Supplementary Material S1

Spiral-wave dynamics in a Mathematical Model of Human Ventricular Tissue with Myocytes and Fibroblasts

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Our principal results have been given in the main paper of this paper. We present additional results of our numerical simulations of (a) MF composites and (b) two-dimensional (2D) arrays of such units (see Section on “Model and Methods”) in this Supplementary Material S1.

I. Results

a. A Myocyte-Fibroblast (MF) Composite

The ranges of parameters, which we use for our composite MF system, are consistent with those found in experimental studies and those used in earlier computational studies. For example, in a cell-culture experiment, Rook, et al. [1] have studied rat-heart fibroblasts and reported that the membrane resistance $R_f$, the fibroblast resting membrane potential $E_f$, and the gap-junctional conductance $G_{gap}$, lie, respectively, in the ranges $3 - 25 \ \Omega$, $-20$ to $-40 \ \text{mV}$, and $0.3 - 8.0 \ \text{nS}$. Kohl et al. [2] have studied non-excitable cardiac, mechanosensitive fibroblasts from the region of the sinoatrial node in a rat heart. Their study, which uses both intact tissue and cell cultures, estimates that $R_f \approx 1 \ \Omega$, $E_f \approx -15 \pm 10 \ \text{mV}$, and $G_{gap} \approx 4 - 6 \ \text{nS}$ for a well-coupled MF pair. In vitro studies, by Kiseleva, et al. [3], have examined rat mechanosensitive fibroblasts attached to the right atrium; they have found $E_f \approx -22 \pm 1.9 \ \text{mV}$ and $R_f = 0.51 \pm 0.01 \ \Omega$, for a control case, and $E_f \approx -46.5 \pm 1.8 \ \text{mV}$ and $R_f = 3.8 \pm 0.03 \ \Omega$, in the case of a large infarct caused by a myocardial infarction. In vitro studies by Kamkin, et al. [4] of non-excitable, mechanosensitive, cardiac fibroblasts from the atrium of a human heart have reported $E_f \approx -15.9 \pm 2.1 \ \text{mV}$, $R_f \approx 4.1 \pm 0.1 \ \Omega$. In vitro studies, by Kamkin et al. [5], of rat atrial fibroblasts attached to the sinoatrial node region yielded $E_f \approx -22 \pm 2 \ \text{mV}$ and $R_f = 510 \pm 10 \ \Omega$, for the control case, and for the case with myocardial infarction, and $E_f \approx -41 \pm 3 \ \text{mV}$ to $-28 \pm 3 \ \text{mV}$. Recent experiment, in culture, by Chilton et al. [6] have measured the cellular capacitance $C_{f,tot}$ of rat-ventricular fibroblasts by using a patch-clamp recording and found $C_{f,tot} \approx 6.3 \pm 1.7 \ \text{pF}$; they have shown that the input resistance of fibroblasts $R_f \approx 10.7 \pm 2.3 \ \Omega$. Their measurements have shown that $E_f$ depends on the inwardly rectifying $K^+$ current (Kir) and the potassium ion concentration $[K^+]_o$; e.g. when Kir is expressed, $E_f$ is $\approx -65 \pm 5 \ \text{mV}$ and $-80 \pm 1.8 \ \text{mV}$ for $[K^+]_o = 10 \ \text{mM}$ and $5.4 \ \text{mM}$, respectively. However, when Kir is absent, $E_f$ is $\approx -34 \pm 2 \ \text{mV}$. Furthermore, in culture, Shibukawa, et al. [7] have found, in patch-clamp recordings from rat-ventricular fibroblasts (active), that $C_{f,tot} \approx 4.5 \pm 0.4 \ \text{pF}$, $E_f \approx -58 \pm 3.9 \ \text{mV}$, $R_f \approx 5.5 \pm 0.6 \ \Omega$.

