Supplemental Table 1. Contractile Properties. Percent change relative to before (5V), data are mean ± SEM for all beats in each group CCM (10V), and After (5V). n = 23. **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.

Supplemental Table 2. Calcium Handling Properties. Percent change relative to before (5V), data are mean ± SEM for all beats in each group, CCM (10V), and After (5V). n = 13. **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.

Supplemental Table 3. Electrophysiological Properties. Percent change relative to before (5V), data are mean ± SEM for all beats in each group; CCM (10V), and After (5V). n = 12. **P* < 0.05, ***P* < 0.01, ****P* < 0.001, *****P* < 0.0001.

Supplemental Table 4. Baseline hiPSC-CM Properties**.** Absolute values of baseline (i.e., Before, 5V) cardiomyocyte excitation-contraction coupling properties for action potential (i.e., electrophysiology), calcium handing and contraction, data are mean ± SEM; n = 5 – 23. N/A = not applicable.

Supplemental Figure 1. Schematic of human in vitro CCM Model. A: hiPSC-CMs are pre-plated in monolayer format on gelatin (0.1%) coated 6-well plates. B: After 2 – 28 days in culture hiPSC-CMs are dissociated and prepared for plating on Matrigel mattress substrate. C: Isolated hiPSC-CMs are plated at high density on Matrigel mattress arrayed in 48-well format (left) and assayed in [0.5 mM] $[Ca]_0$ Tyrode solution (right). D: Commercial pulse generator and standard clinical CCM pulse parameters (right) are used stimulate hiPSC-CMs, cardiac function is assessed by video and florescence measurements (left). E: Representative contraction recording before CCM (5V), CCM (10V) and after (5V).

Supplemental Figure 2. Percent Change for the Effect of Extracellular Calcium Modulation on CCM Response. hiPSC-CMs were exposed to increasing concentrations of extracellular Ca [Ca_o] 0.25 – 2 mM. Summary bar graphs of immediate effects. n = 6 - 8 per group. Transformed data from figure 5. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001.

Supplemental Figure 3. Electric Field Numerical Modeling. A: Prospective and top view of the geometry of the platinum electrodes inserted in a glass bottom well. B: Electric field intensity in the YZ plane perpendicular to the electrodes for 1 V applied. For quantitative analysis, the values of the |E| field were extracted in the region of interest (ROI). C:|E| field along the y axis; the ROI is highlighted by a rectangle. D: Scaling table to convert the |E| field in the ROI obtained at 1 V applied to significant experimental values, 5 V and 10 V, respectively.

Supplemental Figure 4. Effect of Voltage Amplitude on CCM Response. A: Contraction traces for each group, Before (5V), CCM (0 - 15V), After (5V), hiPSC-CMs were exposed to increasing CCM pulse amplitude (0 – 15) Volts. [Ca_o] 0.5 mM. B: Transformed data demonstrating the effect of CCM pulse amplitude on contraction amplitude During CCM (Hill slope = 8.0). n = 1. EV_{50} = Effective Voltage 50%.

Supplemental Figure 5. Effect of 0V CCM on hiPSC-CM Contractility. A: Contraction traces for each group, Before (5V), CCM (0V), After (5V). [Ca_o] 0.5 mM.

Supplemental Video. hiPSC-CMs on Matrigel Mattress. Matrigel Mattress in one well of 48-well glass bottom plate 4x. hiPSC-CMs form monolayer morphology and robust contraction at ~ 24 hours post plating. White arrow indicated edge of Matrigel mattress. Scale bar, 1 mm.

Supplemental Table 1. Contractile Properties

Parameter	CCM	After
Amplitude	**16 ± 4%****	**4 ± 5%**
Time to Peak 50%	**-20 ± 9%***	**7 ± 5%**
Time to Peak 90%	**-22 ± 8%***	**6 ± 5%**
Time to Baseline 50%	**-8 ± 5%**	**4 ± 4%**
Time to Baseline 90%	**-12 ± 6%***	**5 ± 5%**
Contraction Duration 10%	**-13 ± 6%**	**3 ± 5%**
Contraction Duration 50%	**-6 ± 5 %**	**3 ± 5%**
Contraction Duration 90%	**0 ± 5%**	**3 ± 4%**
N	**23**	**23**

Supplemental Table 2. Calcium Handling Properties

Parameter	CCM	After
Amplitude	**13 ± 5%***	**-10 ± 2%****
Time to peak	**-22 ± 3%******	**-1 ± 3%**
Ca Rise Time	**-33 ± 3%******	**5 ± 2%***
Ca Duration 50%	**-10 ± 2%*****	**0 ± 1%**
Ca Duration 90%	**-2 ± 1%**	**1 ± 1%**
N	**13**	**13**

