Supplemental Table 1. Mathematical expressions for a selection of diffusion models. Related to Figures 2 and 3.

Type of Diffusion	Diffusion Model [a]	Mean squared displacement [b] $MSD_{theory}(nt_{lag})$	Diffusion coefficient [c] $D(nt_{lag}) = \frac{MSD(nt_{lag})}{2d\,nt_{lag}}$	$\lim_{nt_{lag}\to 0} D(nt_{lag})$	$\lim_{nt_{lag}\to \tau} D(nt_{lag})$	$\lim_{nt_{lag}\to \infty} D(nt_{lag})$
Constant diffusion [d]	Free (Brownian)	$2d\,D\,nt_{lag}$	D	D	D	D
	Free with directed motion	$2d\,D\,nt_{lag} + v^2(nt_{lag})^2$	$D + \frac{v^2 nt_{lag}}{2d}$	D	$D + \frac{v^2\tau}{2d}$	$D + \lim_{n\,t_{lag}\to\infty} \frac{v^2 n\,t_{lag}}{2d}$
Continuous time-dependent diffusion [e]	Anomalous [g]	$2d\,D(nt_{lag})^{\alpha}$	$D\left(nt_{lag}\right)^{\alpha-1}$	$\begin{Bmatrix} \infty & \alpha<1 \\ D & \alpha=1 \\ 0 & \alpha>1 \end{Bmatrix}$	$\begin{Bmatrix} D\tau^{\alpha-1} & if & \alpha\neq 1 \\ D & if & \alpha=1 \\ D & if & \tau=1 \end{Bmatrix}$	$\begin{Bmatrix} 0 & \alpha<1 \\ D & \alpha=1 \\ \infty & \alpha>1 \end{Bmatrix}$
	Normalized Anomalous [h]	$2d\,D\tau(\frac{nt_{lag}}{\tau})^{\alpha}$	$D\,(\frac{nt_{lag}}{\tau})^{\alpha-1}$	$\begin{Bmatrix} \infty & \alpha<1 \\ D & \alpha=1 \\ 0 & \alpha>1 \end{Bmatrix}$	D	$\begin{Bmatrix} 0 & \alpha<1 \\ D & \alpha=1 \\ \infty & \alpha>1 \end{Bmatrix}$
Transient time-dependent diffusion [f]	Confined [i]	$2d\,D_{\mu}\tau(1-e^{-\frac{n\Delta t}{\tau}})$	$D_{\mu}\frac{\tau}{n\Delta t}(1-e^{-\frac{n\Delta t}{\tau}}])$	D_{μ}	$D_{\mu}(1-e^{-1})$	0
	Hop [j]	$2d\,n\Delta t\left(D_M + D_{\mu}\frac{\tau}{nt_{lag}}(1-e^{-\frac{n\Delta t}{\tau}})\right)$	$D_M + D_{\mu}\frac{\tau}{n\Delta t}(1-e^{-\frac{n\Delta t}{\tau}})$	$D_M + D_{\mu}$	$D_M + D_{\mu}(1-e^{-1})$	D_M
	Channeled [k]	$2D\tau(1-e^{-\frac{n\Delta t}{\tau}}) + 2(d-1)D\,nt_{lag}$	$\frac{D}{d}\frac{\tau}{nt_{lag}}(1-e^{-\frac{n\Delta t}{\tau}}) + \frac{D}{d}(d-1)$	D	$\frac{D}{d}(1-e^{-1}) + \frac{D}{d}(d-1)$	$\frac{D}{d}(d-1)$

Footnotes:

[a] The following parameters are defined for all diffusion models as follows: MSD is the mean squared displacement, d is the dimensionality of the diffusion process, i.e. d=2 for diffusion in a 2-dimensional plane, D is the diffusion coefficient, n is the number of experimental data points, t_{lag} is the lag time between consecutive data points, τ is a specific time point n t_{lag}, v is the directed flow velocity, and α is an anomaly constant where $\alpha < 1$ for sub-diffusion and $\alpha > 1$ for super-diffusion. The remaining parameters are defined below.

