

Motility coefficient

The motility coefficient of cells is a concept identical to the diffusion coefficient of molecules. Both are a measure for how fast the cells or molecules displace from their starting positions assuming a random walk or diffusion process. The motility coefficient (M) can be determined from a plot of the mean of the squared displacements ($\overline{r^2}$) versus the time interval (t), or from a plot of the mean displacement ($\bar{r}$) versus square root of time ($\sqrt{t}$), where r equals the length of the displacement vector $\vec{r}$. Here, we derive this relationship for the cases of one, two, and three dimensions separately. For a more general derivation see Beauchemin *et al.*¹.

1D case.

The relationship between displacement and motility coefficient can be derived by considering a single peak of diffusing particles at the origin as initial condition for a diffusion process. For the one-dimensional case, the probability density $P(x)$ of finding a particle at position x at time t follows the Gaussian-like distribution (see Berg²):

$$P(x) = \frac{1}{\sqrt{4\pi Mt}} e^{-\frac{x^2}{4Mt}} . \quad (1)$$

The well-known formula for the mean of the squared displacements is calculated from the second moment of this probability distribution:

$$\overline{r^2} = \int_{x=-\infty}^{\infty} x^2 P(x) = 2Mt . \quad (2)$$

In a similar manner, the mean displacement $\bar{r}$ can be determined by calculating the first moment of the distribution:

$$\bar{r} = \int_{x=-\infty}^{\infty} |x| P(x) = \sqrt{\frac{4Mt}{\pi}} . \quad (3)$$

Hence, solving these equations for M , one can see that M can be derived directly from either the mean of the squared displacements plot, or from the mean displacement plot:

$$M = \frac{\overline{r^2}}{2t} = \frac{\pi \overline{r}^2}{4t} \quad . \quad (4)$$

From a comparison of on the one hand a plot of the mean of the squared displacements versus time, and on the other hand a plot of the squares of the mean displacements versus time, it becomes clear that the slopes of these plots differ by a factor $\frac{1}{2}\pi \approx 1.57$ given the 1D case. When M would be determined from the mean displacement plot while using (erroneously) equation (2) instead of equation (3), this means an error of a factor $\frac{1}{2}\pi$, that is, the values need to be multiplied by that factor to get a correct estimate for the motility coefficient.

2D case.

For the two-dimensional case, the probability density $P(x, y)$ of finding a particle at position (x, y) at time t is a multiplication of two Gaussian-like distributions (one for each dimension):

$$P(x, y) = \frac{1}{\sqrt{4\pi Mt}} e^{-\frac{x^2}{4Mt}} \frac{1}{\sqrt{4\pi Mt}} e^{-\frac{y^2}{4Mt}} = \frac{1}{4\pi Mt} e^{-\frac{x^2}{4Mt} - \frac{y^2}{4Mt}} \quad . \quad (5)$$

The formula for the mean of the squared displacements becomes:

$$\overline{r^2} = \int_{x=-\infty}^{\infty} \int_{y=-\infty}^{\infty} (x^2 + y^2) P(x, y) = 4Mt \quad , \quad (6)$$

and the formula for the mean displacement becomes:

$$\overline{r} = \int_{x=-\infty}^{\infty} \int_{y=-\infty}^{\infty} \sqrt{x^2 + y^2} P(x, y) = \sqrt{\pi Mt} \quad . \quad (7)$$

Again, M can be derived directly from either the mean of the squared displacements plot, or from the mean displacement plot:

$$M = \frac{\overline{r^2}}{4t} = \frac{\bar{r}^2}{\pi t} \quad (8)$$

Hence, when M is determined from the mean displacement plot using the incorrect formula (equation (6) instead of equation (7)), the estimate for the motility coefficient is a factor $4/\pi \approx 1.27$ too low for the two-dimensional case.

3D case.

