|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Unit | Description | Ref |
| Surface area | μm2 | Total area of the surface of a solid 3D object. |  |
| Volume | μm3 | Space that is occupied by a solid 3D object with an enclosed surface. |  |
| Sphericity(*ψ*) | % | Morphometric characteristic of shape which represents how spherical an object is. Sphericity *ψ* is defined as the ratio of the surface area of a sphere with the same volume *V* as the object to the surface area of the object *A*:$$ψ=\frac{π^{\frac{1}{3}} \left(6V\right)^{\frac{2}{3}}}{A} , 0<ψ\leq 1$$In the case of a sphere with volume $V=\frac{4}{3}πr^{3}$ and surface area $A=4πr^{2}$, the sphericity formula is reduced to $ψ=1$. For 3D objects which have $A\gg V$, the sphericity $ψ\rightarrow 0$. | [1] |
| Compactness(*C*) | dim\* | Measure of shape compactness which represents the degree to which a shape is compact. The classical compactness of a solid 3D object is defined as the given ratio between surface area *A* and volume *V* of the object:$$C=\frac{A^{3}}{V^{2}} , 36π\leq C<\infty $$This measure is dimensionless and is minimized by a sphere with volume $V=\frac{4}{3}πr^{3}$ and surface area $A=4πr^{2}$, having the most compact shape for $C=36π$. | [2] |
| Minimal distance$$(d\_{min})$$ | μm | Distance between centers of mass of FRCs in 3D Euclidean space, which is then minimized ($d\_{min}$) by finding the nearest FRC neighbor. The distance between two FRCs *i* and *j* with Cartesian coordinates $\left(x\_{i},y\_{i},z\_{i}\right)$ and $\left(x\_{j},y\_{j},z\_{j}\right)$ respectively, is given by:$$d\left(i,j\right)=\sqrt{\left(x\_{j}-x\_{i}\right)^{2}+\left(y\_{j}-y\_{i}\right)^{2}+\left(z\_{j}-z\_{i}\right)^{2}}$$ |  |
| Connected protrusions | # \*\* | Number of protrusions per 3D reconstructed FRC body, counted before the first branching point and connected to another FRC. |  |
| Number of nodes | # \*\* | Total number of nodes *n* connected in a network. |  |
| Number of edges | # \*\* | Total number of edges for all nodes in a network. |  |
| Average number of edges per FRC$$(\overbar{e})$$ | # \*\* | The arithmetic mean of the number of edges $e\_{i}$ per node *i*, for the network with *n* nodes:$$\overbar{e}=\frac{1}{n}\sum\_{i=1}^{n}e\_{i}$$ |  |
| Average local clustering coefficient$$(\overbar{C})$$ | % | The local clustering coefficient $c\_{i}$ of a node *i* is defined as the number of edges $e\_{i}$ among neighbors of *i* divided by the total possible number of edges among its neighbors:$$c\_{i}=\frac{2}{δ\_{i}\left(δ\_{i}-1\right)}e\_{i} , 0\leq c\_{i}\leq 1$$where $δ\_{i}$ represents the number of neighbors of node *i*.The average local clustering coefficient of a network with *n* nodes is the arithmetic mean of clustering coefficients of all the nodes:$$\overbar{C}=\frac{1}{n}\sum\_{i=1; δ\_{i}>1}^{n}c\_{i} , 0\leq \overbar{C}\leq 1$$ | [3] |
| Average shortest path length($\overbar{L}$) | dim\* | The average shortest path length *L* of a network is determined as the arithmetic mean of all pairs of shortest distances between nodes *i* and *j*:$$\overbar{L}=\frac{2}{n\left(n-1\right)}\sum\_{i=1}^{n}\sum\_{j=i+1}^{n}l\_{ij} , 1\leq \overbar{L}<\infty $$ | [4] |
|  |  | where $l\_{ij}$ is the length (number of edges) of the shortest path between nodes *i* and *j*, namely how many nodes one needs to pass in order to get from node *i* to node *j*. The maximum distance $\overbar{L}\_{max}$ is called the diameter of the network.In case of a complete network where all possible connections are present, all the node distances $l\_{ij}=1$, thus the sum $\sum\_{i=1}^{n}\sum\_{j=i+1}^{n}l\_{ij}=\frac{n\left(n-1\right)}{2}$, which gives the minimal $\overbar{L}\_{min}=1$. |  |
| Sigma factor(*σ*) | dim\* | The small-world measure $σ$ is determined by comparing the average clustering coefficient $\overbar{C}$ and average shortest path length $\overbar{L}$ of the network in question to an equivalent Erdos-Renyi random network with the same number of nodes and edges:$$σ=\frac{{\overbar{C}}/{C\_{R}}}{{\overbar{L}}/{L\_{R}}} , 1\leq σ<\infty $$where $C\_{R}$ and $L\_{R}$ are the average clustering coefficient and average shortest path length of the random network, respectively, averaged across 100 simulation runs of an equivalent random network.In the case of a random network $\overbar{C}=C\_{R}, \overbar{L}=L\_{R}$, the sigma factor $σ=1$.A network will be classified as a small-world network if $\overbar{C}\gg C\_{R}, \overbar{L}\geq L\_{R}$ which implies ${\overbar{C}}/{C\_{R}}\gg 1$ and ${\overbar{L}}/{L\_{R}}\geq 1$ and therefore $σ>1$. | [5,6] |