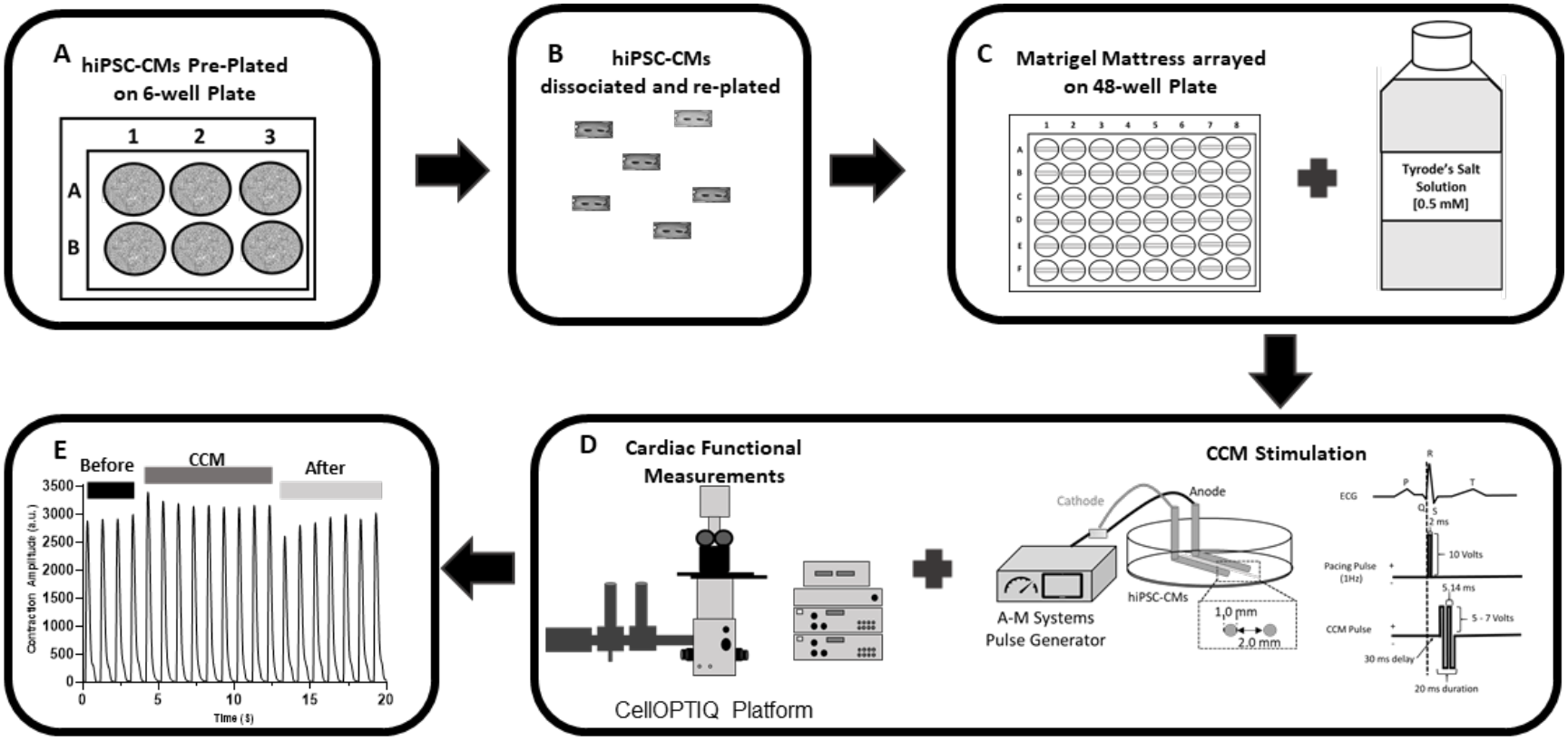
Supplemental Table 3. Electrophysiological Properties

Parameter	CCM	After
TRise	-13 ± 5%*	-6 ± 17%
APD50	-8 ± 2%**	18 ± 6%
APD75	-9 ± 1%****	18 ± 4%
APD90	-10 ± 1%****	17 ± 5%
n	12	12

