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Causes of Transient Instabilities in the Dynamic Clamp

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Abstract

The dynamic clamp is a widely used method for integrating mathematical models with electrophysiological experiments. This method involves measuring the membrane voltage of a cell, using it to solve computational models of ion channel dynamics in real-time, and injecting the calculated current(s) back into the cell. Limitations of this technique include those associated with single electrode current clamping and the sampling effects caused by the dynamic clamp. In this study, we show that the combination of these limitations causes transient instabilities under certain conditions. Through physical experiments and simulations, we show that dynamic clamp instability is directly related to the sampling delay and the maximum simulated conductance being injected. It is exaggerated by insufficient electrode series resistance and capacitance compensation. Increasing the sampling rate of the dynamic clamp system increases dynamic clamp stability; however, this improvement, is constrained by how well the electrode series resistance and capacitance are compensated. At present, dynamic clamp sampling rates are justified solely on the temporal dynamics of the models being simulated; here we show that faster rates increase the stable range of operation for the dynamic clamp system. In addition, we show that commonly accepted levels of resistance compensation nevertheless significantly compromise the stability of a dynamic clamp system.

Index Terms

Action potential; biological cells; control systems; nervous system

I. Introduction

The Dynamic clamp technique combines computational modeling with biological experiments. It is an extremely versatile tool that enables an experimentalist to artificially create voltage-dependent and time-dependent conductances within neurons [1]–[3] and other electrically excitable cells [4], [5]. This ability has significantly contributed to our knowledge of electrically excitable cells through the wide range of experiments it permits [6]–[8]. The dynamic clamp can be used to create new ion channels or enhance existing ion channels in excitable cells [9]–[12]. It is also frequently used to study networks of excitable cells by creating synaptic conductances that are dependent on the membrane voltage of a different, presynaptic cell [13]. Computational synaptic time constants can be modified to study their effect on network behavior [14]. Furthermore, complex synaptic conductance waveforms can

be injected to study synaptic integration [3], [15], [16]. These networks can either be exclusively biological cells [13], [17] or hybrid networks, which combine live cells and computational ones simulated by the dynamic clamp system [18]–[23].

Though the dynamic clamp technique has significantly contributed to our understanding of single neurons and networks of neurons, the method has several limitations. As with current and voltage clamping techniques, the accuracy of the dynamic clamp is limited by the constraints of injecting current and recording voltage with the same electrode. The resistance and capacitance of the electrode and electrophysiology amplifier cause measurement error and transient artifacts in the measured membrane voltage. There are techniques to ameliorate these artifacts; however, there are residual electrode effects [24]–[26]. The remaining uncompensated microelectrode series resistance causes an error in the voltage measurement used to solve computational models in the dynamic clamp, while uncompensated capacitance causes transient artifacts and affects the time course of the voltage measurement.

Another major limitation of the dynamic clamp technique is the sampling of the digital system. Dynamic clamps are predominantly discrete-time digital systems that sample the membrane voltage periodically, convert it to a digital value, and use that to solve the conductance equations being simulated in real-time. The overhead in dynamic clamp systems limits the maximum possible sampling rate, limiting the accuracy and temporal dynamics of the simulation [27]. The amount of delay is mainly determined by the hardware platform running the dynamic clamp. Dynamic clamp implementations include digitally controlled analog circuits [3], [28], dedicated digital hardware [29]–[32], and personal computer based systems running dynamic clamp software [33]–[36]. Dynamic clamp sampling rates are currently chosen based on the limits of the hardware platform being used and the temporal dynamics being simulated.

We previously quantified how the properties of voltage-dependent state variables, numerical integration time step (and the sampling delay imposed by it), and measurement noise affect numerical solution accuracy [37]. Bettencourt *et al.* further show that time step duration, integration method, jitter, and latency also affect dynamic clamp accuracy [27]. Here we focus on dynamic clamp stability. Fig. 1 shows an example of dynamic clamp instability that appears as the magnitude of an ionic current created with the dynamic clamp is increased. Similar transients have been reported by others [38]–[40]. Previously, instabilities have been described for dynamic clamp conductances whose magnitude approached the resting resistance of the cell [41], which were alleviated by low-pass filtering the membrane potential recording. While instabilities do not preclude using the dynamic clamp, they impose an upper bound on allowable conductance values, often at values less than those desired by the investigator. Preliminary reports of these results have been made in conference proceedings [42]; this paper quantifies those qualitative observations and investigates the phenomena in more depth.

