Supplementary Materials for
CompuCell3D Model of Cell Migration Reproduces Chemotaxis

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I. TABLE OF RESULTS

Table I. For cell radius R = 10 without chemotactic response, these are the results from the MSD fit and drift speed calculation. ϕ_f is the Lamel volume relative to cell volume, $\lambda_{F-actin}$ is the protrusion coefficient. D is the diffusion coefficient, P is the persistent time, S relates to the short time interval diffusive regime, and V_d is the drift speed.

R = 10	mu = 0				
ϕ_f	$\lambda_{F-actin}$	$D[R^2/\text{MCS}]$	P[MCS]	S	$V_d[R/\text{MCS}]$
0.05	125	4.18E-04	1.30E+03	8.39E-01	5.32E-04
0.05	150	1.88E-03	3.52E+03	9.21E-01	7.31E-04
0.05	175	3.16E-03	7.20E+03	9.54E-01	7.37E-04
0.1	125	1.84E-04	1.05E+03	8.08E-01	3.81E-04
0.1	150	1.86E-03	2.90E+03	9.06E-01	8.06E-04
0.1	175	5.40E-03	7.18E+03	9.54E-01	9.65E-04
0.2	125	–	–	–	–
0.2	150	7.18E-04	2.49E+03	8.92E-01	4.86E-04
0.2	175	3.17E-03	4.60E+03	9.29E-01	8.64E-04

Table II. For cell radius R = 10 with chemotactic response, these are the results from the MSD, drift speed and chemotactic efficiency. V_T is the terminal velocity and ε is the chemotactic efficiency.

R = 10	mu = 10^6							
ϕ_f	$\lambda_{F-actin}$	$D[R^2/\text{MCS}]$	P[MCS]	S	$B[R^2/\text{MCS}^2]$	$V_d[R/\text{MCS}]$	$V_T[R/\text{MCS}]$	ε
0.05	125	3.20E-04	1.20E+03	5.90E-02	1.07E-07	5.75E-04	3.28E-04	5.70E-01
0.05	150	1.45E-03	3.15E+03	1.33E-02	1.00E-07	7.61E-04	3.17E-04	4.16E-01
0.05	175	4.79E-03	9.27E+03	3.97E-03	3.97E-08	7.47E-04	1.99E-04	2.67E-01
0.1	125	1.85E-04	9.95E+02	9.78E-02	2.32E-08	4.49E-04	1.52E-04	3.39E-01
0.1	150	1.73E-03	2.76E+03	1.11E-02	4.61E-08	7.83E-04	2.15E-04	2.74E-01
0.1	175	6.80E-03	7.15E+03	2.80E-03	2.88E-08	9.72E-04	1.70E-04	1.74E-01
0.2	125	–	–	–	–	–	–	–
0.2	150	7.54E-04	2.58E+03	2.51E-02	9.69E-09	5.14E-04	9.84E-05	1.91E-01
0.2	175	3.19E-03	3.69E+03	5.87E-03	1.49E-08	9.13E-04	1.22E-04	1.34E-01

II. 4-REGIMES MSD FIT STEP-BY-STEP WITH EXAMPLE

Fitting an MSD curve can be difficult due to the multiple regimes for very different time scales. Some parameters depend on each other and it can be hard to separate them. A direct implementation of a gradient descent algorithm may not give the best result, even if

you weight the data appropriately. Fitting regions of the curve separately and iterating this process over and over again may work but it demands a lot of work and has a big margin of arbitrary decisions.

Here we present a step-by-step fitting of Eq. 1 over a MSD curve that presents all four regimes of movement (short time diffusive, intermediate ballistic, long term diffusive and long term ballistic). This method gives very good fits, although it is more complicated than simply hitting play on a data analysis software, but it is faster and less arbitrary than the brute force iterative fitting in each curve region. You also do not need any sophisticated algorithm for fitting. You only need to do differentiation, selection of specific data range, and to perform any gradient descent fitting iteration.

$$\langle|\Delta\vec{r}|^2\rangle = 2D(\Delta t - P(1 - e^{-\Delta t/P})) + A\Delta t + B\Delta t^2 \quad . \tag{1}$$

We start with a text file containing two columns, one for the Δt and the other for MSD. We assume this file is already the average MSD of all cell trajectories. Plot MSD vs Δt and set log scale in both x and y coordinates to get a graph like Fig. 1, where you can see clearly the four regimes. We are using the software OriginPro 2017 (64-bit) from OriginLab Corporation, Northampton, MA, USA. Be careful how you track your cells: tracking by the nucleus center of mass or by the whole cell center of mass yield different MSD curves, specially in the first diffusive regime.