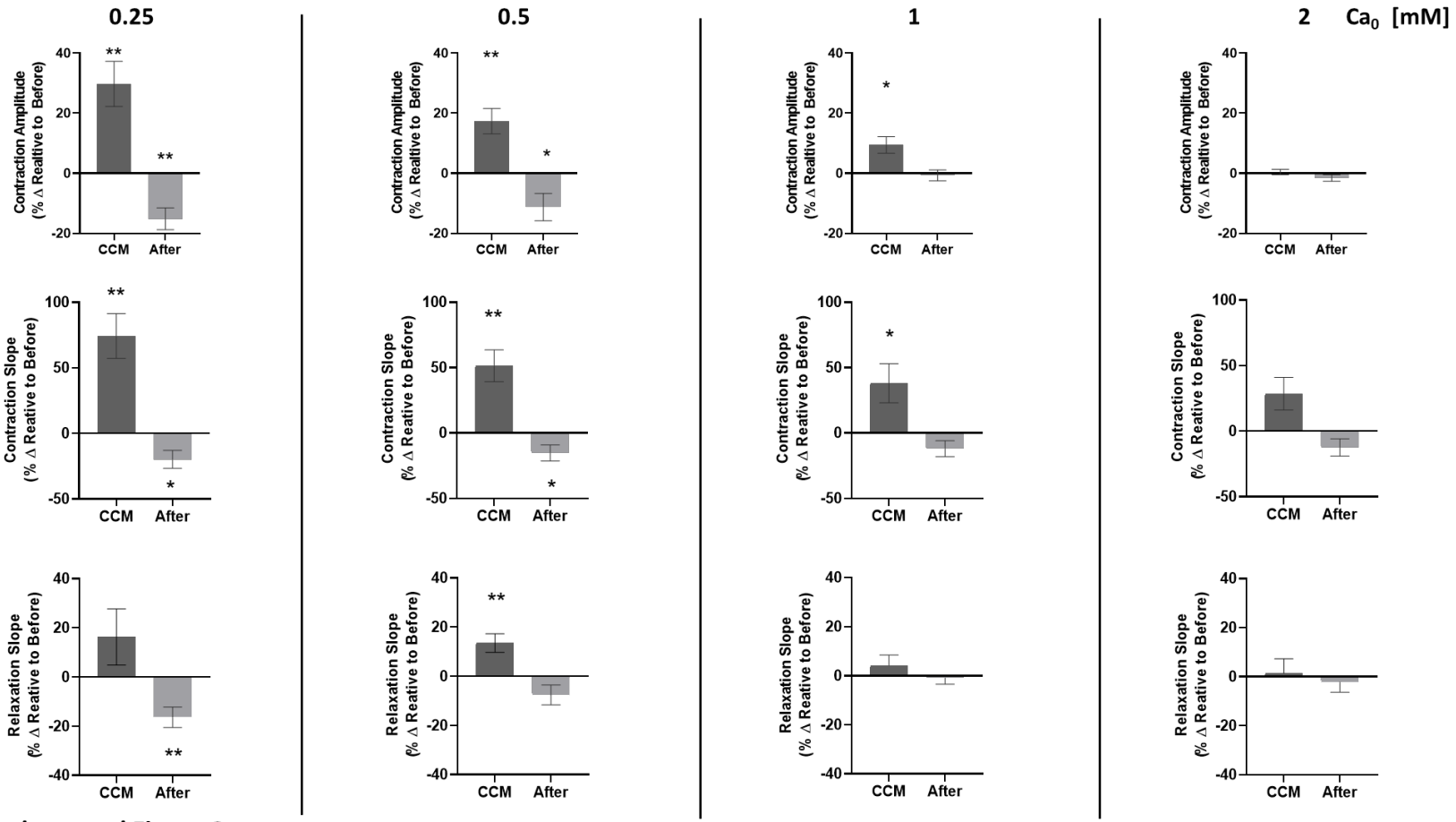
Supplemental Table 4. Baseline hiPSC-CM Properties