[b] The typical main aim in investigations of lateral dynamics is to determine the time- dependence of the diffusion process and the magnitude of the diffusion coefficient, D. A standard approach for this is to perform a curve fitting of the time-dependence of the MSD (n t_{lag}) to a suitable diffusion model. It has in this case further become customary to also include plots of the time dependence of the raw MSD (n t_{lag}) data in order to directly be able to compare lateral dynamics data from different experimental conditions. However, this approach suffers from that it is not amendable for a direct, model-independent, assessment of the time-dependence of the diffusion process in terms of D, and furthermore that it is very difficult to directly assess the impact of experimental noise for data acquired at fast sampling frequencies (Supplemental Figure 1).

[c] An alternative method that is better suited for direct comparison of lateral dynamics data in terms of the time-dependence of D is to instead define a time dependent diffusion coefficient, D(n t_{lag}), as given in the table. This approach has the advantage that it is then possible to directly evaluate the time-dependence of the lateral dynamicsdata in terms of D in a model independent way, and furthermore to directly assess the impact of experimental noise in the measurements (Supplemental Figure 2).

[d] Constant diffusion processes are the only type of diffusion processes for which the magnitude of D can be directly compared between studies. This is because this is the only case where the magnitude of D is independent of the sampling time n t_{lag}.

[e] Continuous time-dependent diffusion processes have a time-dependent diffusion coefficient, D(n t_{lag}), that varies continuously with the sampling time n t_{lag}. Direct comparisons of the magnitude of the time-dependent diffusion coefficient, D (n t_{lag}), from different studies in this case is thus only possible at specific times, τ=n t_{lag}.

[f] Transient time-dependent diffusion processes are defined by having a diffusion coefficient, D(n t_{lag}), that approaches constant, but separate, magnitudes in the limits of time $n\, t_{lag} \to 0$ and $n\, t_{lag} \to \infty$, with some intermediate temporal transition zone. It is in this case possible to compare the magnitude of D but only then at the limiting values or at specific times, τ=n t_{lag} .

[g] This conventional definition of the anomalous diffusion has the disadvantage that D has units that is also dependent on the magnitude of the anomaly constant α. It is thus not possible to compare the magnitude of D unless the magnitude of the anomaly constant α is also considered.

[h] This revised time normalized anomalous diffusion model has the advantage that the units of D are always in the traditional format of $(distance)^2/time$ for all values of the anomaly constant α and the time constant τ. This expression is furthermore directly amendable for calculating the magnitude of D independent of the anomaly constant α for any specific value of the time $\tau = n\, t_{lag}$, and is thus also suitable for direct comparison of the magnitude of D at specific times.

[I] This expression is for completely confined diffusion in a confinement area that is given by $L^2 = 12\, D_\mu\, \tau$ where L is the linear confinement dimension, D_μ is the unhindered diffusion coefficient within the confinement area and τ is a time constant at which the magnitude of D_μ has been reduced by a factor of 1/e.

[j] This expression is for transiently confined diffusion, or so called hop-diffusion, where the time-dependent diffusion coefficient, $D(n\, t_{lag})$, consists of a long-range, intracompartmental, time-independent, diffusion coefficient component, D_M, and a short-range, intercompartmental, time-dependent diffusion coefficient component, D_μ. The confinement area is given, as above, by $L^2 = 12\, D_\mu\, \tau$ where τ is a time constant at which the magnitude of D_μ has been reduced by a factor of 1/e.

[k] This expression is for channeled diffusion, where a molecule is confined along one spatial dimension, but diffuses freely along the other spatial dimensions. The channel width is given by $L = (12\, D\tau)^{1/2}$ where τ is a time constant at which the magnitude of D, in a direction that is perpendicular to the channel has been reduced by a factor of 1/e