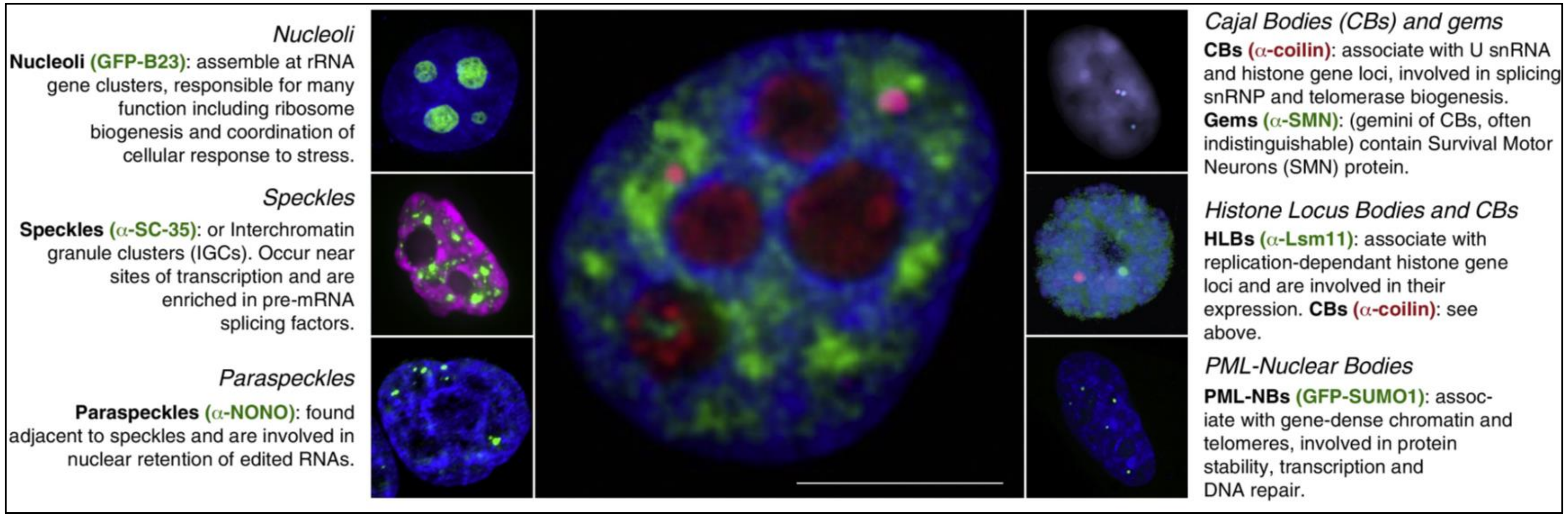
Literature Report

Chen Jie

2021-03-04

Nuclear subcompartments (nuclear bodies)

- consist of specific proteins and RNAs, entirely mediated by protein-protein and protein-RNA interactions



Nuclear body	Defining protein	Size (μM)	Related functions
Cajal bodies	Coilin	0.1–2	Biogenesis, maturation and recycling of small RNAs
Clastosome	19S, 20S proteasome	0.1–1.2	Sites of proteasomes, ubiquitine conjugates, and protein substrates of the proteasome
Gems nuclear bodies	SMN	0.1–2	pre-mRNA splicing
Histone body	NPAT, FLASH	0.2–1.2	Histone gene synthesis
Nuclear speckles	SRSF2, SRSF1, Malat1	0.8–1.8	Storage and recycling of splicing factors
Nuclear stress body	HSF1, HAP	0.3–3	Regulation of transcription and splicing under stress
Nucleolus	RNA Pol I machinery	0.5–8	Ribosome biogenesis
Paraspeckle	PSP1, P54NRB, PSF	0.5	mRNA regulation, RNA editing
Perinucleolar compartment	PTB, CUGBP	0.2–1	Post-transcriptional regulation of a subset of Pol III RNAs
PML bodies	PML	0.3–1	Regulation of genome stability, DNA repair, control of transcription, viral defense
Polycomb body	Bmi1, Pc2	0.3–1	Involved in polycomb proteins-mediated gene paring and silencing in Drosophila