Parameter	Action Potential	Calcium	Contraction
Amplitude (a.u.)	N/A	0.20 ± 0.03	1882.5 ± 187.2
Time to Peak 50% (ms)	N/A	N/A	166.4 ± 15.5
Time to Peak 90% (ms)	N/A	272.6 ± 15.0[#]	245.4 ± 18.1
TRise (ms)	70.0 ± 23.9	100.5 ±7.2	N/A
Contraction / CaT (Up), Slope (a.u./s)	N/A	22104 ± 5517	20088.6 ± 1920.0
Time to Baseline 50% (ms)	N/A	N/A	666.2 ± 29.0
Time to Baseline 90% (ms)	N/A	N/A	807.5 ± 21.1
Relaxation or CaT (Down), Slope (a.u./s)	NA	-8926 ± 2144	-9055.8 ± 843.8
Duration 10% (ms)	N/A	N/A	375.4 ± 21.1
Duration 50% (ms)	519.7 ± 24.2	517.1 ± 17.0	500.0 ± 19.3
Duration 75% (ms)	581.1 ± 24.2	N/A	N/A
Duration 90% (ms)	613.7 ± 19.4	676.0 ± 10.3	561.8 ± 13.0
Beat Rate, Spontaneous (BPM)	N/A	N/A	33.3 ± 6.4
Interval, Spontaneous (ms)	N/A	N/A	2353.2 ± 472.4
Interval, Paced 1 Hz (ms)	N/A	N/A	998.18 ± 2.7
Beat Rate, Paced 1 Hz (BPM)	60	60	60

