# Supporting material

## Universal algorithm for identification of fractional Brownian motion. A case of telomere subdiffusion

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# 1 Experimental results

The diffusion of telomeres was described and analyzed in ref. (1). We extended this data set using similar experimental set-up. U2OS osteosarcoma cells are transiently transfected with a plasmid coding for a fused TRF2-GFP protein which is then independently expressed. The TRF2 subunit of the fused protein binds to the telomeric chain as a part of the shelterin complex while the GFP subunit is used to track the location of the telomeres with fluorescent microscopy. An inverted fluorescent Olympus IX71 microscope is used with an oil objective lens of 60X and a NA=1.35. The microscope is connected to both a sensitive and fast CCD camera that has an electron-multiplication mechanism (EMCCD, Andor DU-885), as well as, to a confocal setup (Olympus IV-1000).

Typically several dozens of telomeres are observed in each cell, however, only the brightest are used for data analysis. In order to track the telomeres in an extended time scale, the measurements are separated into three overlapping time domains. For measuring the shortest times, a horizontal slice of the cells is imaged in 2D by selecting a single plane in focus using the CCD camera with wide field illumination. Data acquisition rate is 84 Hz. However, bleaching limits the total time of the acquisition to $\sim$1000 measurement points (i.e., 11.2 seconds). 2D confocal fluorescent microscopy is used to image cells at 2.3 Hz up to 85 seconds in the intermediate time domain. Here too only a single focal slice is imaged, thus enabling faster acquisition. Since illumination is not wide field, bleaching is prevented. At times larger than 100 seconds, cell motion in 3D becomes significant and must be corrected for. Thus, a full 3D confocal scan of each cell is performed at each time point and the motion of the cells is corrected by calculating the nucleus center of mass and shifting all tracks accordingly. The 3D measurements span 35 minutes with a full imaging scan completed every 18.5 seconds. The 3D data for each telomere is analyzed in 2D so that it can be combined with the 2D confocal and CCD data. Overall, a coverage of six time orders, $10^{-2} - 10^{3}$, seconds is achieved.

The PSF of the fluorescent signal gives a resolution of 200 nm in the horizontal plain. The Imaris program is used to identify the center of the signal from each telomere and thus improve tracking accuracy. The overall accuracy was evaluated by measuring dead fixated cells. Since there is no motion inside these cells, the experimental error can be estimated according to the apparent motion of the telomeres. In all time domains, the error could be described by a normally distributed random variable with a zero mean and standard deviation of about 22 nm, Fig S1 - S3.

We analyze the $X$ and $Y$ coordinate of a telomere motion. As explained above, the datasets are recorded in three time regimes related to three different measurement methods: $10^{-2} - 10$ [s] (CCD), $1 - 10^2$ [s] (2D confocal) and $10 - 10^3$ [s] (3D confocal). The CCD dataset consists of 180 trajectories of length 1000, the 2D confocal dataset of 94 trajectories of length 200, and the 3D confocal dataset of 1090 tracks of length 100. Observe that for the 3D confocal measurements we analyze the 2D projections. In Fig. S4 we plot all 2 dimensional CCD measurements. It is clear that the spread of the different trajectories in the $xy$ plane is much larger than the dynamics of each telomere. Thus, we shifted all trajectories to make them start at the origin. In Fig. 1 sample trajectories of $X$ time series corresponding to each of the time regimes are presented. It is important to note that there is no physical difference between the $X$ and $Y$ directions and these are chosen simply by the orientation of the microscope.

## 2 Ergodicity and mixing

In Fig. S5A we show the ergodicity test results (calculated as the ensemble average over all trajectories within a certain time range), while in Fig. S5B the mixing test results. Note, that the test indicates ergodicity and mixing, respectively, since the plotted curves converge to zero.

## 3 Generalized p-variation test

One can show that for data from an $H$-self-similar process with stationary increments and finite moments $V_m^{(p)} \sim m^{Hp-1}$. In particular, this implies that in the case of FBM for $p > 1/H$ sample $p$-variation is an increasing function of $m$ (it tends to zero as $m$ gets smaller), whereas for $p < 1/H$ it is a decreasing function of $m$ (it diverges to infinity when $m$ gets smaller) (2). In the case of CTRW $V_m^{(p)}$ as a function of $m$ changes its behavior from increasing to decreasing for $p = 1/0.5 = 2$, exactly as for a BM (3).