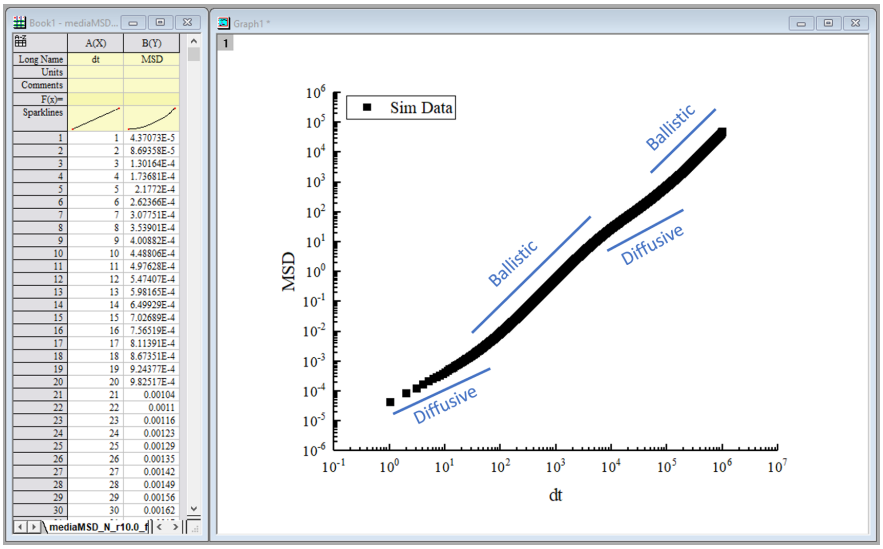

Figure 1. Plot of MSD vs Δt in log-log scale.

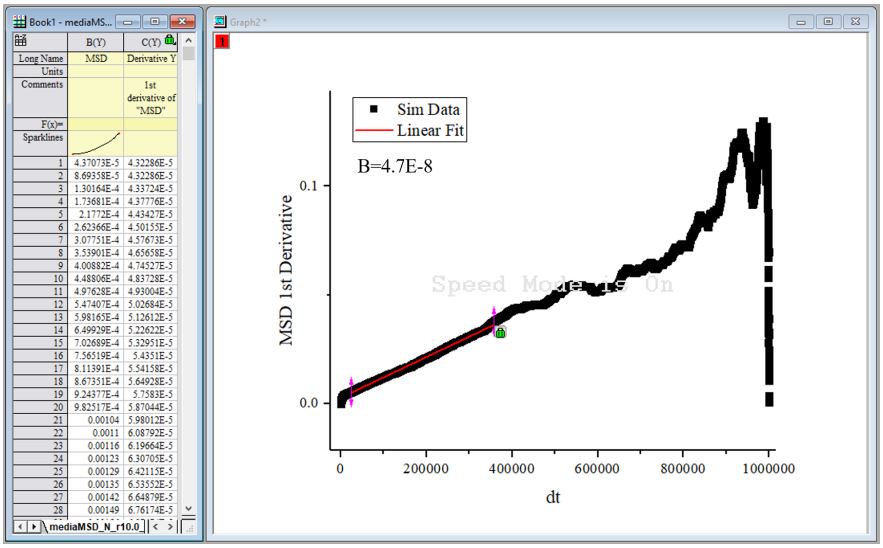

Figure 2. Plot and linear fit of the linear region in the 1st differentiated MSD curve (linear scale).

The easiest parameter to extract is B, since the squared term is the only to survive for large Δt.. Since humans can identify a line much better than a parabola, we first differentiate our MSD curve once (in linear x and y coordinates). After identifying the straight line region, you can perform a linear fit. We show this first result in Fig. 2 Just remember that the angular coefficient output will be $2B$ because we differentiated Eq. 1 once.

We found our parameter B. Now we recalculate our MSD without the Δt^2 term by subtracting it MSD-$B\Delta t^2$. We plot the MSD curve in Fig. 3 again just to show you how it looks without the long term ballistic regime.