The computational studies of mathematical models for fibroblasts, discussed in the “Introduction” Section of the main paper, have also used a wide range of values for parameters for the cellular capacitance $C_{f,tot}$, the membrane conductance $G_f$, the fibroblast resting membrane potential $E_f$, and the gap-junctional coupling $G_{gap}$ between myocyte and fibroblasts. For example, Xie, et al. [8] have used $C_{f,tot} = 25 \ \text{pF}$, $G_f = 0.1 - 4 \ \text{nS}$, $E_f = -50 - 0 \ \text{mV}$, and $G_{gap} = 0 - 20 \ \text{nS}$ for an MF composite. The study of
Sachse, et al. [9] has used $C_{f,tot} = 4.5$ pF, $E_f = -58$ mV, and $G_{gap} = 0.1 - 100$ nS for an MF composite with active fibroblasts. Jacquemet, et al. [10] have studied the MF composite with active fibroblasts by using $C_{f,tot} = 4.5$ pF, $E_f = -58$ mV, and $G_{gap} = 0.09 - 4.05$ nS. MacCannell, et al. [11] have used $C_{f,tot} = 6 - 60$ pF, $E_f = -49.6$ mV and $G_{gap} = 1 - 3$ nS for their studies of an active-fibroblast model. To investigate in detail the effect of fibroblasts on a myocyte, we use the following wide ranges of parameters (these encompass the ranges used in the experimental and computational studies mentioned above): $C_{f,tot} = 6 - 60$ pF, $G_f = 0.1 - 1$ nS, $E_f = -39$ to 0 mV, and $G_{gap} = 0.3 - 8.0$ nS for our MF composites. However, to observe some special properties, such as autorhythmicity of MF composites, we vary the fibroblast parameters and gap-junctional conductances.

It has been noted in Refs. [12–14], that a myocyte cell can display autorhythmicity when it is coupled with fibroblasts; in particular, Ref. [12] shows that the cycle length of autorhythmicity activation depends on $E_f$ and $G_{gap}$. We find that $G_f$ and $C_{f,tot}$ play a less important role than $N_f$, $E_f$, and $G_{gap}$ in determining whether such autorhythmicity is obtained. In Fig. S4 we give some illustrative plots for $N_f = 1$, $E_f = 0nV$, and $G_f = 8nS$ that yield autorhythmicity; Fig. S4 (a) shows a plot of $V_m$ versus time; Fig. S4 (b) contains a plot of the frequency of autorhythmicity $f$ versus $G_{gap}$ for our MF composite; for more detailed studies of the dependence of such autorhythmicity on $N_f$ and $E_f$ we refer the reader to Ref. [15]. Figure S4 (b) shows that, for the range 0 nS $\leq G_{gap} \leq$ 16 nS, the myocyte behaves like an excitable cell, which produces one action potential when it is stimulated electrically; in the range 16 nS $\leq G_{gap} \leq$ 23 nS, the myocyte displays autorhythmicity and the cycle length $\lambda_f$, the time difference between the upstrokes of two successive action potentials, decreases with increasing $G_{gap}$; for $G_{gap} \geq 23nS$, the myocyte displays oscillatory behavior. Such autorhythmic and oscillatory responses of an MF composite [15] can occur at lower values of $G_{gap}$, e.g., $G_{gap} = 8$ nS, if we increase $N_f$.