This suggested a generalized $p$-variation test (2) for checking both whether a given sample follows the self-similar dynamics and, in the subdiffusion case, distinguishing between a FBM (a light-tailed model), a fractional Lévy stable motion (FLSM) (a heavy-tailed model) and a CTRW. If the underlying model is a FBM, then sample $p$-variation should change its monotonic character from a decreasing to an increasing one for some $p = 1/H$, $0 < H < 1$. If the underlying model is a FLSM, then sample $p$-variation as a function of $m$ should be a decreasing function for all $p = 1/H$, $0 < H < 1$. Finally,

if the proper model is a CTRW, then sample $p$-variation should change its monotonic character for $p = 2$.

The results of the $p$-variation test are presented in Figs. S6-S8.

## References

1. Bronstein I., et al. 2009. Transient anomalous diffusion of telomeres in the nucleus of mammalian cells. *Phys Rev Lett.* 103:018102.

2. Burnecki K., and A. Weron. 2010. Fractional Lévy stable motion can model subdiffusive dynamics. *Phys Rev E.* 82:021130.

3. Magdziarz M., A. Weron, K. Burnecki, and J. Klafter. 2009. Fractional Brownian motion versus the continuous-time random walk: A simple test for subdiffusive dynamics. *Phys Rev Lett.* 103:180602.

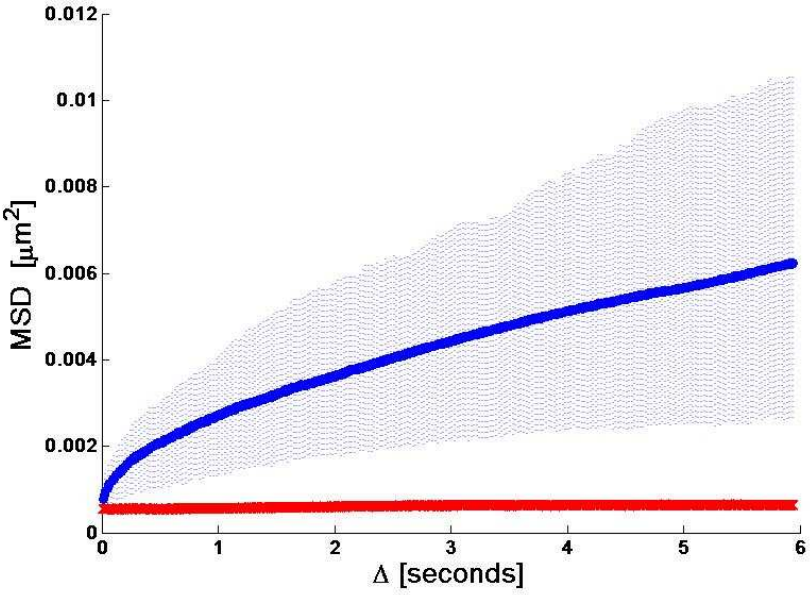


Figure S1: MSD of CCD measurements (blue) and experimental noise (red). vertical lines are the spread of individual MSDs of different telomeres.

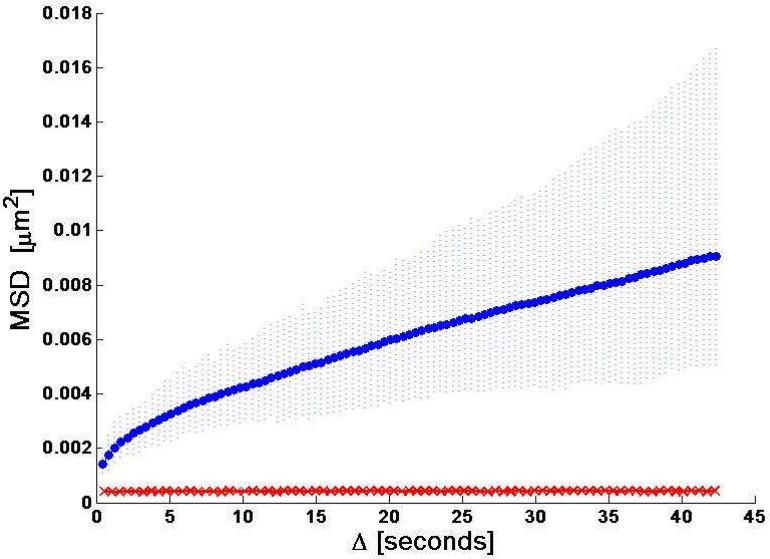


Figure S2: MSD of 2D measurements (blue) and experimental noise (red). vertical lines are the spread of individual MSDs of different telomeres.