| Omega factor(*ω*) | dim\* | The small-world measure $ω$ is determined by comparing the average clustering coefficient of the network in question $\overbar{C}$ to that of an equivalent lattice network $C\_{L}$ and comparing the average shortest path length $\overbar{L}$ to that of an equivalent Erdos-Renyi random network $L\_{R}$ as follows:$$ω=\frac{L\_{R}}{\overbar{L}}-\frac{\overbar{C}}{C\_{L}} , -1<ω<1$$In the case of a random network $\overbar{C}\ll C\_{L}, \overbar{L}≈L\_{R}$, the omega factor $ ω\rightarrow 1$ for $n\rightarrow \infty $, while in the case of a lattice network $\overbar{C}≈C\_{L}$, $\overbar{L}\gg L\_{R}$ will give rise to $ ω\rightarrow -1$.A network will be classified as a small-world network if it has average shortest path length like a random network $\overbar{L}≈L\_{R}$ and average clustering coefficient like a lattice network $\overbar{C}≈C\_{L}$, which gives near-zero values $ ω≈0$.Note that it is suggested that the small-world regime spans in the following range of *ω* values: $-0.5\leq ω\leq 0.5$. Although there is no precise cut-off, the proximity to zero indicates small-world network attributes. | [7] |
| Network robustness(*R*) | dim\* | Network robustness can be assessed by sequentially removing *q* nodes from a network and is defined as:$$R=\frac{1}{n}\sum\_{q=1}^{n}s\left(q\right) , 0<R<0.5$$where $s\left(q\right)={m}/{n}$ is the fraction of nodes *m* in the largest connected cluster (subgraph) when *q* nodes are sequentially removed over the number of nodes *n* of the initial network.The largest connected subgraph must also satisfy the following two conditions:1) Must have the largest number of connected nodes *m* and consequently the largest fraction $s\left(q\right)$.2) The nodes *k* in the largest connected subgraph must be on average connected to at least two other nodes:$$\frac{\overbar{e^{2}}}{\overbar{e}}\geq 2 , \overbar{e^{2}}=\frac{1}{m}\sum\_{k=1}^{m}e\_{k}^{2} , \overbar{e}=\frac{1}{m}\sum\_{k=1}^{m}e\_{k}$$The largest connected subgraph is selected when both conditions are maximized $max\left(s\left(q\right)\right)$ and $max\left({\overbar{e^{2}}}/{\overbar{e}}\right)$.If no subgraph meets these conditions, the fraction $s\left(q\right)=0$.Robustness of a network is calculated in the range of maximal vulnerability (*R=0*) and maximal robustness (*R=0.5*). | [8,9] |
| Average speed($\overbar{v}$) | μm/min | Average 3D speed of a cell is calculated as the mean of all cell velocities estimated at time points numbered with *t* and spanning 30 min time interval with time step $∆t$ as follows:$$\overbar{v}=\frac{1}{T}\sum\_{t=1}^{T}v\left(t\right)$$$$v\left(t\right)=\frac{∆s}{∆t}=\frac{\sqrt{\left(∆x\left(t-1,t\right)\right)^{2}+\left(∆y\left(t-1,t\right)\right)^{2}+\left(∆z\left(t-1,t\right)\right)^{2}}}{∆t}$$where *T* is the number of time points for 30 min total imaging time, $v\left(t\right)$ is the estimated absolute speed of the cell over 20 sec time intervals $∆t$, and $∆x,∆y,∆z$ specify the change in 3D cell position between consecutive time points *(t-1,t)*. |  |
| Arrest coefficient | % | Percentage of the time a cell spends travelling at speed less than 4 μm/min: | [10] |
| (*AC*) |  | $$AC=\frac{t\left(v\_{t}<4μm/min\right)}{T\left(v\_{t}\right)} , 0\leq AC\leq 1$$ |  |
| Motility coefficient(*MC*) | μm2/min | The motility coefficient of a data set can be derived from the mean displacement $∆s$ of all cells within the data set at time point *t = 1 min*:$$MC=\frac{π∙∆s^{2}}{16t}$$The motility coefficient serves as a measure for area scanned by cells. | [11] |
| Meandering index(*MI*) | dim\* | The meandering index, i.e. cell track straightness, is calculated as the ratio of cell displacement $∆s$ and total track length *L*:$$MI=\frac{∆s}{L} , 0\leq MI\leq 1$$The meandering index is a measure of movement straightness. A cell moving in an exact straight line will have *MI = 1*. | [12] |