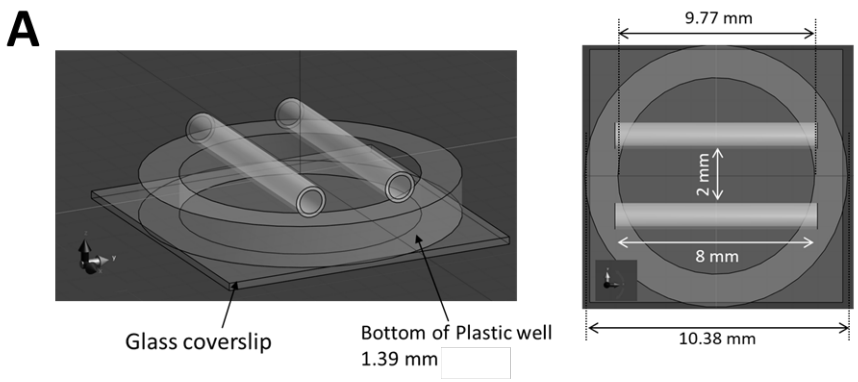
 # = Time to 100%

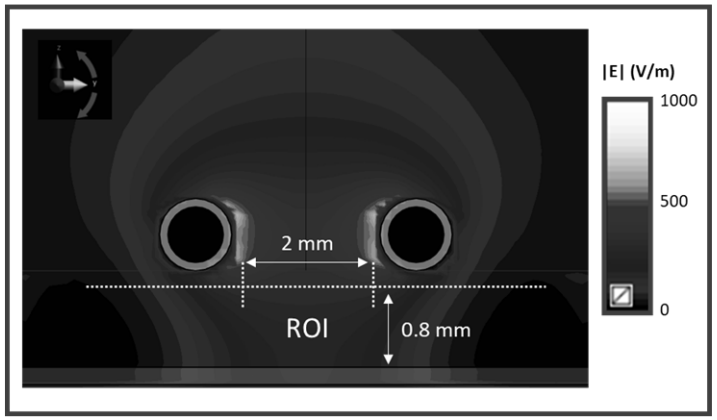


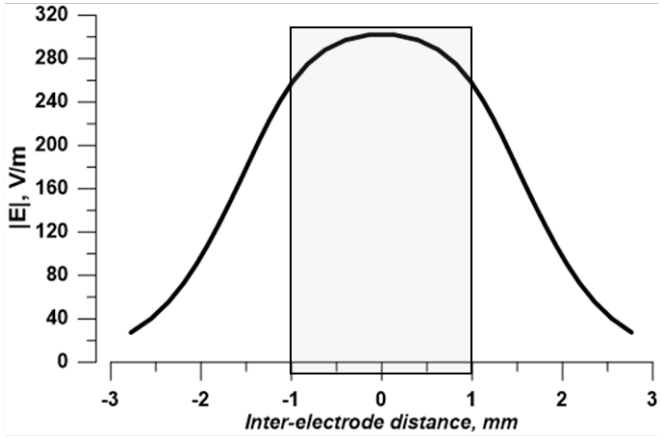
Supplemental Figure 1



Supplemental Figure 2





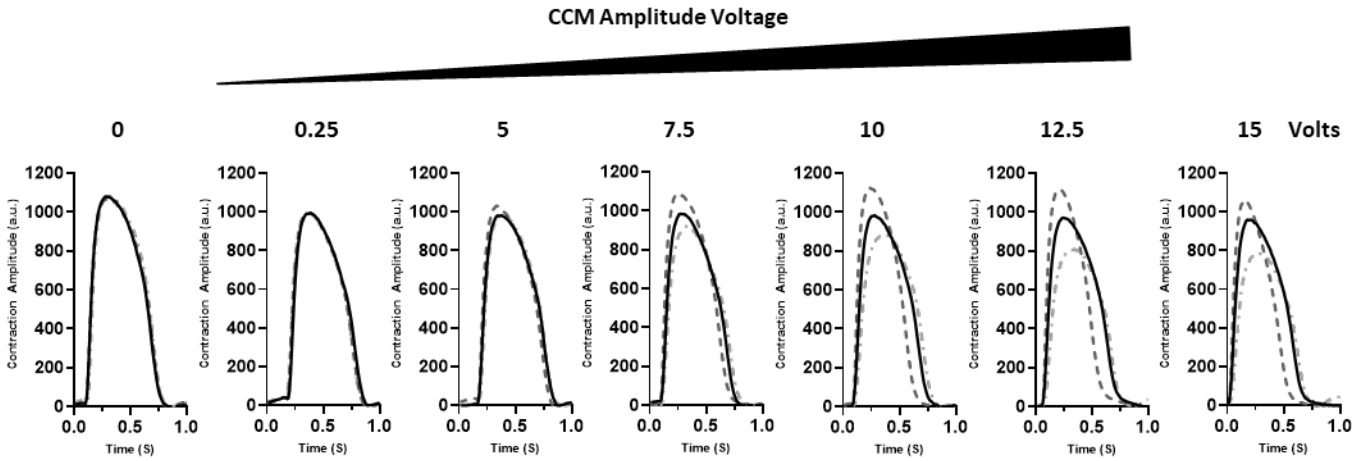


D

V_{app} (V)	E_{ROI} (V/cm)
1	2.8 ± 0.3
5	14 ± 1.5