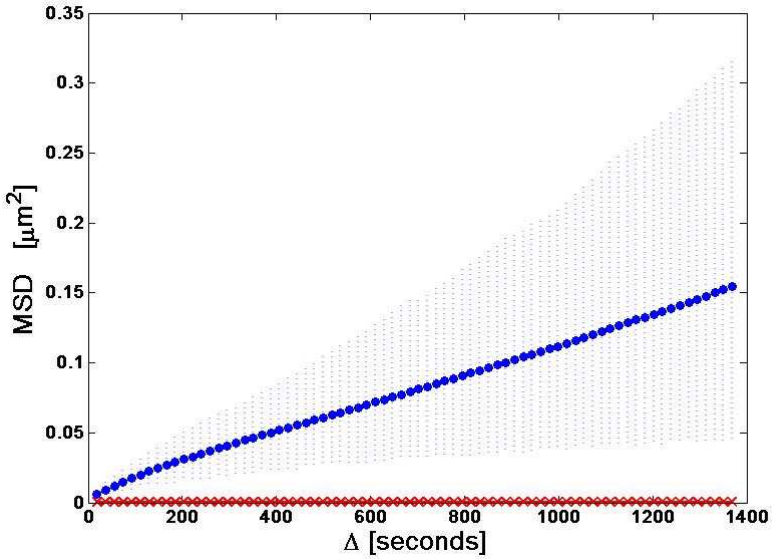


Figure S3: MSD of 3D measurements (blue) and experimental noise (red). vertical lines are the spread of individual MSDs of different telomeres.

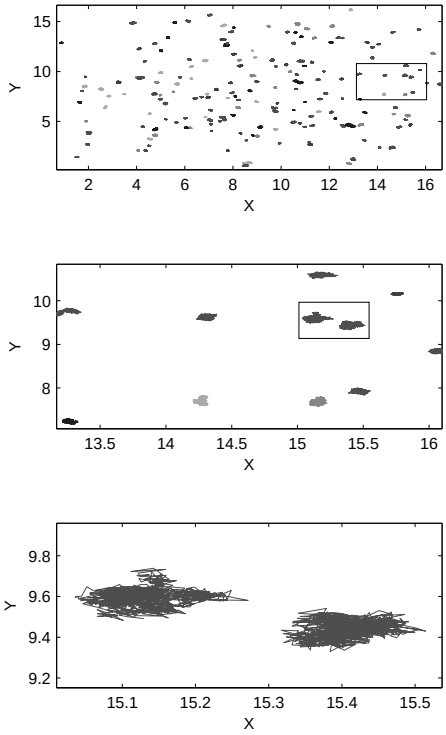


Figure S4: 2-dimensional CCD measurements in different focus. Observe that the rectangles correspond to the zoomed area plotted in the lower panel.