b. Wave dynamics in a 2D simulation domain with MF composites

For the case of zero-sided coupling, with $E_f = 0$ mV and $G_f = 8$ nS, Figs. S6(a)-(c) show, respectively, pseudocolor plots of the myocyte transmembrane potential $V_m$, at time $t = 2$ s, for low-frequency autorhythmicity (e.g., with $G_{gap} = 17$ nS), high-frequency autorhythmicity (e.g., with $G_{gap} = 20$ nS), and when the MF composite displays (cf. Fig. S4) oscillatory behavior (e.g., with $G_{gap} = 23$ nS). In Fig. S6(d), we show the time series of $V_m(x, y, t)$, in the interval 0 s $\leq t \leq 4$ s, obtained from three representative points, shown by asterisks in Fig. S6(a), namely, $(x = 22.5$ mm, $y = 22.5$ mm) (black filled circles), $(x = 67.5$ mm, $y = 67.5$ mm) (blue filled diamonds), and $(x = 112.5$ mm,112.5 mm) (red filled triangles); Fig. S6(g) shows the corresponding power spectra, which we calculate from these time series, each of which has $2 \times 10^5$ data points; each one of these power spectra has discrete, sharp peaks at a fundamental frequency and at its harmonics; the periodic nature of the time series and these peaks in the power spectra provide evidence for the temporally periodic motion of the spiral wave in the region of low-frequency autorhythmicity. The analogs of Figs. S6(d) and (g) are shown in Figs. S6(e) and (h) for the regime of high-frequency autorhythmicity; the time series of $V_m(x, y, t)$, in the interval 0 s $\leq t \leq 4$ s, from $(x = 22.5$ mm, $y = 22.5$ mm) (black filled circles) and $(x = 67.5$ mm, $y = 67.5$ mm) (blue filled diamonds), show irregular behaviors and the corresponding power spectra show subsidiary peaks near the main peaks; however, the time series recorded from $(x = 112.5$ mm,112.5 mm) (red filled triangles) shows periodic behavior and, consequently, the corresponding power spectrum has discrete, strong peaks. The analogs of Figs. S6(d) and (g), for the oscillatory regime, are shown in Figs. S6(f) and (i).

If the value of $G_{mn}/G_{mf}$ is such that conduction failure occurs in a homogeneous, MF-composite simulation domain, then the MF-composite inhomogeneity behaves somewhat like a conduction inhomogeneity inasmuch as the spiral wave does not enter significantly into the region of the inhomogeneity. To check how far the wave penetrates into the MF-composite inhomogeneity, we show in Figs. S8 (a), (b), and (c) pseudocolor plots of $V_m$ at times $t = 2s$, $t = 6s$, and $t = 8s$, respectively, when a square MF-composite inhomogeneity of side $\ell = 33.75$mm, with $G_{mn}/G_{ff} = 1$ and $G_{mn}/G_{mf} = 1$ is placed with its bottom left corner at $(x = 56.25$ mm, $y = 56.25$ mm). Data for the time series of $V_m(x, y, t)$ are recorded at three points of the simulation domain, namely, $(x = 90$ mm, $y = 112.5$mm), which lies outside the inhomogeneity, $(x = 90$ mm, $y = 90$mm), at the top-right corner of the inhomogeneity, and $(x = 90$ mm, $y = 67.5$ mm), on the right-middle side of the inhomogeneity; these points are indicated by asterisks in Fig. S8 (c) and the data recorded from them are represented, respectively, by black circles, blue diamonds, and red triangles in Figs. S8 (d)-(f). Figure S8 (d) contains plots of the time series of $V_m$ (each one of these time series contain $2 \times 10^5$ data points). Figure S8 (e) shows the corresponding plots of the inter-beat intervals (ibis) versus the beat number $n$; and the power spectra $E(\omega)$, which follow from the time series of $V_m$, are
given in Fig. S8 (f).

From the time series of $V_m$ (Fig. S8 (d)), we see small-amplitude oscillations in $V_m$ if the time series are obtained from points at the side and corner of the MF-composite inhomogeneity; however, if the point lies outside the inhomogeneity, this time series shows a periodic pattern of action potentials. These times series and the plots of the ibi (Fig. S8 (e)) show that the oscillations in $V_m$, from these three different points, are in phase; to this extent the MF-composite inhomogeneity acts like a conduction inhomogeneity [16]; however, the spiral wave does penetrate the region of the inhomogeneity marginally, so, in this sense, the MF-composite inhomogeneity acts like an ionic inhomogeneity [16].

