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Supporting Material

Optogenetic versus Electrical Stimulation of Human Cardiomyocytes: Modeling Insights

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Supporting Figures

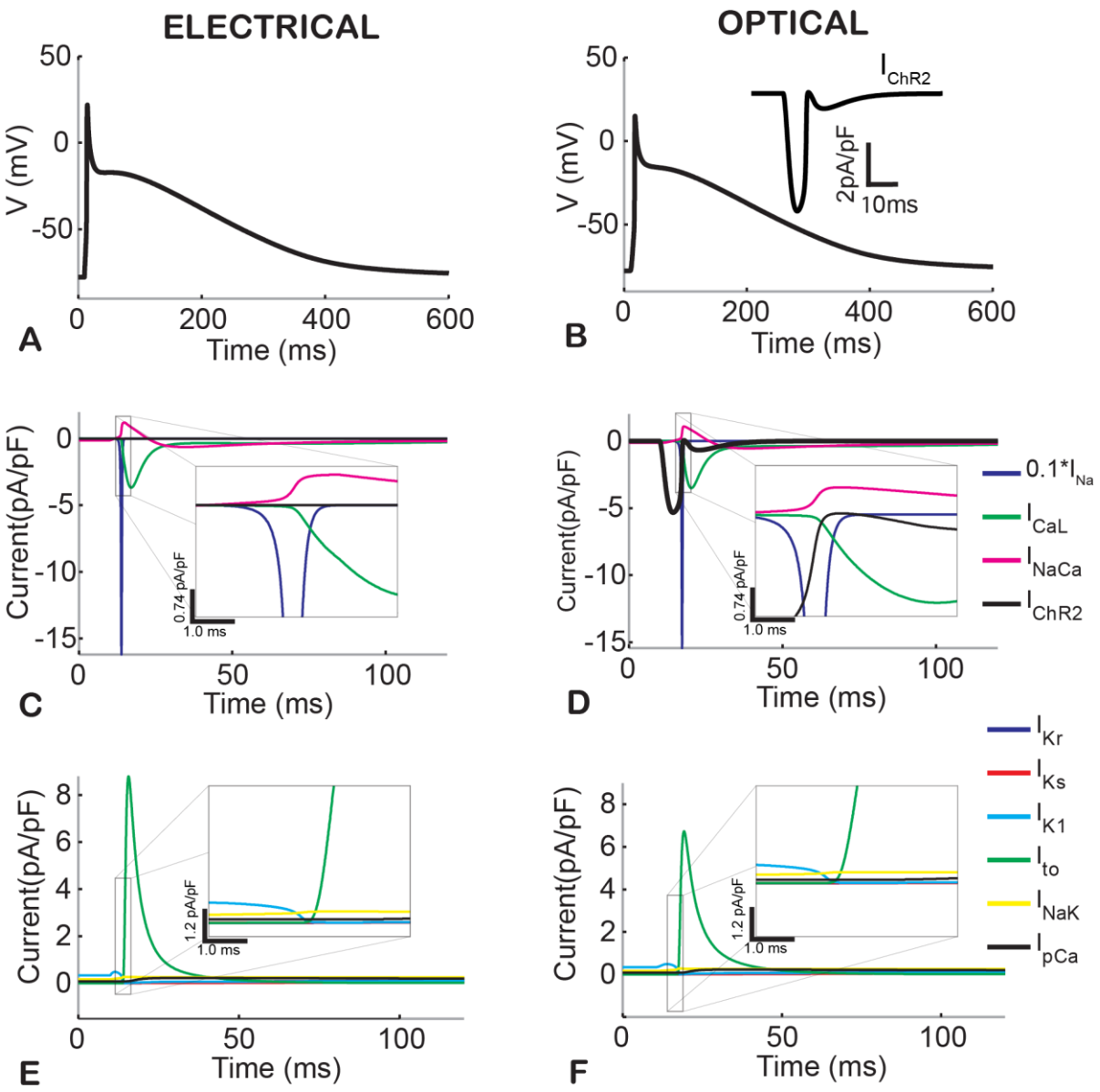

Figure S1. Electrical (left) and optical (right) stimulation produce similar action potential morphology in human atrial cardiomyocytes (the Courtemanche model). **A-B**. Triggered action potentials by injection of electrical current (5 ms, 8 pA/pF) and an optical pulse (10 ms, 0.5 mW/mm^2, 470nm), respectively. Inset in **B** shows the time course of the resultant ChR2 current. **C-D.** Underlying major inward currents and I_{NaCa} during electrical and optical stimulation, respectively. **E-F.** Underlying outward currents during electrical (**E**) and optical stimulation (**F**). Insets are zoomed-in versions of the area of interest in **C-F**.