II. Materials and Methods

A. Electrophysiology

Sharp intracellular microelectrode recordings were performed on neurons from the abdominal ganglia of *Aplysia californica*. The ganglia were removed from the animal, pinned to a Sylgard lined dish (Dow Corning, Midland, MI), and surgically desheathed. Experiments were performed at room temperature, in a high magnesium, low calcium solution, containing (in mM): NaCl, 330; KCl, 10; MgCl₂, 90; MgSO₄, 20; CaCl₂, 2; Hepes, 10 [43], to decrease overall neuronal activity. Fig. 2 contains a block diagram of the experimental setup. Sharp intracellular microelectrodes (6–12 M Ω) filled with 3 M potassium acetate were used to record the membrane voltage and inject current into the cell in bridge balance mode using an Axoclamp-2B electrophysiology amplifier (Molecular Devices Corporation, Sunnyvale, CA). Signals were then amplified and filtered with a Brownlee Precision Model 440 (Brownlee

Precision, San Jose, CA). A Digidata 1322A (Molecular Devices Corporation) was used for data acquisition, and voltage and current signals were recorded using the ClampEx 8.0 software package (Molecular Devices Corporation). Experiments were also performed using the Clamp-1U (Molecular Devices Corporation) passive membrane electrical model cell. This electrical circuit models a passive membrane with properties similar to invertebrate sharp electrode recording ($R_e = 50 \text{ M}\Omega$, $R_m = 50 \text{ M}\Omega$, $C_m = 470 \text{ pF}$).

B. Dynamic Clamp

Dynamic clamping was done with the Real-Time Linux based Model Reference Current Injection system (MRCI) [36]. The dynamic clamp was used to generate a variety of conductances within both real cells and the CLAMP-1U electrical circuit model cell (Molecular Devices Corporation). The membrane voltage was acquired by an NI 6052E multifunction DAQ board (National Instruments, Austin, TX) and used by the MRCI system to generate ionic currents. The current resulting from the calculations was injected into the cell through the Axoclamp-2B in real-time. During dynamic clamp experiments, the Digidata 1322A data acquisition system was solely used for viewing V_m and I_m using ClampEx, as shown in Fig. 2. Simulated currents were in the form of a maximal conductance, $\bar{g}$, multiplied by a time-dependent and/or voltage-dependent term, multiplied by the driving force: $I = \bar{g}f(t; V_m)(V_m - E_{syn})$. E_{syn} for our experiments and simulations was zero.

A variety of dynamic clamp sampling rates, ranging from 5–20 kHz, were used to test the effect of latency on stability. Unless otherwise noted, the data shown in this paper was obtained with the MRCI system running at 10 kHz, or a latency of 0.1 ms.

C. Computational Model

We designed a computational model of the current clamp electrophysiology equipment and dynamic clamp system to simulate the observed instability. We started with a simple ideal current injection circuit with a controllable R and C representing partial compensation. This idealized model was not able to reproduce our results. We then used a simplified version of the model of Wilson and Park [44]. This model (Fig. 3) was chosen to provide a simplified model of existing current clamp technology to isolate the cause of instability, not to replicate the exact experimental system. For example, the Wilson and Park model was simplified by removing the stray capacitance, C_{cur} , because it did not directly affect the instability observed in the dynamic clamp system.

Starting from the bottom left, a simple passive membrane model was used to represent the cell, with membrane resistance and capacitance: R_m and C_m , and a resting potential, V_r . The electrode model, located above the neuron model, consists of a series resistance, R_e , and parallel capacitance, C_e . Current injection into this electrode is done by applying V_{com} to R_{cur} . Capacitance compensation is performed in the bottom center part of the circuit. A portion of the voltage measured at the electrode is amplified by G_c and applied to the C_{comp} capacitor to compensate for the effects of C_{shunt} and C_e . The amount of capacitance compensation is set by the experimentalist with the P_{cc} control. P_{cc} is a value from zero to one that represents what fraction of measured voltage is used to compensate for the electrode capacitance. Full compensation occurs when $P_{cc} = (C_e + C_{shunt} + C_{comp})/(C_{comp} * G_c)$. Compensation for the microelectrode resistance, R_e , is done with the bridge balance circuit. This circuit subtracts a portion of the command voltage from the measured voltage. The amount of voltage subtracted is set by the user with the P_{bb} control. P_{bb} is a value from zero to one that sets how much of the command voltage is subtracted from the measured voltage. Full compensation occurs when $P_{bb} = R_e/R_{curr}$. Both P_{cc} and P_{bb} are commonly implemented as knobs on electrophysiology amplifiers, and the amount of compensation is determined visually by the experimentalist.