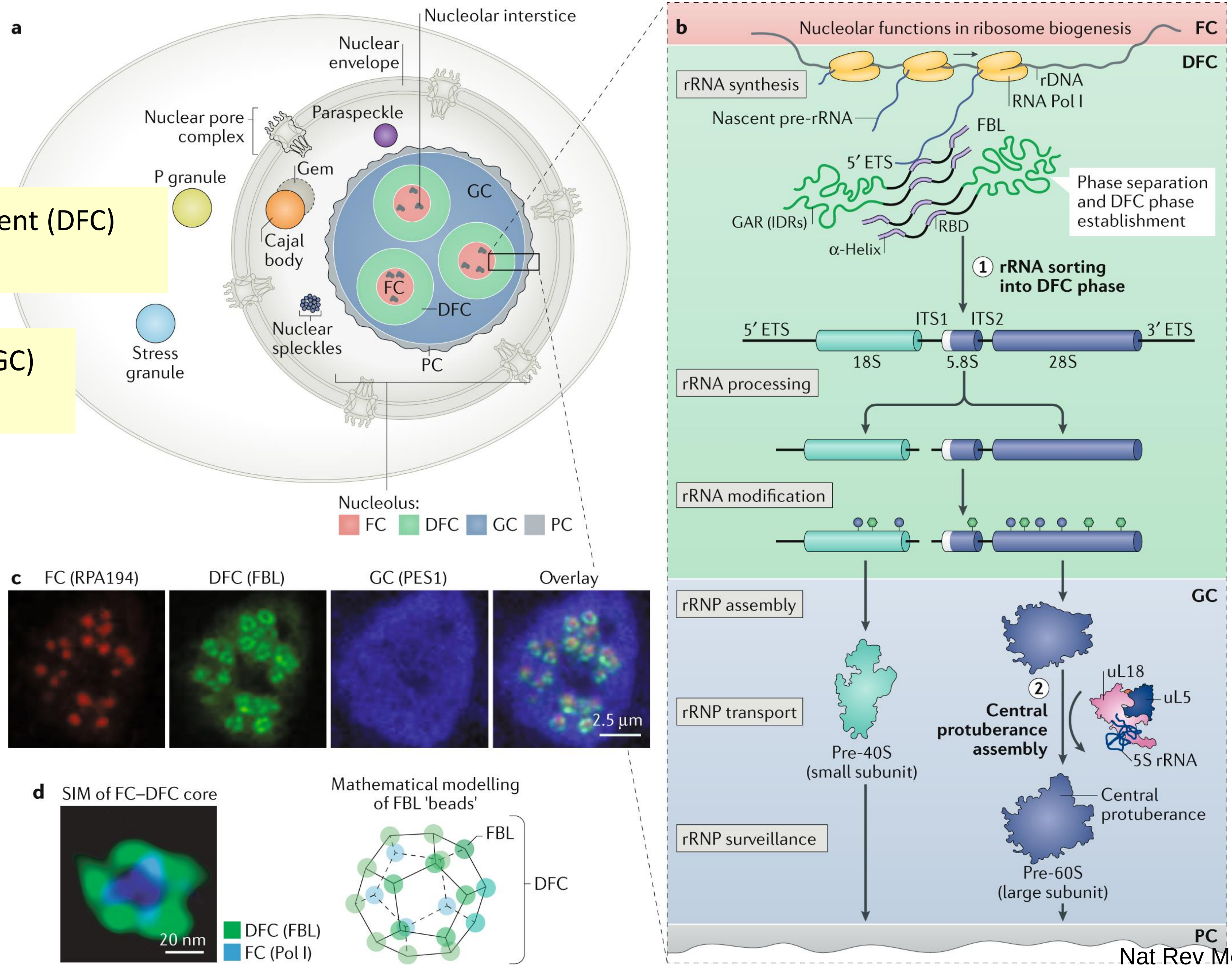
Current Opinion in Cell Biology 2014, 28, 76-83.   Cell Biol Int 2017, 41, 2-7.

Nucleolar organization and its role in ribosome biogenesis

fibrillar centre (FC)
纤维中心

Dense fibrillar component (DFC)
致密纤维组分

Granular component (GC)
颗粒组分



Liquid Liquid Phase Separation (LLPS)