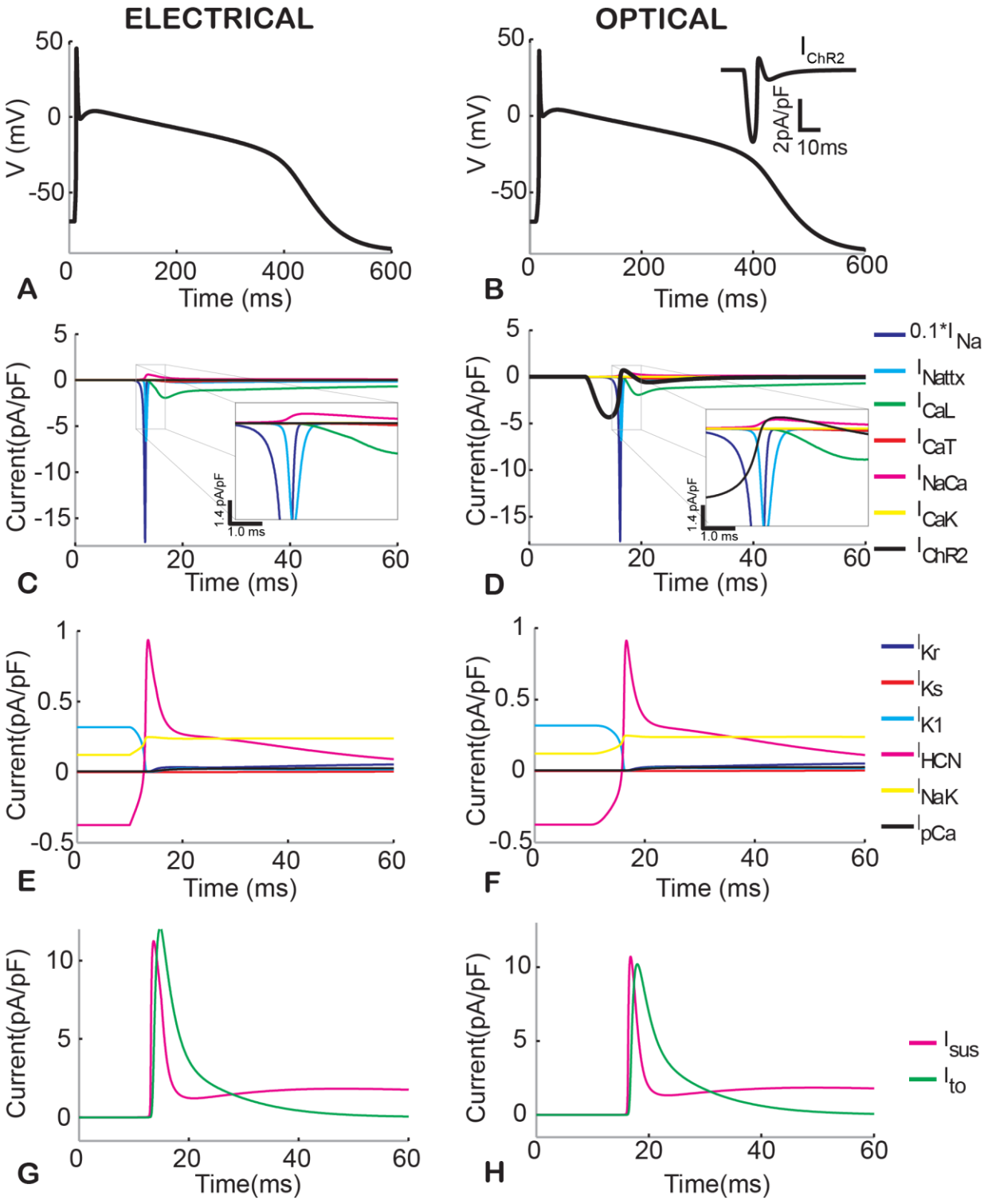

Figure S2. Electrical (left) and optical (right) stimulation produce similar action potential morphology in human Purkinje cardiomyocytes (the Sampson model). **A-B**. Triggered action potentials by injection of electrical current (5 ms, 8 pA/pF) and by an optical pulse (10 ms, 0.5 mW/mm^2, 470 nm), respectively. Inset in **B** shows the time course of the resultant ChR2 current. **C-H.** Underlying major inward and outward currents during electrical and optical stimulation, respectively. Insets are zoomed-in versions of the area of interest in **C-D**.