For the three-dimensional case, the probability density $P(x, y, z)$ of finding a particle at position (x, y, z) at time t is a multiplication of three Gaussian-like distributions (one for each dimension):

$$P(x, y, z) = \frac{1}{\sqrt{4\pi Mt}} e^{-\frac{x^2}{4Mt}} \frac{1}{\sqrt{4\pi Mt}} e^{-\frac{y^2}{4Mt}} \frac{1}{\sqrt{4\pi Mt}} e^{-\frac{z^2}{4Mt}} \quad , \quad (9)$$

which simplifies to

$$P(x, y, z) = \frac{1}{8(\pi Mt)^{3/2}} e^{-\frac{x^2}{4Mt} - \frac{y^2}{4Mt} - \frac{z^2}{4Mt}} \quad . \quad (10)$$

The formula for the mean of the squared displacements becomes:

$$\overline{r^2} = \int_{x=-\infty}^{\infty} \int_{y=-\infty}^{\infty} \int_{z=-\infty}^{\infty} (x^2 + y^2 + z^2) P(x, y, z) = 6Mt \quad , \quad (11)$$

and the formula for the mean displacement becomes:

$$\bar{r} = \int_{x=-\infty}^{\infty} \int_{y=-\infty}^{\infty} \int_{z=-\infty}^{\infty} \sqrt{x^2 + y^2 + z^2} P(x, y, z) = 4\sqrt{Mt/\pi} \quad . \quad (12)$$

So, also in three dimensions, M can be derived directly from either the mean of the squared displacements plot, or from the mean displacement plot:

$$M = \frac{\overline{r^2}}{6t} = \frac{\pi \bar{r}^2}{16t} \quad (13)$$

Hence, when M is determined from the mean displacement plot using the incorrect formula (equation (11) instead of equation (12)), the estimate for

the motility coefficient is a factor $\frac{3}{8}\pi \approx 1.18$ too low for the two-dimensional case.

Correction factors.

In summary, the relation between motility coefficient and displacement is $M = \frac{\overline{x^2}}{2dt} = \frac{c\bar{x}^2}{2dt}$, where d is the number of dimensions that are considered, and c is the correction factor to be applied in case the mean displacement rather than the mean of the squared displacements is used in the calculations. Note that the correction factor depends on the number of dimensions ($c = \frac{\pi}{2} \approx 1.57$ for 1D, $c = \frac{4}{\pi} \approx 1.27$ for 2D, and $c = \frac{3}{8}\pi \approx 1.18$ for 3D; a general formula is derived in Beauchemin *et al.*¹). Because immunologists typically determine the motility coefficient from the mean displacement plot but do not apply the correction factor, this means that the values for M currently reported in the immunological literature, are underestimations and need to be corrected (that is, multiplied with the correction factor).

Confinement ratio

The confinement ratio is a measure of the straightness or confinement of cell tracks, and it is calculated by taking the ratio of the mean displacement of a cell and the total length of the path a cell has traveled. From the previous section it is clear that for random migration the mean displacement $\bar{x}$ is equal to $\sqrt{2dMt/c}$. The total path length of cells can be described by $\bar{s}t$, when cells are assumed to travel with average speed $\bar{s}$. Thus, the confinement ratio can be approximated by $\frac{\sqrt{2dMt/c}}{\bar{s}t}$, which simplifies to $\frac{\sqrt{2dM}}{\bar{s}\sqrt{ct}}$. The latter equation shows that for random motion the confinement ratio is expected to decrease with the track duration as $1/\sqrt{t}$ (see also^{3,4}). Even for non-random motility, the confinement ratio is expected to decrease with track duration, but not necessarily to zero. Multiplying the confinement ratio

by $\sqrt{t}$ gives a measure that is independent of time, namely $\frac{\sqrt{2dM}}{\bar{s}\sqrt{c}}$. This “corrected” confinement ratio can be used for comparison of cell tracks, given that the track durations are longer than the typical duration of persistent motion (to get a good estimate of the motility coefficient), and given that the time interval between subsequent images is shorter than the typical duration of persistent motion (to get a good estimate of the speed).

Supplementary references

- 1 Beauchemin, C., Dixit, N. M. & Perelson, A. S. Characterizing T cell movement within lymph nodes in the absence of antigen. *J. Immunol.* **178**, 5505–12 (2007).
- 2 Berg, H. C. *Random walks in biology*. Princeton University Press, Princeton (1983).
- 3 Benhamou, S. How to reliably estimate the tortuosity of an animal’s path: straightness, sinuosity, or fractal dimension? *J. Theor. Biol.* **229**, 209–20 (2004).
- 4 Bogle, G. & Dunbar, P. R. Simulating T-cell motility in the lymph node paracortex with a packed lattice geometry. *Immunol. Cell Biol.* **86**, 676–87 (2008).