacitance is required. A number of different methods can be used to determine the exact capacitance value, but in such calculations the fact that cell membrane surface - particularly in neurons - is rarely restricted to simple shapes should always be considered. In fact, the area of neurons is almost always distributed over surfaces that are intricate and complex, which affects the accuracy of capacitance measurements.

Measurement of Membrane Capacitance

A capacitor accumulates charge proportional to the voltage across it:

$$Q = c \cdot \Delta V \tag{1}$$

The rate of change of the capacitive charge is the capacitive current:

$$I_C = \frac{dQ}{dt} = c \frac{dV}{dt} \tag{2}$$

From this basic concept, several time-domain methods have been derived to measure the capacitance of a neuron, which essentially measure I_C under voltage clamp conditions.

1. Voltage ramp method. If a voltage ramp with slope dV/dt is applied to a capacitor in parallel with a resistor (an RC circuit), the current response generated includes a step whose amplitude is equal to the capacitive current I_c (Fig. 1a, red), followed by a ramp proportional to the conductance ($1/R$) of the circuit (Fig. 1a). From eq. 2, c can then be calculated.
2. Voltage step method. If a brief voltage step is applied, an initial current transient will be generated which is primarily the current that charges the capacitor (Fig. 1b). By integrating the area under the curve of this transient current ($\int I_c dt$, Fig. 1b, red), the charge Q can be measured and then used to determine c from Eq. 1.
3. Voltage sine wave method. If a sinusoidal voltage waveform is applied to an RC circuit, the current response will also be sinusoidal but shifted relative to the voltage input by a constant time (Δt , Fig. 1c, red). The resulting phase change is related to the capacitance of the circuit (Neef et al. 2007). Lock-in amplifiers in combination with voltage clamp devices generate outputs that are proportional to both impedance and phase, and thus capacitance can be determined (Neher and Marty 1982; Neef et al. 2007).

All voltage clamp methods give accurate measurements of capacitance in cells that are electrically compact (isopotential) and therefore can be described as single-compartment RC circuits. This is the case for many cell types, but is almost never true for neurons whose extensive processes (dendrites and axon) render them non-isopotential. For non-isopotential cells all these methods are inaccurate. Intuitively, the reason for this inaccuracy is that, at locations distal from the point of current injection (i.e., the site of electrode impalement), the membrane voltage decays along the processes relative to the command voltage. The inability to maintain a constant voltage throughout the cell is referred to as the space clamp problem.

As an example, for a simple cell that can be represented by two compartments, one near and one far from the point of current injection, connected by a resistor, r_a , the total capacitance measured with voltage clamp methods can be approximated by

$$c_m = c_n + c_f \frac{1}{(1 + r_a/r_f)^2} \tag{3}$$

where c_n is the capacitance of the compartment near the point of current injection and c_f and r_f are the distal compartment capacitance and membrane resistance, respectively (Golowasch et al. 2009). Thus, the farther the distal compartment, and the lower its membrane resistance, the bigger the error in total capacitance. For cells with more complex morphological structure than two connected compartments, the measured capacitance deviates from the approximation given by Eq. 3. An estimate of the capacitance measured in voltage clamp in cells of more complex morphology is provided by Taylor (2012).

4. Current clamp method. A much more accurate method for measuring capacitance is current clamp pulses. It is appropriate even for cells that have their capacitance distributed over several distal compartments (Golowasch et al. 2009). The principle behind this method is that during a current pulse currents rapidly flow axially along the different cable-like structures of a cell and "equalize" the voltage. These currents generate voltage changes that can be described by multiple exponential terms with short time constants (Rall 1977; Holmes et al. 1992). Meanwhile, the membrane is slowly charged homogeneously over the entire surface of the cell, a process that can be characterized by an additional exponential change of the membrane potential, which has the slowest time constant of all the exponential terms. Thus, the membrane potential V_m can be described as a sum of exponential terms plus the resting potential V_{rest} :

$$V_m(t) = V_{rest} + \sum_{i=0}^{\infty} V_i \left(1 - e^{-t/\tau_i}\right) \tag{4}$$

By dividing Eq. 4 through by the external current I_{ext} , one obtains a series of resistive terms $R_i = V_i / I_{ext}$. The time constant of the slowest exponential term τ_0 is equal to the product $\tau_m = r_m c_m$, and r_m can be determined as the resistive component of the slowest exponential term (R_o), and $c_m = \tau_m / r_m$ (Golowasch et al. 2009).