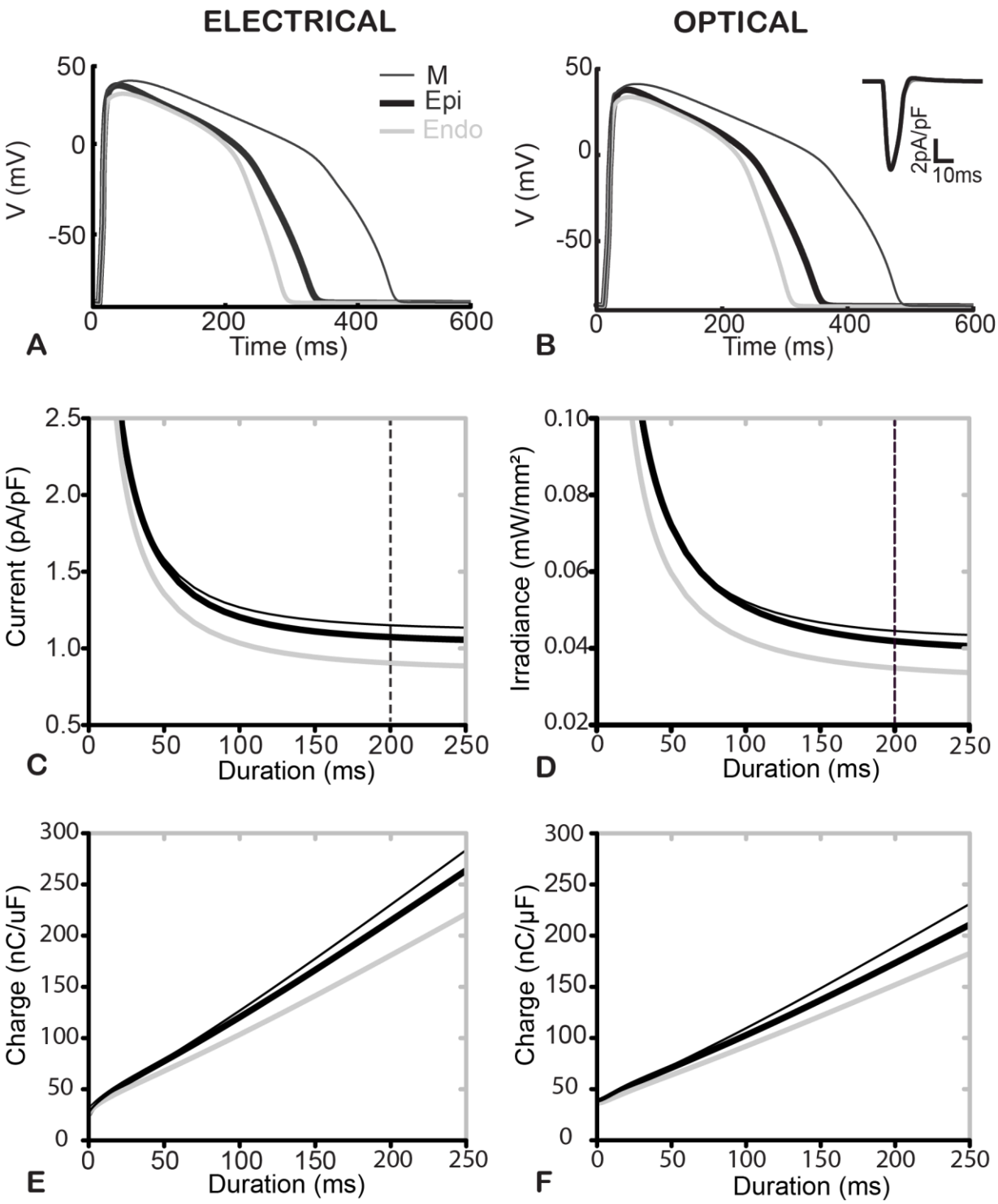

Figure S3. Differential transmural cell response to electrical (left) and optical (right) stimulation and related strength-duration and charge curves in the O'Hara epicardial (Epi), endocardial (Endo), and mid-myocardial (M) ventricular cell. A. Electrically-triggered action potentials in by direct current injection (5 ms, 8 pA/pF). **B.** Optically-triggered action potentials by a light pulse (10 ms, 0.5 mW/mm^2, 470 nm). Dashed vertical line denotes approximate rheobase (200 ms). **C-D.** Strength-duration curves. **E-F.** Minimum stimulus charge needed to excite.