We turn now to an examination of the interaction of spiral waves with an MF-composite inhomogeneity for different values of $G_{gap}$. For the same MF-composite inhomogeneity and parameters as in Fig. 13 (c) in the “Results” Section of the main paper, we show in Figs. S9 (a), (b), and (c) for, respectively, $G_{gap} = 0.5$ nS (low coupling), 2 nS (intermediate coupling), and 8 nS (high coupling), pseudocolor plots of $V_m$, at time $t = 2$ s, with $G_{mm}/G_{mf} = 1$ and $G_{mm}/G_{mf} = 200$. We also obtain time series for $V_m(x, y, t)$ from a point outside the inhomogeneity ($x = 22.5$mm, $y = 22.5$mm) and a point inside it ($x = 67.5$mm, $x = 22.5$mm), both of which are depicted by asterisks in Figs. S9 (a)-(c). These time series, with $2 \times 10^5$ data points each, are plotted in Figs. S9 (d), (e), and (f) for $G_{gap} = 0.5$ nS, 2 nS, and 8 nS, respectively (data from the points outside and inside the inhomogeneity are represented, respectively, by black circles and red triangles); Figs. S9 (g), (h), and (i) show the corresponding plots of the ibi versus the beat number $n$; and the associated power spectra $E(\omega)$ are depicted in Figs. S9 (j), (k), and (l). The Video S10 has four panels that show the spatiotemporal evolution of pseudocolor plots of $V_m$ and the spiral-tip trajectories for $2 \leq t \leq 3$ s for a control myocyte layer with no inhomogeneities (top left panel) and, in addition, the simulation domains of Figs. S9 (a)-(c) (top right, bottom left, and bottom right panels). Here too we obtain a rich variety of spiral-wave behaviors inside and outside of the MF-composite inhomogeneity, as in the cases with zero- and single-sided couplings.

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II. Figures

Figure S1. Schematic diagram: A small part of our square simulation domain with sites occupied by myocyte-fibroblast (MF) composites, connected by the gap-junctional conductance $G_{gap}$, with (a) zero-sided, (b) single-sided, and (c) double-sided couplings between MF composites.
Figure S2. Plots of action potentials: The myocyte action potential $V_m$ (full symbols and lines) and the fibroblast action potential $V_f$ (unshaded symbols and dashed lines), with a passive fibroblast of capacitance $C_{f,tot} = 25.2 \, \text{pF}$ coupled with a myocyte for (a) $E_f = 0 \, \text{mV}$ and $G_f = 0.1 \, \text{nS}$, (b) $E_f = -19 \, \text{mV}$ and $G_f = 0.1 \, \text{nS}$, (c) $E_f = -39 \, \text{mV}$ and $G_f = 0.1 \, \text{nS}$, (d) $E_f = 0 \, \text{mV}$ and $G_f = 1 \, \text{nS}$, (e) $E_f = -19 \, \text{mV}$ and $G_f = 1 \, \text{nS}$, (f) $E_f = -39 \, \text{mV}$ and $G_f = 1 \, \text{nS}$, (g) $E_f = 0 \, \text{mV}$ and $G_f = 4 \, \text{nS}$, (h) $E_f = -19 \, \text{mV}$ and $G_f = 4 \, \text{nS}$, and (i) $E_f = -39 \, \text{mV}$ and $G_f = 4 \, \text{nS}$; red squares (full or unshaded) indicate $G_{gap} = 0.3 \, \text{nS}$; blue diamonds (full or unshaded) indicate $G_{gap} = 1 \, \text{nS}$; gray triangles (full or unshaded) indicate $G_{gap} = 8 \, \text{nS}$; black squares (full or unshaded) indicate an uncoupled myocyte.
Figure S3. Plots of action potentials: The myocyte action potential $V_m$ (full symbols and lines) and the fibroblast action potential $V_f$ (unshaded symbols and dashed lines), with a passive fibroblast of capacitance $C_{f,tot} = 63 \, \text{pF}$ coupled with a myocyte for (a) $E_f = 0 \, \text{mV}$ and $G_f = 0.1 \, \text{nS}$, (b) $E_f = -19 \, \text{mV}$ and $G_f = 0.1 \, \text{nS}$, (c) $E_f = -39 \, \text{mV}$ and $G_f = 1 \, \text{nS}$, (d) $E_f = 0 \, \text{mV}$ and $G_f = 1 \, \text{nS}$, (e) $E_f = -19 \, \text{mV}$ and $G_f = 1 \, \text{nS}$, (f) $E_f = -39 \, \text{mV}$ and $G_f = 1 \, \text{nS}$, (g) $E_f = 0 \, \text{mV}$ and $G_f = 4 \, \text{nS}$, (h) $E_f = -19 \, \text{mV}$ and $G_f = 4 \, \text{nS}$, and (i) $E_f = -39 \, \text{mV}$ and $G_f = 4 \, \text{nS}$; red squares (full or unshaded) indicate $G_{gap} = 0.3 \, \text{nS}$; blue diamonds (full or unshaded) indicate $G_{gap} = 1 \, \text{nS}$; gray triangles (full or unshaded) indicate $G_{gap} = 8 \, \text{nS}$; black squares (full or unshaded) indicate an uncoupled myocyte.