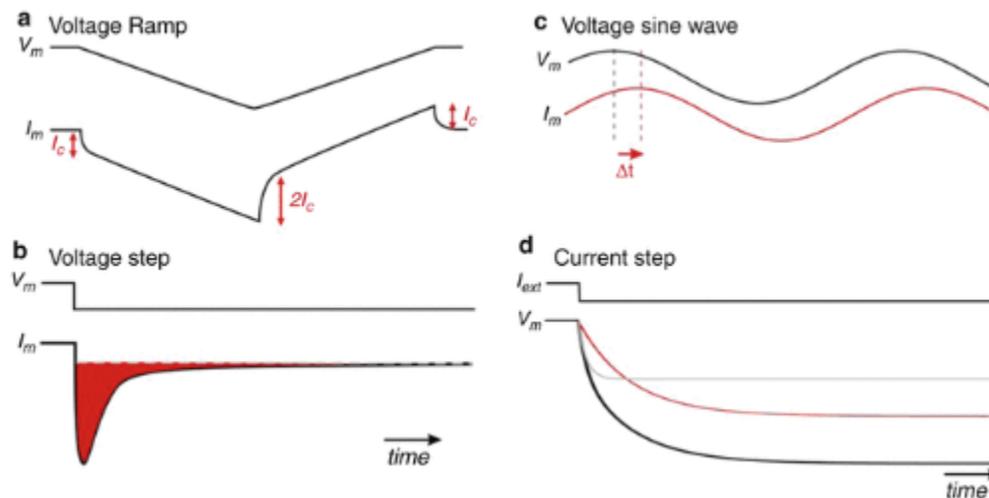


Fig. 1 Capacitance measurement protocols. Top

traces show stimulation waveform. (a-c), voltage clamp protocols. (d), current clamp protocol. Time scales for the different protocols differ, with (a) and (d) typically being slower (seconds) than (b) and (c) (tens to hundreds of milliseconds). Red indicates the response element relevant for the measurement of capacitance

All these methods rely on manipulating voltage in a range where only passive properties of the cell are involved. Any activation of voltage-gated currents will introduce significant errors in the capacitance estimate (Golowasch et al. 2009; White and Hooper 2013).

Specific Membrane Capacitance

The value most used is $1 \mu\text{F}/\text{cm}^2$, which most likely stems from the first measurements ever made in the famous series of experiments of Hodgkin, Huxley, and Katz published in 1952 (Hodgkin and Huxley 1952; Hodgkin et al. 1952). They in fact measured values over a range of 0.8 and $1.5 \mu\text{F}/\text{cm}^2$, with a mean of $0.9 \mu\text{F}/\text{cm}^2$ (Hodgkin et al. 1952), but then used $1 \mu\text{F}/\text{cm}^2$ to simplify the complex calculation used for their final and seminal paper (Hodgkin and Huxley 1952). Later on it was shown that most cells do not have a smooth membrane whose area can be measured optically by making a simplifying geometric assumption (e.g., a perfect cylinder or a perfect sphere). Instead, most cell membranes have a certain degree of rugosity (lack of smoothness), which could lead to an overestimate of the specific membrane capacitance value. Using an inflation method in the whole-cell patch clamp configuration, Solsona and collaborators (Solsona et al. 1998) determined the specific membrane capacitance value to be closer to $0.5 \mu\text{F}/\text{cm}^2$. Furthermore, it has been established that cell capacitance does not significantly vary as a function of ion channel density (Gentet et al. 2000), and the value of $0.5 \mu\text{F}/\text{cm}^2$ obtained from inflated cells is close to that measured in artificial lipid bilayers although this value also depends on lipid composition (Niles et al. 1988).

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