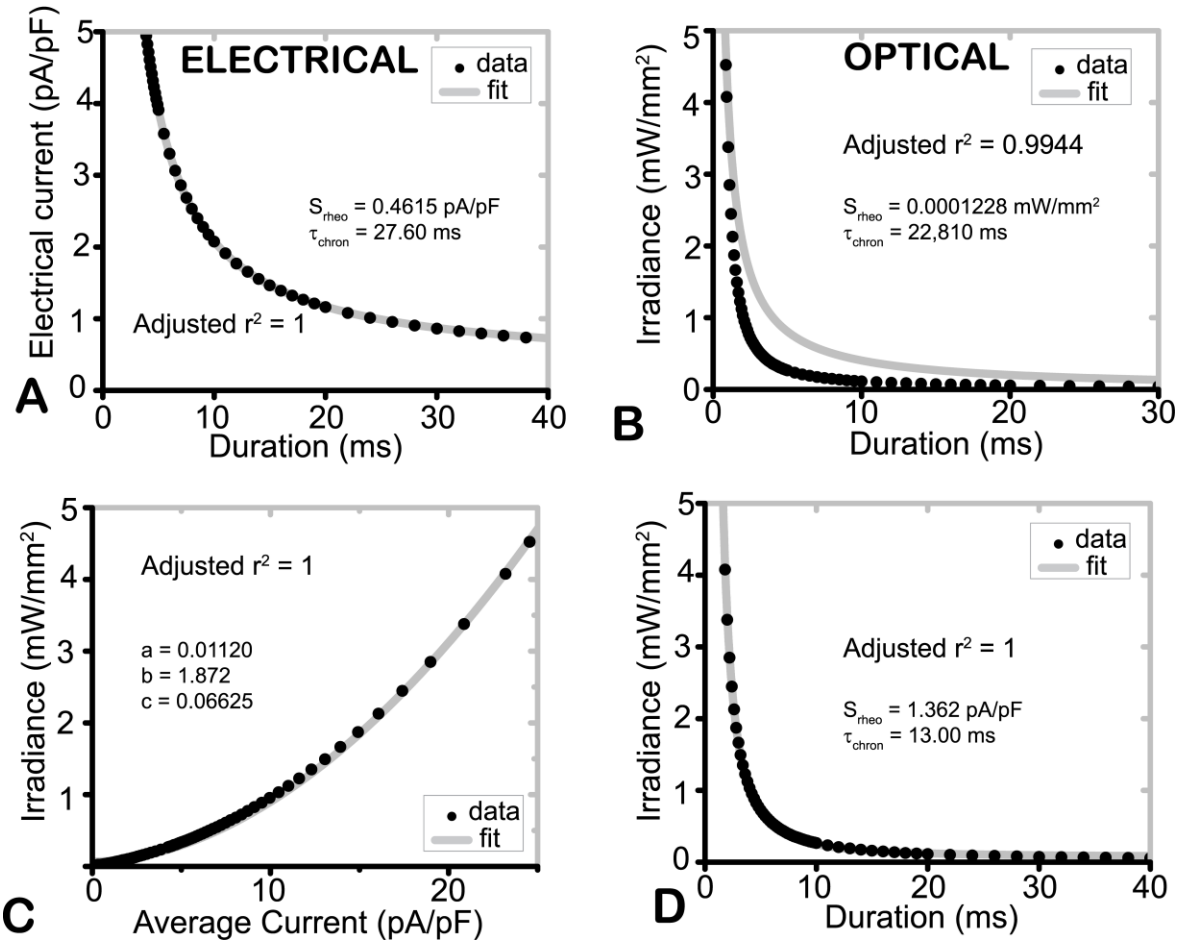

Figure S4. Optogenetic stimulation produces a correctable change in strength-duration curve shape in human atrial cardiomyocytes. A. Electrical SD curves in human atrial cardiomyocytes fit well a theoretical mono-exponential relationship assuming simple equivalent RC-circuit behavior. **B.** Optical SD curves (using irradiance) deviate from the theoretical mono-exponential curve. **C.** Empirical mapping of irradiance to the average inward stimulating current, using a power series model. **D.