Figure S4. Transmembrane potential of myocyte $V_m$ in an MF composite: (a) Plots of $V_m$ versus $t$, with $C_{f,tot} = 6.3 \, \text{pF}$, $G_f = 8.0 \, \text{nS}$, and $E_f = 0 \, \text{mV}$ for $G_{gap} = 17 \, \text{nS}$ (full black circles), $G_{gap} = 20 \, \text{nS}$ (full blue diamond) and $G_{gap} = 23 \, \text{nS}$ (full red triangle). (b) Plot of the frequency $f$ (see text) versus $G_{gap}$. The MF composite shows excitable, autorhythmicity and oscillatory behavior in the regime $0 \leq G_{gap} < 16 \, \text{nS}$, $16 \leq G_{gap} < 23 \, \text{nS}$ and $G_{gap} \geq 23 \, \text{nS}$, respectively.
Figure S5. Initiation of a spiral wave by the S1-S2 parallel field protocol: To inject a spiral wave, the diffusion constant is set to $D_{mm} = 0.000385 \text{ cm}^2/\text{ms}$; this is a quarter of its original value, which is 0.00154 cm$^2$/ms; an S1 stimulus of strength 150 pA/pF is applied for 3 ms at the left boundary; after 560 ms, an S2 stimulus of strength 450 pA/pF is applied for 3 ms just behind the refractory tail of the plane wave initiated by the S1 stimulus; this S2 stimulus is applied over the region $x = 360$ and $1 \leq y \leq 550$. We reset $D_{mm}$ to its original value after 880 ms; this procedure yields a fully developed spiral wave at $t = 976$ ms. The spiral wave configuration in (c) is used as the initial condition for our subsequent studies.
Figure S6. Pseudocolor plots of the myocyte transmembrane potential \( V_m \), at time \( t = 2 \) s, for the case of zero-sided couplings, with \( E_f = 0 \) mV and \( G_f = 8 \) nS: (a) low-frequency autorhythmicity \( (G_{gap} = 17 \) nS), (b) high-frequency autorhythmicity \( (G_{gap} = 20 \) nS), and (c) when the MF composite displays oscillatory behavior \( (G_{gap} = 23 \) nS) (see, Figs. S4 for the boundaries of these regions). Figures (d)-(f) show, respectively, the time series of \( V_m(x,y,t) \), in the time interval \( 0 \) s \( \leq t \leq 4 \) s, obtained from three representative points, shown by asterisks in Fig. S6(a)-(c), namely, \( (x = 22.5 \) mm, \( y = 22.5 \) mm) (black filled circles), \( (x = 67.5 \) mm, \( y = 67.5 \) mm) (blue filled diamonds), and \( (x = 112.5 \) mm, \( y = 112.5 \) mm) (red filled triangles). Figures S6(g)-(i) show the corresponding power spectra, which we calculate from these time series, each of which has \( 2 \times 10^5 \) data points.