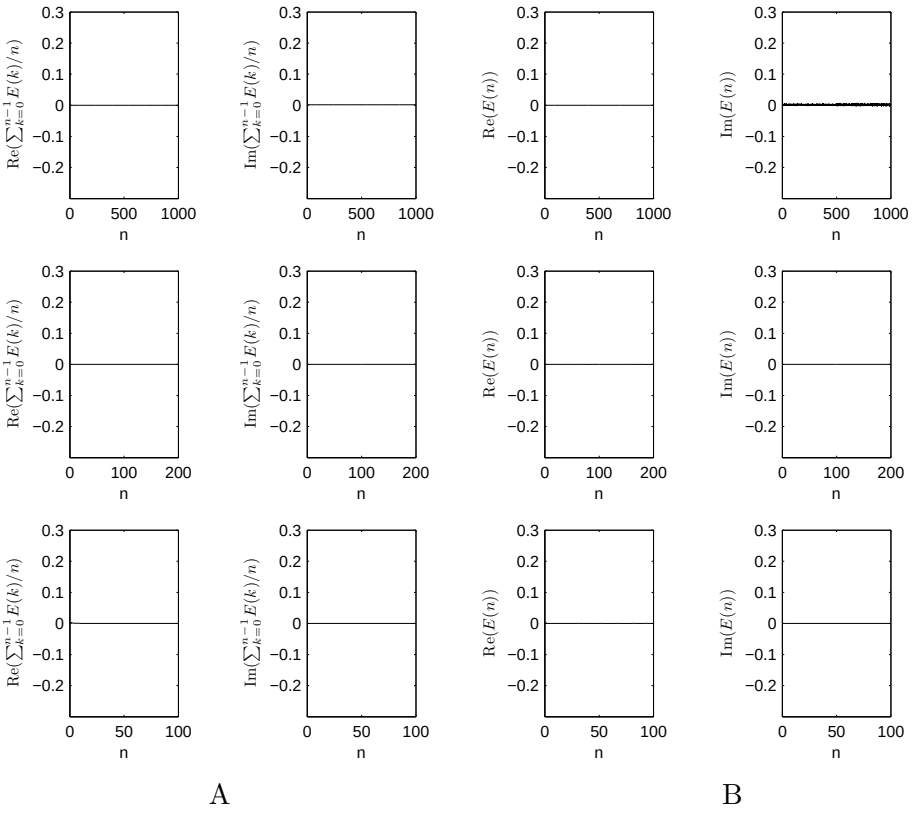


Figure S5: DF test results for the ergodicity (A) and mixing (B) property of the increments of $X$ coordinate corresponding to each of the time regimes: CCD (top panel), 2D (middle panel), 3D (bottom panel).

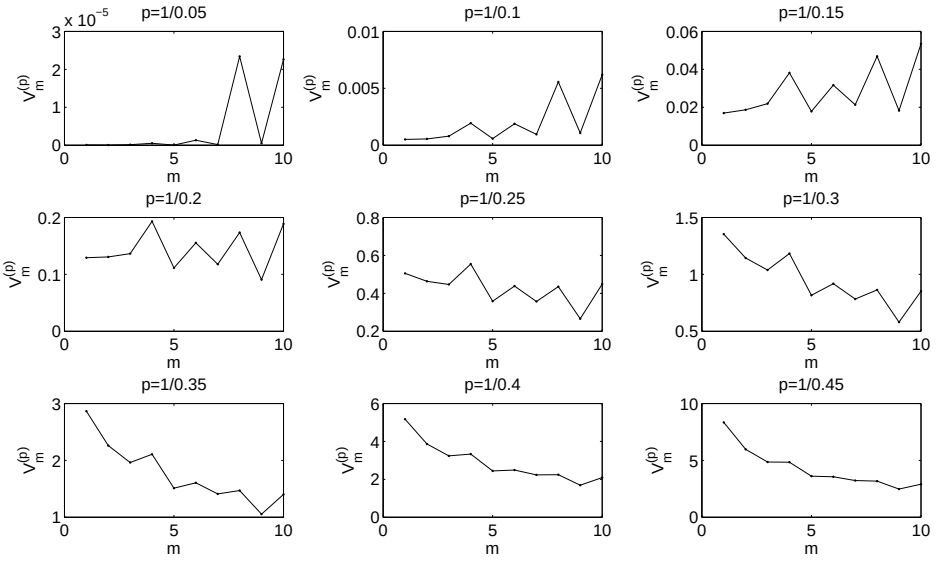


Figure S6: Sample $p$-variation for $m = 1, 2, \ldots, 10$, $H = 0.1, 0.2, \ldots, 0.9$ for the sample trajectory from the CCD regime depicted in Fig. 1A. We observe that in the first three panels sample $1/H$-variation has an increasing trend, it stabilizes in the fourth panel (corresponding to $H = 0.2$), and it has a decreasing trend in the subsequent panels. This behavior is similar to that of FBM with $H = 0.2$.