Now we have to separate at least one of the A, D and P parameters. We opted for getting rid of the linear term $A\Delta t$ by differentiating the MSD twice, giving the exponential

$$\frac{d}{d(\Delta t)}\langle|\Delta\vec{r}|^2\rangle = \frac{2D}{P}e^{-\Delta t/P} \quad . \tag{2}$$

So we have to find a linear region in the MSD 2nd derivative graph (using log scale in the y coordinate only), see Fig. 4. The smoothed curve in blue helps identifying the linear region. Then we perform a nonlinear curve fit using Eq. 2 and get D and P.

Now we recalculate our MSD without the Fürth term by subtracting MSD$-2D(\Delta t - P(1 - exp(-\Delta t/P)))$ so that only the linear term remains. Now you find the linear region in the graph and perform a linear fit fixing the intercept coefficient at zero, as we show in Fig. 5. For this one, it does not matter if the graph is put in log-log or linear-linear (it looks

like a straight line in both systems), provided that you perform a linear fit in the original coordinate system.

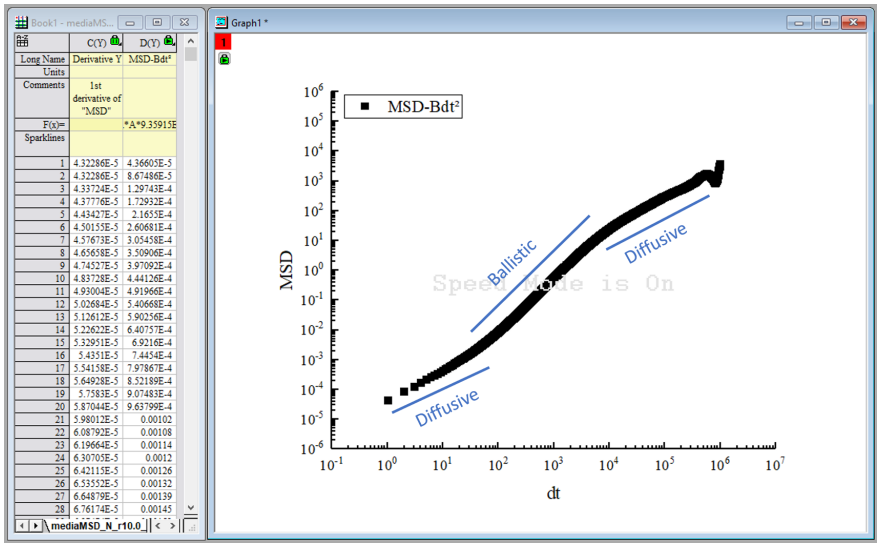

Figure 3. MSD without the ballistic term $B\Delta t^2$.

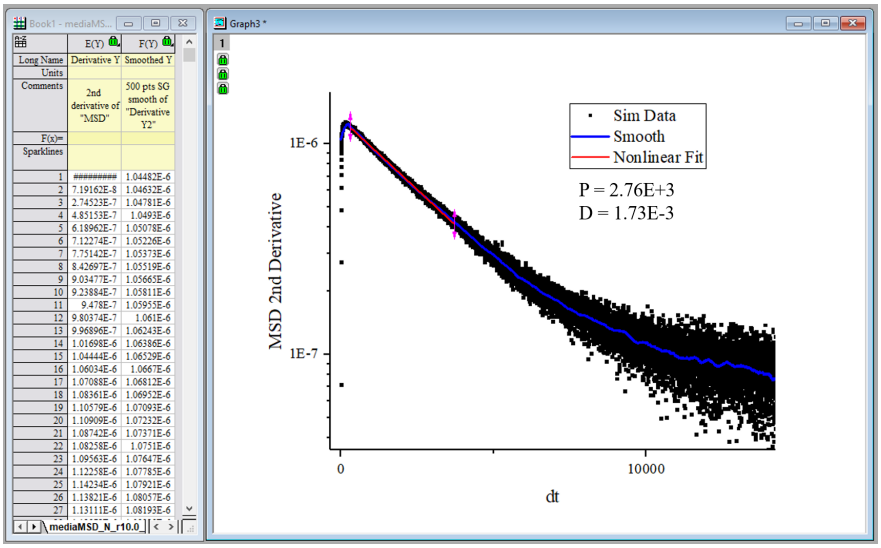

Figure 4. Plot and nonlinear fit (using Eq. 2) of MSD 2nd derivative, finding parameters D and P. Graph scales are log-linear.