Figure S7. Pseudocolor plots of the transmembrane potential $V_m$ of the myocyte at time, $t = 2$ s, in the presence of a square MF-composite inhomogeneity, of side $\ell = 33.75$ mm, for the case of single-sided coupling with $G_{mm}/G_{mf} = 1$; the bottom-left corner of the inhomogeneity is fixed at (a) $(x = 33.75$ mm, $y = 67.5$ mm), (b) $(x = 56.25$ mm, $y = 56.25$ mm), and (c) $(x = 78.75$ mm, $y = 45$ mm); the white solid lines in these figures show the spiral-tip trajectories in the time interval $2\ s \leq t \leq 3\ s$ and the local time series data are recorded from points that are shown by asterisks. The plots in (d)-(f) show the time series for $V_m$, in the interval $0\ s \leq t \leq 4\ s$, which are obtained from the points outside ($(x = 112.5$ mm, $y = 112.5$ mm) for all cases) and inside the fibroblast inhomogeneity ($(x = 45$ mm, $y = 90$ mm), $(x = 67.5$ mm, $y = 67.5$ mm), and $(x = 90$ mm, $y = 67.5$ mm) for (a), (b), and (c), respectively), represented by black circles and red triangles, respectively; (g), (h), and (i) show plots of the inter-beat intervals (ibis) versus the beat number $n$ for the time series of $V_m$ mentioned above; each one of these time series contain $2 \times 10^5$ data points; the power spectra $E(\omega)$, which follow from these time series, are given in (j), (k), and (l).
Figure S8. Pseudocolor plots of $V_m$ with an MF-composite inhomogeneity: The transmembrane potential of the myocyte $V_m$ at time, (a) $t = 2$ s, (b) $t = 4$ s, and (c) $t = 6$ s, when a square MF-composite inhomogeneity with, $G_{mm}/G_{ff} = 1$ and $G_{mm}/G_{mf} = 1$, and of length $\ell = 33.75$ mm, is placed with its lower-left corner at $(x = 67.5$ mm, $y = 67.5$ mm); (d) shows the time series of $V_m(x, y, t)$, in the time interval $0 \leq t \leq 4$ s, obtained from three representative points, shown by asterisks in (c), namely, $(x = 90$ mm, $y = 112.5$ mm) (black filled circles), $(x = 90$ mm, $y = 90$ mm) (blue filled diamonds), and $(x = 90$ mm, $67.5$ mm) (red filled triangles); the corresponding ibi’s, calculated from data sets of $4 \times 10^5$ points, are shown in (e); (f) shows the power spectrum of the above time series of $V_m$ of length $2 \times 10^5$ data points (after removing the initial $2 \times 10^5$ iteration steps).
