

1 Problem 1: Cell Migration

Calculations:

Path length (um) = $\sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2}$ for each time interval. Sum over total time for total path length.

Speed ($\frac{um}{min}$) = path length/time for each time interval. Average over all time intervals.

MSD = $abs(x_f - x_0)^2 + abs(y_f - y_0)^2$ where f denotes the final time point and 0 denotes the initial time point.
→ mean squared displacement

Displacement (um) = $\sqrt{(x_f - x_0)^2 + (y_f - y_0)^2}$ where f denotes the final time point and 0 denotes the initial time point.

$$MSD = 2S^2P \left(t - P \left(1 - e^{t/P} \right) \right)$$

CI = Displacement/Path length

See Excel spreadsheet for answers.

Persistence time. Use

Will need to use

A) Solver, or

B) Excel Goal Seek (Iterative Method)

Speed: known (calculated earlier)

MSD: known (can be calculated)

Fix these, solve for P.

Cell 1			
x	y	Path Length (um)	Speed (um/min)
91.23	12.42		
86.07	3.24	10.53081193	0.702054129
102.84	-4.92	18.64989276	1.243326184
109.29	1.2	8.891394716	0.592759648
119.61	18.54	20.17865209	1.345243472
117.03	-1.86	20.56249985	1.370833323
115.74	0.18	2.41364869	0.160909913
113.16	1.2	2.774310725	0.184954048
110.58	4.26	4.002499219	0.266833281
108	6.3	3.289072818	0.219271521

Average Speed (um/min) 0.676242836
MSD 318.6873
Displacement (um) 17.85181503
Total Path Length (um) 91.2927828
CI 0.195544648
Time (min) 15
Persistence (min) 10.24
MSD calc 459.5426956

Cell 3			
x	y	Path Length (um)	Speed (um/min)
109.29	23.18		
122.19	23.18	12.9	0.86
111.87	31.34	13.15629127	0.877086085
108	30.32	4.002161916	0.266810794
89.94	24.2	19.06877028	1.271251352
3.81	31.34	86.42543896	5.761695931
93.81	43.58	90.82850654	6.055233769
102.84	44.6	9.087425378	0.605828359
95.1	47.66	8.322932176	0.554862145
96.39	50.72	3.320798097	0.22138654

Average Speed (um/min) 1.830461664
MSD 924.8616
Displacement (um) 30.41153728
Total Path Length (um) 247.1123246
CI 0.123067667
Time (min) 15
Persistence (min) 7.5
MSD calc 3162.182249

Cell 5			
x	y	Path Length (um)	Speed (um/min)
109.34	113.04		
119.66	114.06	10.37028447	0.691352298
124.82	116.16	5.57096042	0.371397361
113.21	106.92	14.83811646	0.989207764
104.18	111	9.908950499	0.6605967
105.47	99.78	11.29391429	0.752927619
97.73	106.92	10.53029914	0.702019943
91.28	107.94	6.530153138	0.435343543
99.02	103.86	8.749514272	0.583300951
105.47	114.06	12.06824345	0.804549563

Average Speed (um/min) 0.66563286
MSD 16.0173
Displacement (um) 4.002161916
Total Path Length (um) 89.86043614
CI 0.044537531
Time (min) 15
Persistence (min) 7.5
MSD calc 418.1529147

Cell 7			
x	y	Path Length (um)	Speed (um/min)
-4.76	-23.7		
2.98	-4.32	20.86844508	1.391229672
13.3	-11.46	12.54918324	0.836612216
33.84	-18.6	21.84008242	1.456005494
17.17	-7.38	20.17724709	1.345149806
0.4	-6.36	16.80099104	1.120066069
-4.76	2.82	10.53081193	0.702054129
-13.21	13.02	12.06824345	0.804549563
-22.82	-9.42	25.26550415	1.684366943
-3.47	-1.26	21.00019286	1.400012857

Average Speed (um/min) 1.199338528
MSD 505.2177
Displacement (um) 22.47704829
Total Path Length (um) 161.1007013
CI 0.139521728
Time (min) 15
Persistence (min) 7.52
MSD calc 1343.987682

Cell 2			
x	y	Path Length (um)	Speed (um/min)
9.96	25.46		
-2.94	68.3	44.74008941	2.982672627
-4.23	59.12	9.270194173	0.618012945
4.8	48.92	13.62280808	0.908187205
3.51	29.54	19.42288599	1.294859066
20.28	32.69	17.06327636	1.137551757
46.08	38.72	26.49529958	1.766353306
53.82	34.64	8.749514272	0.583300951
84.78	32.6	31.02713651	2.068475767
88.65	14.24	18.76343519	1.250895679

Average Speed (um/min) 1.401145478
MSD 6318.0045
Displacement (um) 79.4858761
Total Path Length (um) 189.1546396
CI 0.420216371
Time (min) 15
Persistence (min) 49.47720273
MSD calc 6318.0045

Cell 4			
x	y	Path Length (um)	Speed (um/min)
12.25	41.64		
22.57	39.6	10.51969581	0.701313054
23.86	55.92	16.37090407	1.091393605
27.73	70.2	14.79511068	0.986340712
34.18	56.94	14.74551118	0.983034079
41.92	54.9	8.004323832	0.533621589
56.11	31.44	27.41765307	1.827843538
66.43	23.28	13.15629127	0.877086085
78.04	33.48	15.45419361	1.030279574
62.56	45.72	19.73443691	1.315629127

Average Speed (um/min) 1.038504596
MSD 2547.7425
Displacement (um) 50.47516716
Total Path Length (um) 140.1981204
CI 0.360027417
Time (min) 15
Persistence (min) 35.0240479
MSD calc 2547.7425