** Corrected optical SD curve according to **Eq. 14** (correction using the mapping in **C**) fits the theoretical mono-exponential relationship for irradiance vs. pulse duration.

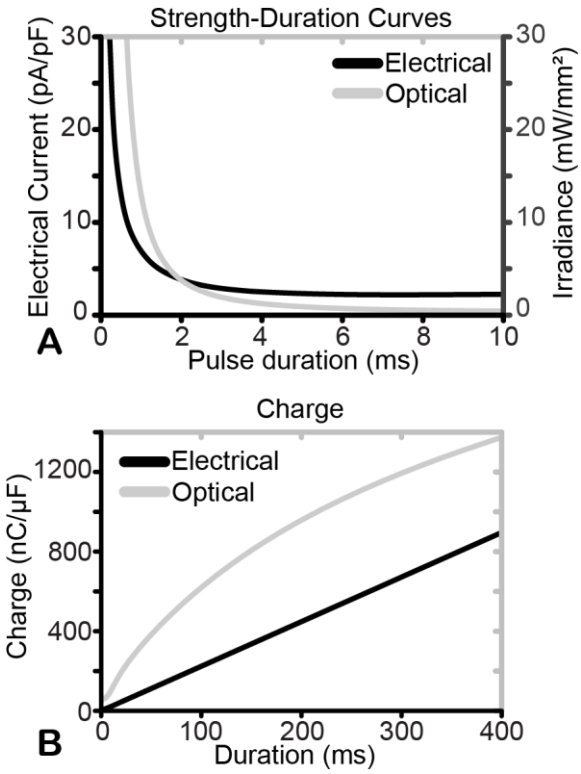

Figure S5. Neuronal response differs from cardiac: optical and electrical strength-duration and charge curves in a modified Hodgkin-Huxley giant squid axon model. A. SD curves for electrical stimulation by direct current injection and for optical stimulation by a light pulse (470 nm). **B.** Minimum charge needed to excite (nC/μF).