Figure S9. Pseudocolor plots of the transmembrane potential of the myocyte $V_m$, at time $t = 2$ s, in the presence of a square, MF-composite inhomogeneity, of side $\ell = 33.75$ mm and with its lower-left-hand corner placed at $(x = 56.25$ mm, $y = 56.25$ mm) for the case of doubled-sided coupling with $G_{mm}/G_{ff} = 1$ and $G_{mm}/G_{ff} = 200$: (a) $G_{gap} = 0.5$ nS, (b) $G_{gap} = 2$ nS, and (c) $G_{gap} = 8$ nS. Video S10 illustrates the spatiotemporal evolution of these spiral waves. The time series for $V_m(x, y, t)$, with $2 \times 10^5$ data points each, from a point outside the inhomogeneity $(x = 22.5$ mm, $y = 22.5$ mm) and a point inside it $(x = 67.5$ mm, $x = 67.5$ mm), both of which are depicted by asterisks in (a)-(c), are plotted in (d), (e), and (f) for $G_{gap} = 0.5$ nS, 2 nS, and 8 nS, respectively (data from the points outside and inside the inhomogeneity are represented, respectively, by black circles and red triangles); (g), (h), and (i) show the corresponding plots of the ibi versus the beat number $n$; and the associated power spectra $E(\omega)$ are depicted in (j), (k), and (l).
| \( C_{f,tot} \) (pA) | \( G_f \) (nS) | \( G_{gap} \) (nS) | \( E_f \) (mV) | \( N_f \) | \( \Delta APD_{70\%} \) (ms) | \( \Delta APD_{80\%} \) (ms) | \( \Delta APD_{90\%} \) (ms) | \( \Delta V_{\text{max}} \) (mV/ms) | \( \Delta V_{\text{rest}} \) (mV) |
|---|---|---|---|---|---|---|---|---|---|
| 6.3 | 0.1 | 0.3 | -9 | 1 | 0.82 | 0.90 | 1.06 | -2.41 | 0.12 |
| | 0.1 | 0.3 | -9 | 2 | 1.66 | 1.82 | 2.14 | -5.49 | 0.25 |
| | 0.1 | 0.3 | -9 | 3 | 2.52 | 2.78 | 3.26 | -9.28 | 0.38 |
| | 0.1 | 0.3 | -9 | 4 | 3.42 | 3.76 | 4.42 | -13.83 | 0.52 |
| | 0.1 | 0.3 | -9 | 5 | 4.32 | 4.76 | 5.62 | -19.16 | 0.67 |
| | 0.1 | 0.3 | -9 | 6 | 5.26 | 5.80 | 6.86 | -22.21 | 0.82 |
| | 0.1 | 0.3 | -9 | 7 | 6.22 | 6.86 | 8.12 | -25.40 | 0.99 |
| | 0.1 | 0.3 | -9 | 8 | 7.22 | 7.96 | 9.44 | -29.41 | 1.16 |
| | 0.1 | 0.3 | -9 | 9 | 8.24 | 9.08 | 10.80 | -34.21 | 1.34 |
| | 0.1 | 0.3 | -9 | 10 | 9.28 | 10.24 | 12.20 | -39.74 | 1.52 |
| | 0.1 | 0.3 | -9 | 11 | 10.36 | 11.44 | 13.64 | -45.68 | 1.72 |
| | 0.1 | 0.3 | -9 | 12 | 11.48 | 12.66 | 15.14 | -48.79 | 1.92 |
| | 0.1 | 0.3 | -19 | 1 | 0.26 | 0.34 | 0.50 | -2.08 | 0.10 |
| | 0.1 | 0.3 | -19 | 2 | 0.56 | 0.70 | 1.00 | -4.64 | 0.21 |
| | 0.1 | 0.3 | -19 | 3 | 0.86 | 1.08 | 1.54 | -7.72 | 0.33 |
| | 0.1 | 0.3 | -19 | 4 | 1.18 | 1.50 | 2.12 | -11.34 | 0.45 |
| | 0.1 | 0.3 | -19 | 5 | 1.52 | 1.92 | 2.70 | -15.53 | 0.57 |
| | 0.1 | 0.3 | -19 | 6 | 1.86 | 2.36 | 3.34 | -20.29 | 0.70 |
| | 0.1 | 0.3 | -19 | 7 | 2.24 | 2.84 | 3.98 | -22.61 | 0.84 |
| | 0.1 | 0.3 | -19 | 8 | 2.64 | 3.32 | 4.68 | -25.34 | 0.98 |