Cell 6			
x	y	Path Length (um)	Speed (um/min)
72.68	67.22		
71.39	75.38	8.261337664	0.550755844
7.52	86.6	64.84801693	4.323201129
77.84	96.8	71.05591038	4.737060692
84.29	72.32	25.3154676	1.68769784
90.74	54.98	18.50075944	1.233383963
107.51	41.72	21.37897331	1.425264888
110.09	39.68	3.289072818	0.219271521
103.64	47.84	10.40135087	0.693423392
106.22	46.82	2.774310725	0.184954048

Average Speed (um/min) 1.672779257
MSD 1541.0916
Displacement (um) 39.25673955
Total Path Length (um) 225.8251998
CI 0.173836842
Time (min) 15
Persistence (min) 7.51
MSD calc 2640.848437

Cell 8			
x	y	Path Length (um)	Speed (um/min)
11.49	74.94		
34.71	81.06	24.01297149	1.600864766
32.13	95.34	14.51119568	0.967413045
25.68	94.32	6.530153138	0.435343543
25.68	102.48	8.16	0.544
8.91	95.34	18.22669745	1.215113163
-11.73	104.52	22.58942223	1.505961487
-11.73	104.52	0	0
-10.44	102.48	2.41364869	0.160909913
-11.73	105.54	3.320798097	0.22138654

Average Speed (um/min) 0.738999162
MSD 1475.5284
Displacement (um) 38.41260731
Total Path Length (um) 99.76488685
CI 0.385031332
Time (min) 15
Persistence (min) 40.75889141
MSD calc 1475.00027

2. Cell adhesion strength (20 points)

5 pts. each A-D

Taken from *Tissue Engineering* exercise 6.5.

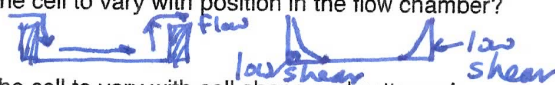
An adherent cell is exposed to shear forces from a buffered water flowing in a parallel plate flow chamber. The gap thickness is $250\mu\text{m}$, and the channel width is 14mm . The flow rate is adjusted so that the wall shear stress varies from 0.25 to 4 dyne/cm^2 . Attach additional pages as necessary.

- A) Calculate the volumetric flow rate that is required to achieve each value of shear stress in the following table.

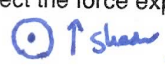
Shear stress at the wall (dyne/cm^2)	0.25	0.5	1	2	4
Volumetric flow rate (cm^3/s)	8.19×10^{-3}	1.64×10^{-2}	3.28×10^{-2}	6.55×10^{-2}	1.31×10^{-1}
Force on adherent cell (dyne/cell)					

- B) Calculate the force experienced by an "average" endothelial cell attached to the surface of the lower plate. Make and justify whatever assumptions are necessary to perform this calculation.

- C) How much would you expect the force experienced by the cell to vary with position in the flow chamber?

→ Very likely position dependent 

- D) How much would you expect the force experienced by the cell to vary with cell shape and pattern of attachment?

Shape:  $\uparrow$ shear  $\downarrow$ shear (flat cells experience less shear)
Dense cells, shear only at top (less shear)

A)

$$\mu = 8.9 \times 10^{-3} \text{ dyn}\cdot\text{s}/\text{cm}^2$$

$$a = 0.0125 \text{ cm}$$

$$b = 1.4 \text{ cm}$$

Eqn. 6-8 in Tiss Eng.

$$\tau = \frac{3}{2} \frac{\mu Q}{2a^2b}$$

fluid shear stress @ wall

Vol. flow rate

B) Will accept multiple answers.

This can be estimated in a number of ways.

Can assume cell diameter (spherical) = $10\mu\text{m}$ 

Cell on a surface is different

Can assume height is $\sim 5\mu\text{m}$, where cell would experience shear force.

Use. $\tau = -\mu \left. \frac{dv_y}{dx} \right|_{x=a}$

3. Engineered Tissue (50 points)

In class on March 10th, we heard a wiki presentation on cell sheets used for tissue engineering. If you can remember, way back on February 7th, we heard a wiki on dialysis. Dialysis has been typically used for replacing kidney function, i.e. to clean waste from blood and concentrate urea; however, one could envision a similar technique being used to supplement both liver and pancreas function, where blood is "sampled" and enzymes are then released back into the bloodstream to break down carbohydrates. Replacements for liver and pancreas, if made financially effective, obviously, could have a huge impact on global human health.

Think, for a moment, about how cell sheet engineering techniques could be implemented in *ex vivo* liver or pancreas replacements (i.e. not implanted, but will run outside the body). Pick one target (i.e. liver or pancreas), research the literature, and use resources from lecture and the wikis to answer each of the following:

- (A) What disease(s) might you impact with such a device?
- (B) What physiological functions must your device perform to be a substitute for a liver or pancreas?
- (C) What will your device look like (draw a sketch)?
- (D) What biomaterials, if any, will have to be incorporated into the device and why?
- (E) What **SINGLE** cell type would use as a cell sheet, and why?
- (F) Since you only want to incorporate one cell type in the engineered device, what features are you missing that are normally provided by other cell types? Can you replace this function with structural or chemical aspects of the device?
- (G) Where will you get the cell type of interest, how will you grow up the cells, and how will you incorporate them into the device?
- (H) Do you think this will work? If yes, why doesn't it already exist? If not, what advances need to be made to get it to work?

Attach additional pages if necessary. Cite your references used. **Limit your response to no more than 2 total pages.**

A-H 5 pts. each
page length +
turn it in : } 5 pts.
grammar / spelling: 5 pts.