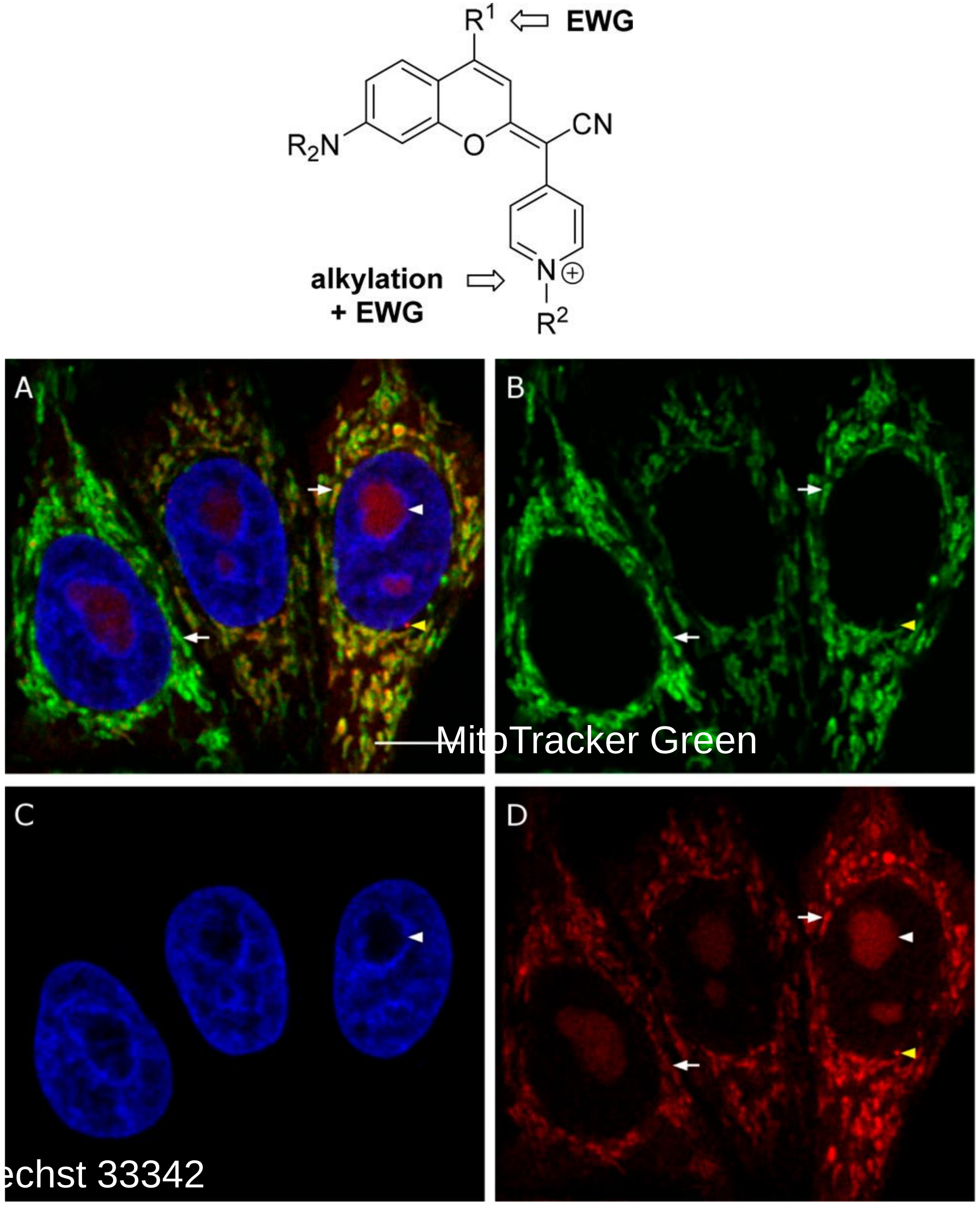
Nat Rev Mol Cell Biol, 2021, 22, 165-182.