| | 0.1 | 0.3 | -19 | 9 | 3.06 | 3.84 | 5.40 | -28.67 | 1.13 |
| | 0.1 | 0.3 | -19 | 10 | 3.50 | 4.38 | 6.16 | -32.58 | 1.28 |
| | 0.1 | 0.3 | -19 | 11 | 3.96 | 4.94 | 6.94 | -37.04 | 1.44 |
| | 0.1 | 0.3 | -19 | 12 | 4.44 | 5.52 | 7.78 | -41.99 | 1.60 |
| | 0.1 | 0.3 | -29 | 1 | -0.28 | -0.22 | -0.08 | -1.76 | 0.09 |
| | 0.1 | 0.3 | -29 | 2 | -0.54 | -0.40 | -0.12 | -3.85 | 0.18 |
| | 0.1 | 0.3 | -29 | 3 | -0.80 | -0.58 | -0.16 | -6.29 | 0.28 |
| | 0.1 | 0.3 | -29 | 4 | -1.04 | -0.76 | -0.18 | -9.10 | 0.37 |
| | 0.1 | 0.3 | -29 | 5 | -1.28 | -0.90 | -0.18 | -12.29 | 0.48 |
| | 0.1 | 0.3 | -29 | 6 | -1.50 | -1.04 | -0.14 | -15.89 | 0.58 |
| | 0.1 | 0.3 | -29 | 7 | -1.70 | -1.16 | -0.08 | -19.87 | 0.69 |
| | 0.1 | 0.3 | -29 | 8 | -1.88 | -1.26 | 0.02 | -22.37 | 0.81 |
| | 0.1 | 0.3 | -29 | 9 | -2.04 | -1.32 | 0.10 | -24.49 | 0.93 |
| | 0.1 | 0.3 | -29 | 10 | -2.20 | -1.38 | 0.24 | -27.02 | 1.05 |
| | 0.1 | 0.3 | -29 | 11 | -2.32 | -1.42 | 0.40 | -29.96 | 1.18 |
| | 0.1 | 0.3 | -29 | 12 | -2.44 | -1.44 | 0.60 | -33.30 | 1.31 |
| | 0.1 | 0.3 | -39 | 1 | -0.82 | -0.76 | -0.64 | -1.45 | 0.07 |
| | 0.1 | 0.3 | -39 | 2 | -1.64 | -1.52 | -1.26 | -3.11 | 0.15 |
| | 0.1 | 0.3 | -39 | 3 | -2.46 | -2.26 | -1.86 | -4.99 | 0.22 |
| | 0.1 | 0.3 | -39 | 4 | -3.26 | -2.98 | -2.46 | -7.10 | 0.30 |
| | 0.1 | 0.3 | -39 | 5 | -4.04 | -3.70 | -3.02 | -9.45 | 0.39 |
| | 0.1 | 0.3 | -39 | 6 | -4.82 | -4.40 | -3.58 | -12.05 | 0.47 |
| | 0.1 | 0.3 | -39 | 7 | -5.58 | -5.08 | -4.10 | -14.90 | 0.56 |
| | 0.1 | 0.3 | -39 | 8 | -6.32 | -5.74 | -4.62 | -18.00 | 0.65 |
| | 0.1 | 0.3 | -39 | 9 | -7.04 | -6.40 | -5.10 | -21.36 | 0.74 |
| | 0.1 | 0.3 | -39 | 10 | -7.76 | -7.04 | -5.56 | -23.17 | 0.83 |
| | 0.1 | 0.3 | -39 | 11 | -8.46 | -7.64 | -5.98 | -24.89 | 0.93 |
| | 0.1 | 0.3 | -39 | 12 | -9.14 | -8.24 | -6.38 | -26.87 | 1.03 |

Table S1. The values of \( C_{f,tot} \), \( G_f \), \( G_{gap} \), \( E_f \), and \( N_f \) for a single MF composite and the changes in the AP morphology, relative to that of an uncoupled myocyte. We concentrate on the APD, \( V_{\text{max}} \), and \( V_{\text{rest}} \) and list the changes, indicated by \( \Delta \), in these parameters. \( \Delta APD_{70\%} \), \( \Delta APD_{90\%} \), and \( \Delta APD_{90\%} \) denote, respectively, the changes in the APD at 70%, 80%, and 90% repolarization. Note that here we have low values (see text) for both \( G_f \) (0.1 nS) and \( G_{gap} \) (0.3 nS).