The final portion of this circuit is the dynamic clamp system. The computational model that would be running on the dynamic clamp is simulated at the dynamic clamp rate being tested, while the rest of the computational model is simulated with a time step of 1×10^{-5} ms. This difference is denoted by dashed lines in the diagram. The output voltage from the bridge balance circuitry is sampled, but not discretized, at the dynamic clamp rate with a zeroth-order sample and hold and used by the dynamic clamp differential equations. The resulting command voltage is used to inject current into the cell.

The stimulus current most commonly used in this study was a step of conductance, $g * u(t)$, multiplied by the driving force of the current, $(V_m - E_{Syn})$. Stability was measured as the step size of conductance that could be injected, while still maintaining a system whose oscillations converged to steady state. This maximum possible step size was measured for a variety of conditions to examine how the amount of bridge balance, P_{bb} , the amount of capacitance compensation, P_{cc} , and the sampling rate affect the amount of current that can be simulated and injected with the dynamic clamp.

This entire computational model is described by

$$\frac{dV_m}{dt} = \frac{1}{C_m} \left(\frac{V_{in} - V_m}{R_m} - \frac{V_m - V_r}{R_m} \right) \quad (1)$$

$$\frac{dV_{in}}{dt} = \frac{1}{C_e} \left(I_{prep} - \frac{V_{in} - V_m}{R_e} \right) \quad (2)$$

$$V_{out} = V_{in} - P_{bb} V_c \quad (3)$$

$$I_{prep} = I_{cur} + I_{cc} - I_{shunt} \quad (4)$$

$$I_{cur} = \frac{V_c}{R_{cur}} + C_{cur} \frac{dV_c}{dt} \quad (5)$$

$$I_{shunt} = C_{shunt} \frac{dV_{in}}{dt} \quad (6)$$

$$I_{cc} = C_{comp} G_c P_{cc} \frac{dV_{in}}{dt} - C_{comp} \frac{dV_{in}}{dt}. \quad (7)$$

Table I includes the values that were used for simulations. The invertebrate values are similar to those found during sharp electrode invertebrate electrophysiology and the values used by Wilson and Park [44]; the passive membrane and electrode parameters are those of the CLAMP-1U model cell. The vertebrate values are based on whole-cell patch-clamping

experiments; these values are the same as those used for the MCW-1U model cell (Molecular Devices Corporation). For these parameters, the microelectrode resistance is completely compensated when $P_{bb} = R_e/R_{curr}$, or 0.5 for invertebrate parameters and 0.1 for vertebrate parameters. The electrode and shunt capacitance are exactly compensated when P_{cc} equals 0.5 for both cases. The computational model contains the positive feedback configuration present in the physical amplifier, which causes the system to be unstable at or above exact capacitance compensation, so simulations were not performed for a P_{cc} greater than 0.495.

III. Results

A. Physical System

The experiments that initially identified a transient instability in the dynamic clamp system involved adding a slow potassium current, I_{inj} , to a live spiking neuron, as shown in Fig. 1 (Equations for this current are listed in the Appendix). The current contained a time-dependent and voltage-dependent activation variable and an instantaneous voltage-dependent inactivation function. As the maximum conductance of the current was increased, a transient ringing was observed at the end of the action potential. We have frequently encountered such transient instabilities as the value of an injected conductance is increased.

We verified that the instability was not caused by saturation of the electronics, as injected currents were not near the limits of the electronic equipment. The instability was also not caused by the numerics of the dynamic clamp system, which were well within the bounds described in [37]. We also duplicated these instabilities using another computational and data acquisition platform to implement the dynamic clamp (dSPACE DS1104, Paderborn, Germany), verifying that the instability was not an artifact of the MRCI system or the PC hardware. This type of transient instability was also reproduced in experiments using discontinuous current clamp instead of bridge balance mode.

To simplify the system, the neuron was hyperpolarized to prevent tonic firing, and the voltage-dependent conductance was reduced to a voltage independent up/down conductance ramp at a constant rate. This conductance, which increased/decreased linearly in time, was multiplied by the driving force, Fig. 4(a). This simplified conductance waveform developed a transient instability as well. The live neuron was then replaced with the CLAMP-1U artificial electrical model of a passive membrane, Fig. 4(b). We utilized the voltage-offset of the Axoclamp to provide a resting potential of -50 mV. As with the real neuron, the system developed a transient instability in response to a sufficiently large ramp conductance. Finally, the instability was reproduced in simulations of the computational model described above. Fig. 4(c) shows the instability in the computational model, in response to an up/down ramp of conductance of similar magnitude to the experimental results. While the neuron is clearly more complex than the RC cell or simulation, in all cases the transient instability occurred shortly after the peak of the conductance ramp.