Nucleolar biophysical properties and Functional characteristics

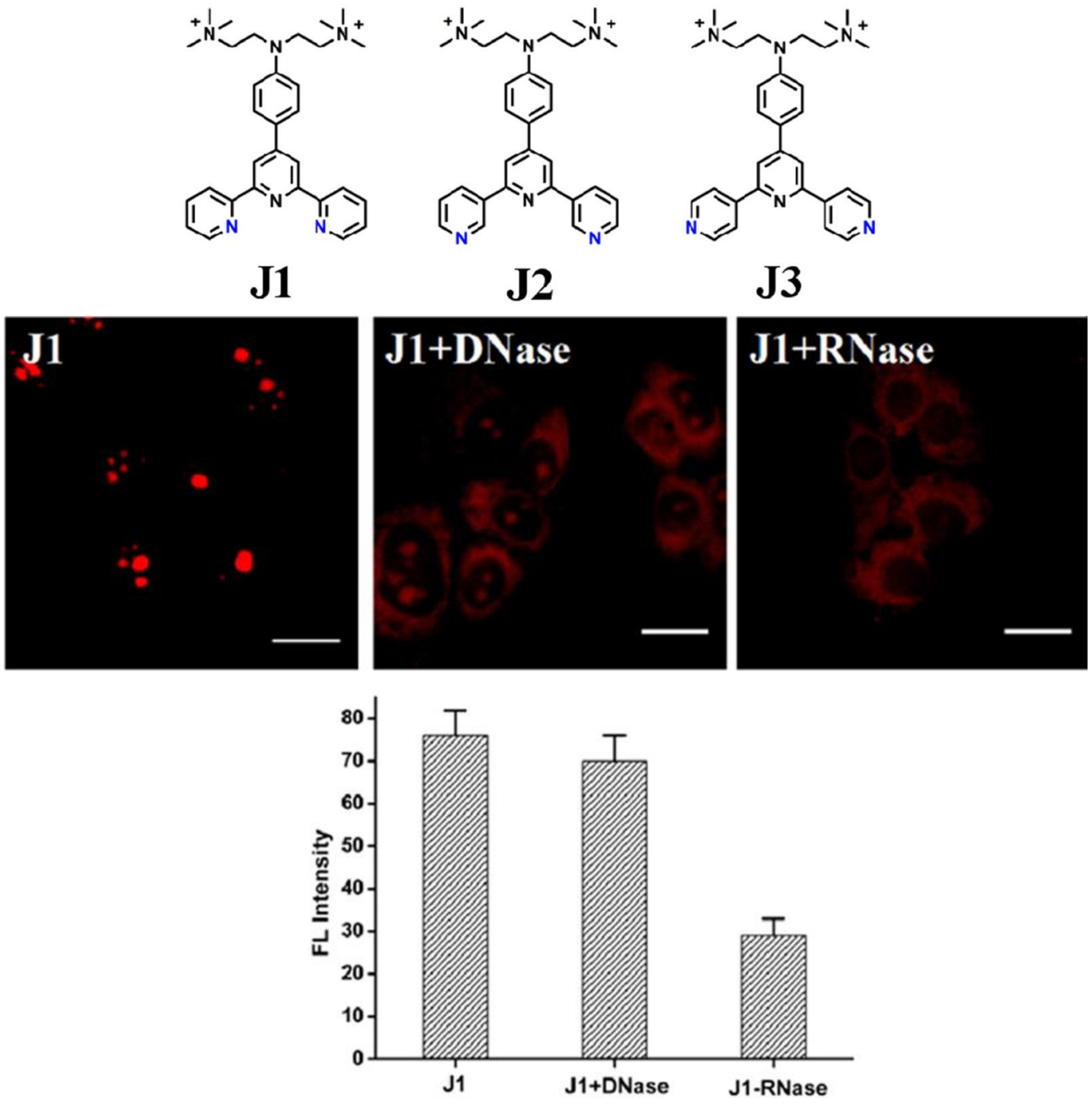
- The average number of nucleoli per cell nucleus ($N_{nucleoli}$): ~2–5 in HeLa cells[106].
- The size (diameter) of the nucleolus (ℓ): ~1–5 μm in HeLa cells, ~1–10 μm in *Xenopus laevis*[15].
- The number of fibrillar centre (FC)–dense fibrillar component (DFC) modules per nucleolus (N_{DFC}): several dozen in human cells. This number is relatively constant within a particular cell type but varies considerably between cell types, making it a powerful biomarker[23].
- The size of the DFC: outer diameter ~630 nm and inner diameter ~360 nm in human cells[23].
- The number of different nucleolar proteins (N_{prot}): >1,300 in human cells[35].
- The average residency time of nucleolar protein in the mammalian nucleolus (τ_{prot}): ~10–100 s[28].
- The percentage of disorder in nucleolar proteins: the median fraction of disordered residues per protein in human cells is 14% (12% in mouse), 20% (22% in mouse) and 36% in cytosolic-associated, nucleolar-associated and perichromosomal region-associated proteins, respectively[35].
- The viscosity (η): ~10 Pa·s for the granular component (GC)[16]. For reference, the viscosity of water is 10^{-3} Pa·s.
- The surface tension (GC–nucleoplasm interface) (γ): ~10^{-6} N/m[16,107]. For reference, the surface tension of an air–water interface is 0.07 N/m.
- The density (average) (ρ): 1.155 g/ml[29], estimates from the *X. laevis* germinal vesicle.
- The volume fraction of biomolecules (average) (ϕ): 0.16 (REF.[29]). For reference, for equal-sized spheres, the highest possible density of their packing in a given volume is represented by a volume fraction of 0.74.
- The number of transcriptionally active ribosomal DNAs per FC–DFC module in human cells (N_{rDNA}): 2–3 (REF.[23]).
- The ribosomal RNA transcription rate (k_{rib}): ~10^3–10^4 transcripts/min[108–110].
- The average nucleolar residency time of ribosomal RNA (τ_{rRNA}): ~30–60 min[74].
- The number of ribosomes per cell (N_{rib}): ~10^5 in yeast and ~10^6–10^7 in animal cells[110,111].
- The organization of ribosomal assembly factors in the DFC: in human cells, DFCs establish a spherical network of 18–24 regularly spaced 'beads' of ~130 nm in diameter, with a distance between two adjacent beads of ~180 nm (see FIG. 1d). Considering that early maturation-stage yeast pre-ribosomes are ~25 nm × 30 nm and human counterparts are likely a bit larger, each bead may correspond to multiple maturing pre-ribosomes.