10	28 ± 3.0

Supplemental Figure 3

A



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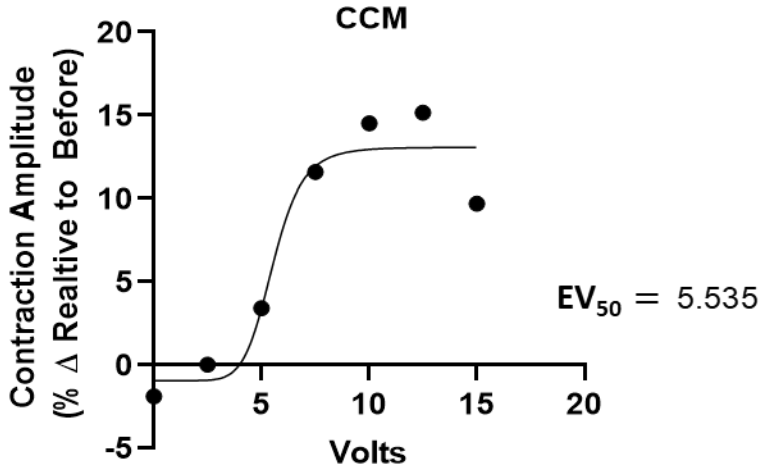
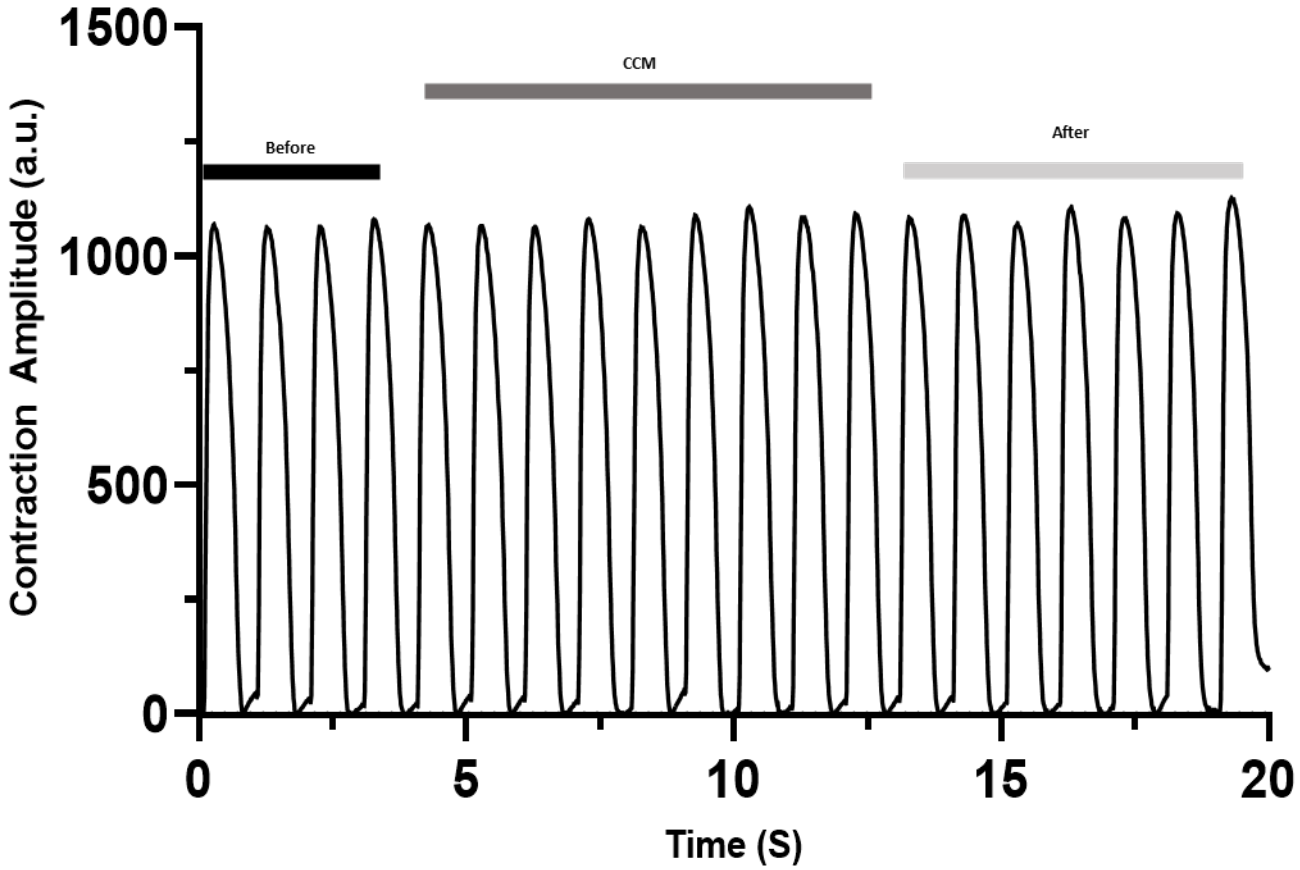
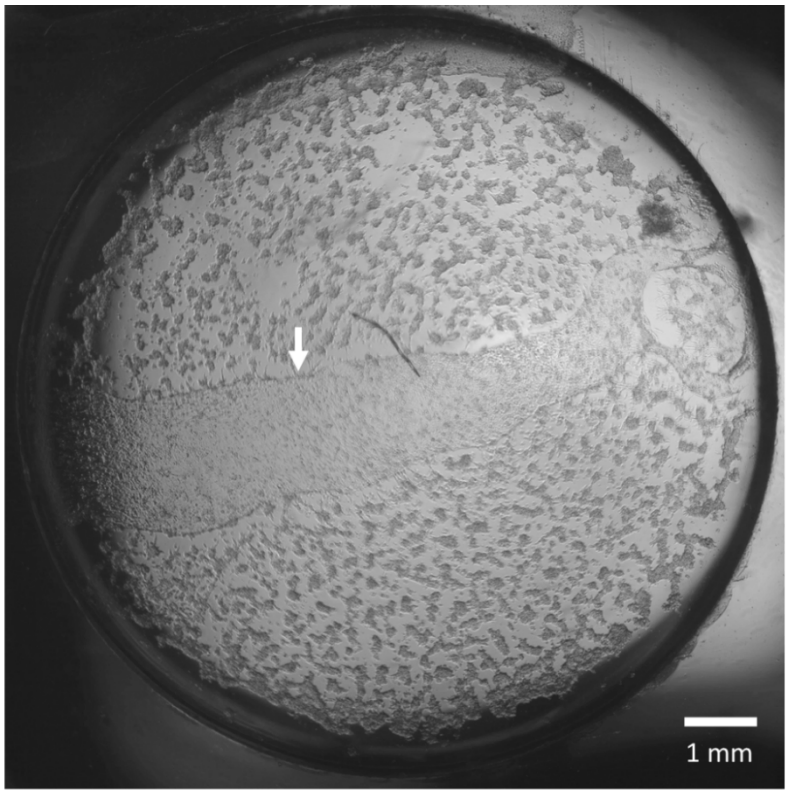


Supplemental Figure 4



Supplemental Figure 5



Supplemental Video