To summarize, we were able to reproduce a qualitatively similar transient instability by replacing the voltage and time-dependent conductance in an *in vitro* neuron with a simple up/down ramp. This instability was consistent in experiments on live neurons, experiments on an RC model cell, and simulations of the electrophysiology circuitry and an RC cell. Because of this consistency, the remainder of this study focuses on utilizing the computational model of the system to analyze factors affecting the instability.

B. Computational Results

Once the physical results were qualitatively replicated, the computational model system was used to quantitatively examine how the bridge balance, capacitance compensation, and

sampling rate affect the maximum possible step size of conductance that maintains a stable system. For each set of parameters, a step of conductance was applied to the system. The size of this conductance was increased until the system became unstable. This process was repeated for different parameter values to measure the stability as the resistance compensation, capacitance compensation, and sampling rate change. Fig. 5(a) and (b) shows the results obtained when the amount of bridge balance, P_{bb} , and the amount of capacitance compensation, P_{cc} , were varied for a dynamic clamp sampling rate of 10 kHz and the parameters listed in Table I. For these values, full bridge balancing occurs when $P_{bb} = R_e/R_{Curr}$, 0.5 for the invertebrate parameters, and 0.1 for the vertebrate experiments. For both preparations, the capacitance is fully compensated at $P_{cc} = (C_e + C_{shunt} + C_{comp})/(C_{comp} * G_c)$, 0.5 for these parameters. Fig. 5 shows that the maximum stable conductance is a function of both P_{bb} and P_{cc} and contains a sharp peak where the electrode resistance and capacitance are well compensated. For invertebrate parameters, this is extremely pronounced, with a wider band of improvement when both resistance and capacitance are nearly compensated. The increased stability for the vertebrate parameters is less dramatic, although the overall range of values of stable conductance are inclusive of those values most commonly used in mammalian experiments.

These computational results were verified using the experimental set up and the *RC* model cell. As with the computational procedure, steps of conductance were applied to the *RC* model cell using the dynamic clamp. These steps were increased in magnitude until the system became unstable. Fig. 6 shows a plot of the maximum stable conductance as a function of the percent of resistance compensation and the amount of capacitance compensation.

Resistance compensation was measured visually from the step response of the *RC* model cell in bath setting to a 1 nA step of current. Using the Axoclamp-2B, there is no clear way to quantify capacitance compensation. Here it is measured as “whole turns of the capacitance compensation knob.” Responses were measured for 0, 1, 2, and 3 turns of the knob. Four turns resulted in instability, indicating overcompensation. While these physical experiments lack precision, they qualitatively show the same trends observed computationally, with a peak in the maximum stable conductance occurring when the series electrode resistance is completely compensated and increasing peaks occurring as the amount of capacitance compensation increases.

Fig. 7 illustrates how sampling rate changes the maximum stable step size as a function of both bridge balance and capacitance compensation. Fig. 7(a) and (b) shows that for the exactly bridge balanced case there is a significant increase in the maximum stable conductance. These trends are reproduced in Fig. 7(c) and (d), which show the maximum stable conductance as a function of sampling rate, for the exactly balanced case. This shows a steady increase in stability, as the sampling rate increases.

In contrast, Fig. 7(a) also indicates that as the sampling rate increases, the amount of capacitance compensation becomes important. The peak of the nearly compensated 5 kHz trace is higher than the 10 kHz one; however, the well compensated case shows the opposite relationship. This is because the amount of uncompensated capacitance affects how quickly the circuit responds to current transients. For less compensated circuits, more time is required for current transients to settle, so there must be more time between samples for the oscillation to die out.

IV. Discussion

The dynamic clamp technique has been used to greatly enhance our knowledge of neurons and networks of neurons. By adding or subtracting ionic currents through real-time model

simulation, the dynamic clamp has shown how individual currents affect the activity of a cell, as well as how pharmacological agents affect cell properties. The dynamic clamp is also used to generate synaptic coupling between neurons to study how individual neurons and synapses affect network behavior.