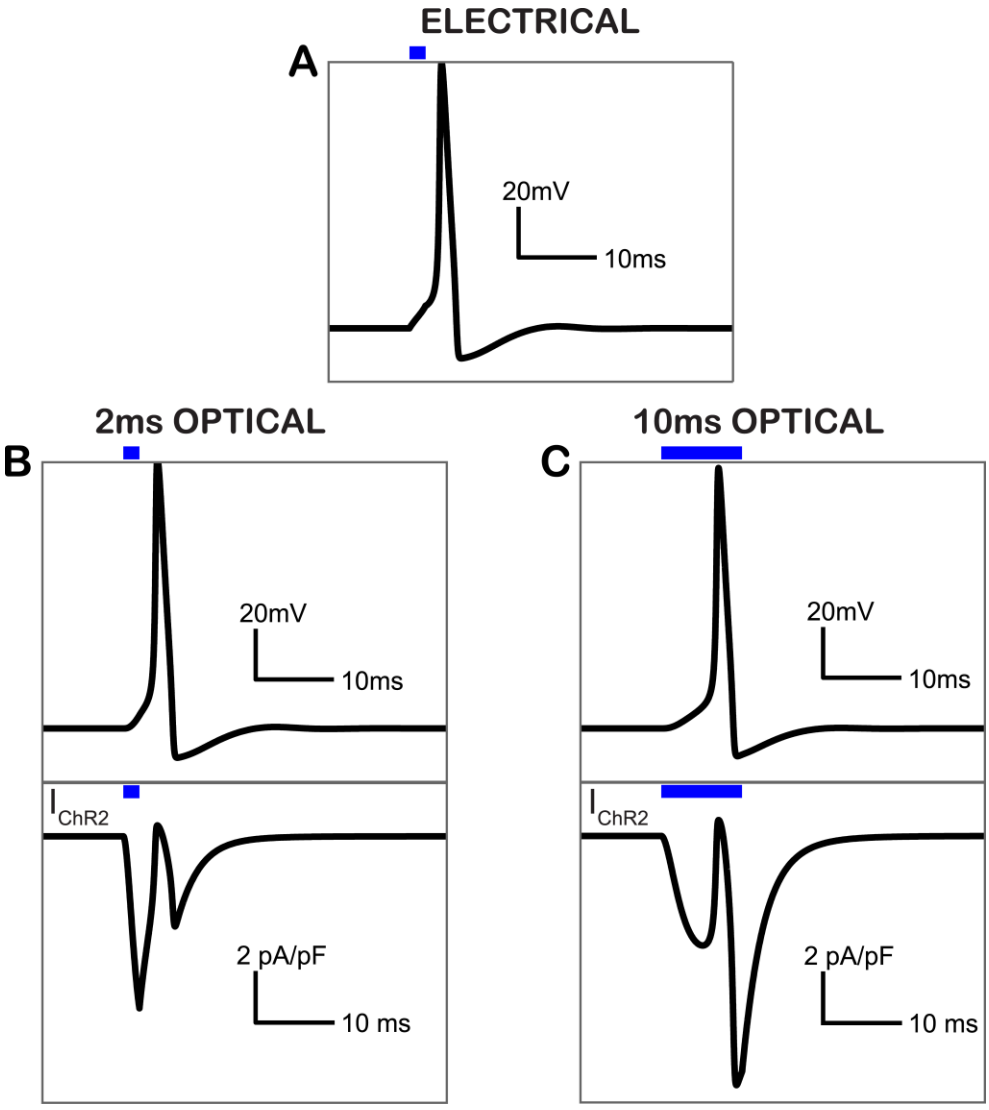

Figure S6. Transmembrane voltage (left) and ChR2 current (right) during an action potential in a modified Hodgkin-Huxley squid axon model. Blue bars show period of electrical (A) and optical (B-C) stimulus. **A.** Action potential from 2 ms, 5 pA/pF rectangular electrical pulse. **B-C.** Action potential and corresponding ChR2 current from 2 ms 2 mW/mm^2 and 10 ms 0.5 mW/mm^2 470nm light pulse, respectively. Simulations were done at 6 °C.