With all 4 parameters, we can plot both MSD data points and the final fitted curve, showed in Fig. 6. As you may have noticed, not all steps are user independent, different decisions will impact the final result, for example: 1) what exactly is the range of data points I have to set in each fit step? 2) do I ignore this noisy part? 3) do I ignore this curvy part in my supposedly linear region? 4) in which order do I fit the parameters? 5) do I repeat

the process for some of the parameters? To be practical, we don't care about obtaining precise values as much as we care about the relationship between the fitting parameters and cell behavior. For example: cells with clear and stable polarization should present higher P relative to those with less stable polarization; cells that walk longer distances over same periods of time should present a higher D relative to those that do not move as much; cells that present higher fluctuations in its structure should present a higher A; and cells that walk faster towards a chemical field source should present a higher B.

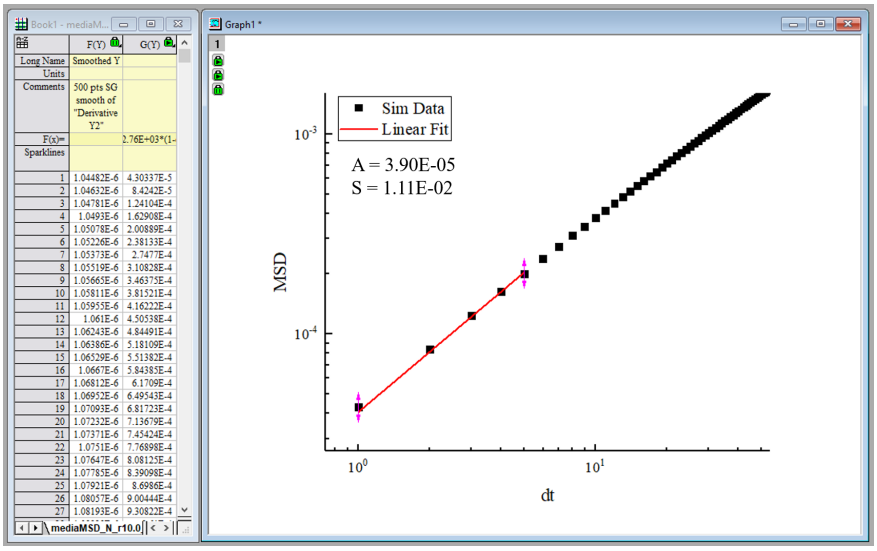

Figure 5. MSD curve only with the remaining $A\Delta t$ term.

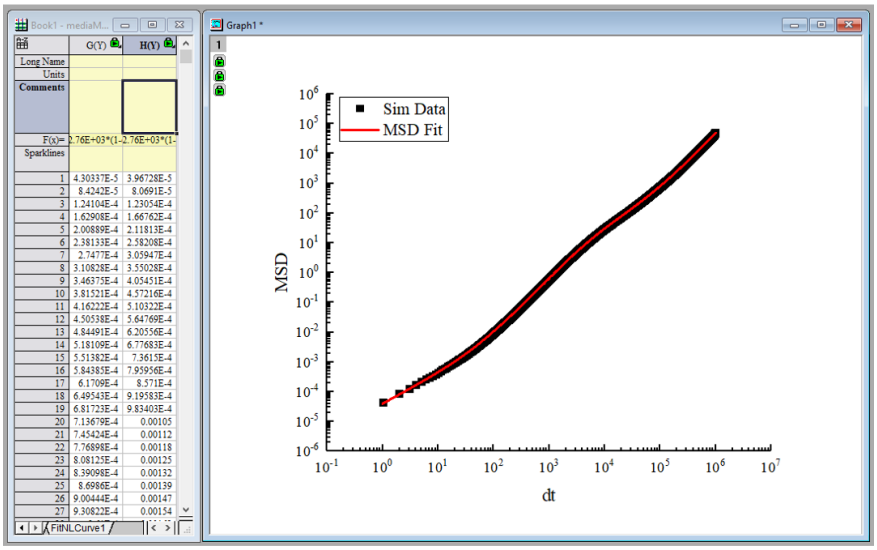

Figure 6. Final MSD fit in log-log scale.