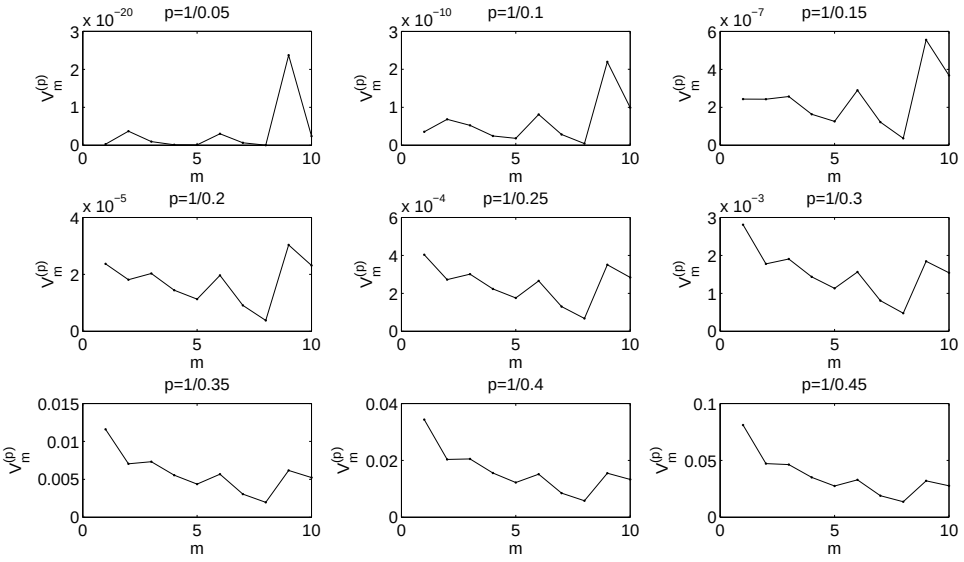


Figure S7: Sample $p$-variation for $m = 1, 2, \ldots, 10$, $H = 0.1, 0.2, \ldots, 0.9$ for the sample trajectory from the 2D regime depicted in Fig. 1A. We observe that in the first three panels sample $1/H$-variation has an increasing trend, it stabilizes in the fourth panel (corresponding to $H = 0.2$), and it has a decreasing trend in the subsequent panels. This behavior is similar to that of FBM with $H = 0.2$.

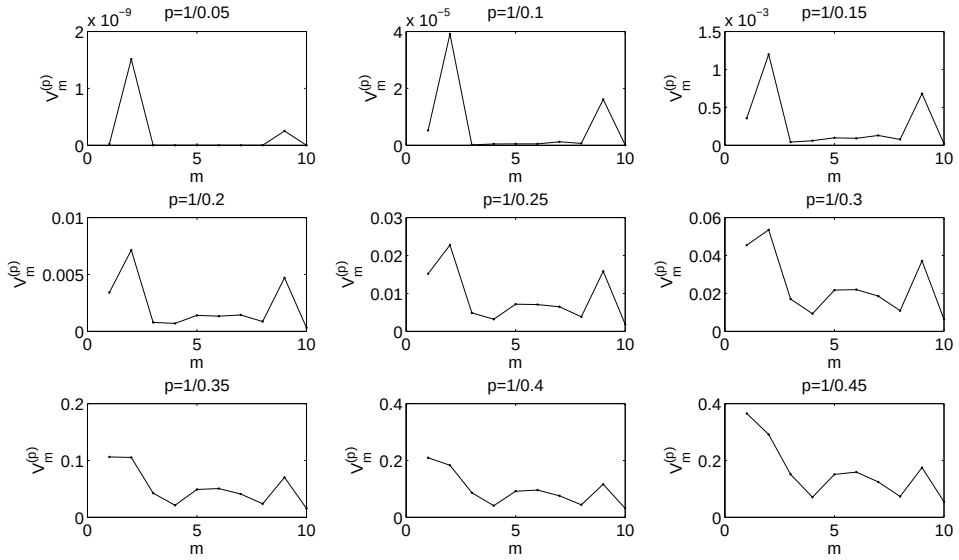


Figure S8: Sample $p$-variation for $m = 1, 2, \ldots, 10$, $H = 0.1, 0.2, \ldots, 0.9$ for the sample trajectory from the 3D regime depicted in Fig. 1A. We observe that in the first six panels sample $1/H$-variation is neither decreasing nor increasing and it has a decreasing trend starting from the seventh panel onwards (corresponding to $H = 0.35$). The conclusions cannot be definite since the sample size is very small (100 observations). Nevertheless, the behavior in the last three panels is similar to that of FBM with $H = 0.35$.