**S1 Table References:**

[1] Wadell H (1935) Volume, Shape and Roundness of Quartz Particles. J. Geol 43: 250-280.

[2] Bribiesca E (2000) A measure of compactness for 3D shapes. Comput Math Appl 40: 1275-1284.

[3] Watts DJ and Strogatz S (1998) Collective dynamics of 'small-world' networks. Nature 393: 440-442.

[4] Wiener H (1947) Structural determination of paraffin boiling points. J Am Chem Soc 69: 17-20.

[5] Humphries MD, Gurney K, Prescott TJ (2006) The brainstem reticular formation is a small-world, not scale-free, network. Proc Biol Sci 273: 503-511.

[6] Humphries MD, Gurney K (2008) Network 'small-world-ness': a quantitative method for determining canonical network equivalence. PLoS ONE 3: e0002051.

[7] Telesford QK, Joyce KE, Hayasaka S, Burdette JH, Laurienti PJ (2011) The ubiquity of small-world networks. Brain Connect 1: 367-375.

[8] Schneider CM, Moreira AA, Andrade JS Jr, Havlin S, Herrmann HJ (2011) Mitigation of malicious attacks on networks. Proc Natl Acad Sci USA. 108: 3838-3841.

[9] Cohen R, Erez K, ben-Avraham D, Havlin S (2000) Resilience of the internet to random breakdowns. Phys Rev Lett. 85: 4626-4628.

[10] Hugues S, Fetler L, Bonifaz L, Helft J, Amblard F, Amigorena S (2004) Distinct T cell dynamics in lymph nodes during the induction of tolerance and immunity. Nat Immunol. 5: 1235-1242.

[11] Beltman JB, Marée AF, de Boer RJ (2009) Analysing immune cell migration. Nat Rev Immunol. 9: 789-798.

[12] Worbs T, Mempel TR, Bölter J, von Andrian UH, Förster R (2007) CCR7 ligands stimulate the intranodal motility of T lymphocytes in vivo. J Exp Med. 204: 489-495.