This widely used technique has some known limitations. The temporal dynamics of the simulated currents are limited by the speed of the dynamic clamping system. The accuracy of the calculations is limited by the numerical methods used, quantization error, latency, and jitter present in the dynamic clamp system. Often faster integration techniques, such as the exponential Euler method [37], [45], [46] are used to perform computations faster, at the sacrifice of precision.

Here we present a final limitation resulting from a combination of these factors. This phenomenon has been personally reported by numerous dynamic clamp users, using different dynamic clamp implementations. It is present in both vertebrate and invertebrate setups, under both bridge balance and discontinuous current clamp modes. We have verified that it is not a direct result of quantization error or the type of dynamic clamp system used.

System instability primarily results from the maximum conductance of the simulated current, the sampling done by the digital dynamic clamp system, and the uncompensated electrode resistance and capacitance. Small oscillations in dynamic clamp simulations can become unstable when the settling time of the electrode does not decay sufficiently faster than the sampling rate of the dynamic clamp system. This time constant is set by the residual uncompensated electrode resistance and capacitance. These oscillations are also aggravated by the maximal conductance of the simulated current and by measurement errors caused by the uncompensated resistance and capacitance. As these parameters are reduced, the dynamic clamp becomes more stable. This stability increases as the sampling rate is also increased.

Currently, the sampling rate of the dynamic clamp is determined by the time needed to sample the membrane voltage and perform the required calculations. Existing dynamic clamp systems typically run at speeds from 2–20 kHz. The dynamic clamp running speed depends on both the complexity of the model being simulated and the dynamic clamp system. Investigators typically justify their choice of dynamic clamp rate in terms of the kinetics of the ion channel being simulated. This work shows that stability may impose more stringent rate requirements, especially when using higher value conductances.

The second major cause of system instability is related to the inaccuracy of voltage measurement and the settling time of the electrode. In electrophysiology experiments using bridge balance techniques to compensate for electrode resistance, the membrane voltage measurement is affected by the residual uncompensated resistance. As the amount of uncompensated resistance increases, the maximum stable conductance of the system falls sharply. The same types of effects also occur under discontinuous current clamp. In this case, measurement error manifests itself as a voltage error proportional to the injected current (due to an insufficient settling time). Here we show that commonly accepted levels of electrode compensation (80%–90%) for current injection nevertheless compromise the stability of a dynamic clamp system for sufficiently large conductances. Although electrode compensation directly affects the maximum stable conductance, the dynamic clamp stability was still limited for simulations performed with no electrode effects, indicating that delay is the primary cause of instability.

These results were obtained using a traditional single electrode amplifier, with dedicated current injection and voltage-follower circuitry. Modern patch clamp amplifiers often utilize a modified design for current injection [47] that has been shown to compromise the fidelity of the specified injected current. Nevertheless, similar instabilities to those reported here have

been anecdotally reported by users of patch-clamp amplifiers as well. We strove to identify the simplest possible circuit model that could replicate the instabilities.

We suggest two ways to reduce the presence of the unstable regime in experiments. The first is to develop faster dynamic clamp systems. A present-data limit of approximately 50 kHz is imposed by architectural aspects of modern desktop computers; this can be averted by hardware-specific solutions [29], [31], [32]. At present, such hardware-based systems require a significant degree of hardware and software skills; however, recent advances in operating system technology and price reductions in various hardware platforms will eventually make such technology accessible and easy to use.

The second method for reducing the effects of delay instability is to reduce the error caused by microelectrode resistance. Currently, this is done in sharp electrode experiments through either the bridge balance or discontinuous current clamp techniques. However, resistance compensation is not always done in patch clamp experiments, as the voltage offset error is often considered negligible due to the magnitude of applied currents, and lower electrode resistances. Both of these compensation methods greatly reduce electrode effects. Discontinuous current clamping allows for a greater range of maximum stable conductance; however, the sampling rate limits the speed the dynamic clamp system can run at. Even when electrode resistance is within acceptable ranges (10% of fully compensated), the stability of the system is compromised. The development of active compensation that can adapt to changing electrode resistance throughout an experiment would significantly reduce the effects of measurement error on the stability of dynamic clamping systems [48].

In summary, we have documented a well-known “nuisance” to dynamic clamp experiments. While the existence of such an instability is obvious and does not compromise the presentation or interpretation of existing results, it provides an obstacle that in many cases has hindered investigators from using desired levels of conductances. These results suggest that improved system stability may be achieved by 1) faster dynamic clamp systems (which previously have only considered gating kinetics to justify a choice of speed) and 2) improved resistance and capacitance compensation, above and beyond commonly accepted practices by investigators. We note that we have not tried to validate either of these approaches in that 1) our dynamic clamp system (as with many PC-based systems) often cannot run faster than 20 kHz for a typical membrane model and 2) improved methods for highly accurate series and resistance compensation have yet to be developed.

Biography

Amanda J. Preyer received the B.S. degree in electrical engineering from Lafayette College, Easton, PA, in 1999 and the M.S. and Ph.D. degrees in electrical and computer engineering from the Georgia Institute of Technology, Atlanta, in 2002 and 2007, respectively.

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Appendix

Appendix: Dynamic Clamp Equations

These are the equations for the M current injected via dynamic clamp for the experiments shown in Fig. 1. V_m is the measured membrane voltage. The model was implemented and solved with the MRCI system as described in the Section II.

$$\begin{aligned}
 I_m &= g_m \omega h_\infty (V_m - E_m) \\
 \frac{d\omega}{dt} &= \frac{\omega_\infty - \omega}{\tau_\omega} \\
 \omega_\infty &= \frac{1}{1 + \exp\left(\frac{V_m - \omega_{1/2}}{\omega_{\text{slope}}}\right)} \\
 h_\infty &= \frac{1}{1 + \exp\left(\frac{V_m - h_{1/2}}{h_{\text{slope}}}\right)} \\
 E_m &= -85\text{mV} \\
 \omega_{1/2} &= -24 \\
 \omega_{\text{slope}} &= -6 \\
 \tau_\omega &= 100\text{ms} \\
 h_{1/2} &= -30 \\
 h_{\text{slope}} &= 1 \\
 g_m &\approx .06\mu\text{s}.
 \end{aligned}$$

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Fig. 1.
 Example of transient instability in spiking neuron. As the maximal conductance of a slow potassium current, I_{inj} , was increased, transient instability was observed.

Fig. 2.

Experimental system. The experimental system consisted of a standard sharp intracellular recording setup with an added MRCI RT Linux dynamic clamp.

Fig. 3. Computational model block diagram. See text for component descriptions.

Fig. 4.

Model simplification. A: The instability appeared with a simple up/down ramp conductance in a live neuron that was hyperpolarized to prevent tonic firing. B: Instability is also reproduced using the Clamp-1U passive membrane model. C: Instability can be reproduced in the computational model using similar magnitudes of injected current. Recordings were taken when the series resistance and capacitance were compensated using standard visual techniques.

Fig. 5.

Maximum stable conductance for invertebrate and vertebrate parameters for 10 kHz sampling rate. A: Invertebrate parameters show sharp peak in maximum stable conductance when the capacitance and resistance are well compensated. B: Vertebrate simulations show improvements as resistance is compensated, but capacitance compensation has less effect. Dashed lines show $\pm 10\%$ changes in R_e .

Fig. 6.

Maximum stable conductance for a physical experiment using the *RC* model cell, with a 10 kHz sampling rate. Percent resistance compensation was measured visually by applying a 1 nA step of current to the model cell in bath setting. Capacitance compensation is defined as “whole turns of the capacitance compensation knob,” as there is no way to determine full compensation. For these experiments four turns of the knob resulted in instability, indicating overcompensation. Traces are shown for 0, 1, 2, and 3 turns of the capacitance compensation knob.

Fig. 7.

Maximum stable conductance as a function of sampling rate. A: Invertebrate results for 5 and 10 kHz sampling rates. B: Vertebrate results for 5 and 10 kHz sampling rates. C: Maximal conductance as a function of sampling rate for the invertebrate parameters with $P_{bb} = 0.5$ and $P_{cc} = 0.495$. D: Maximal conductance as a function of sampling rate for the vertebrate parameters with $P_{bb} = 0.1$ and $P_{cc} = 0.495$.

Table I
Computational Model Parameters for RC Cell and Current Clamp Circuit

Parameter	Invertebrate Value	Vertebrate Value
$R_e(\text{M}\Omega)$	50	10
$C_e(\text{pF})$	5	5
$R_m(\text{M}\Omega)$	50	500
$C_m(\text{pF})$	470	33
$R_{cur}(\text{M}\Omega)$	100	100
$C_{shunt}(\text{pF})$	1	1
$C_{comp}(\text{pF})$	1	1
$G_c(\mu\text{S})$	10	10
$E_{syn}(\text{mV})$	0	0