Nat Rev Mol Cell Biol, 2021, 22, 165-182.

Nucleolus (rRNA) fluorescent imaging

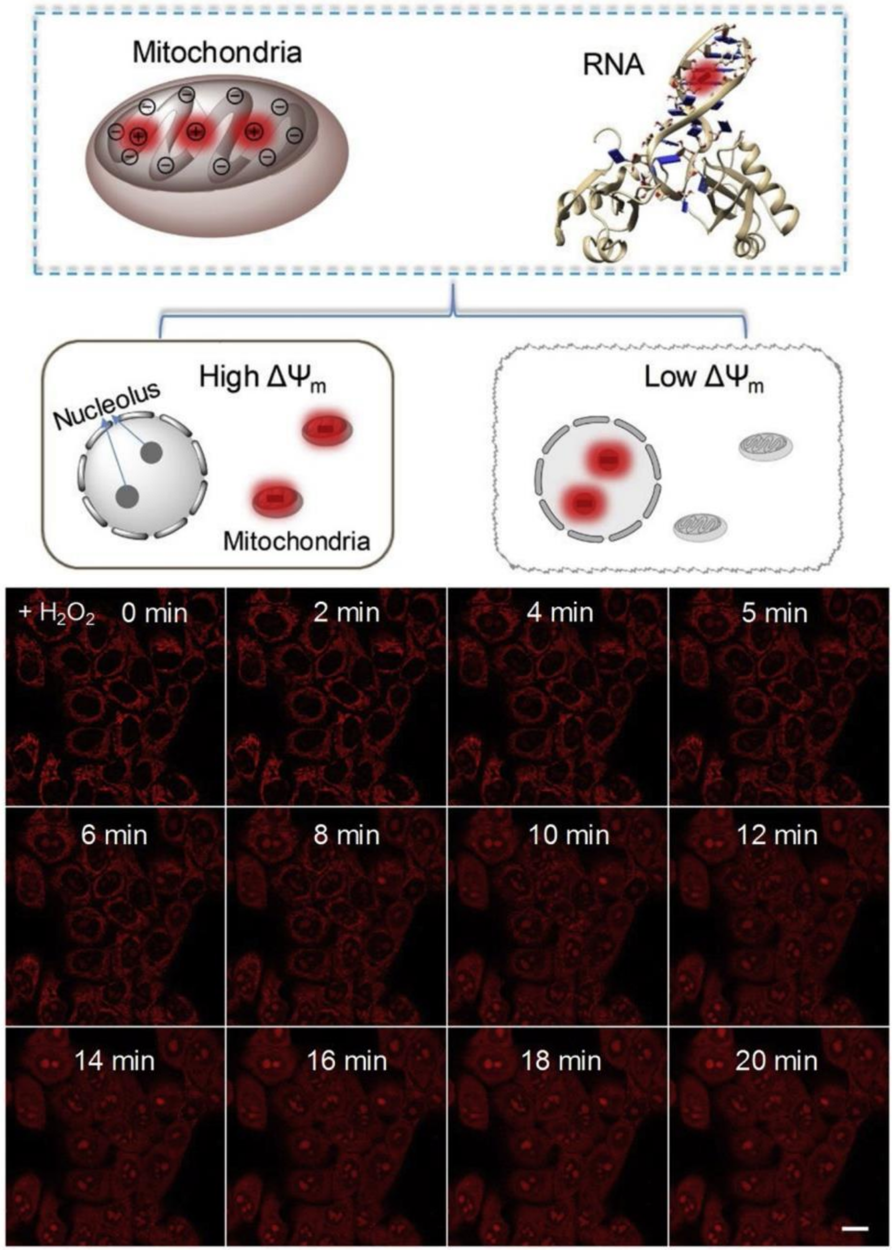


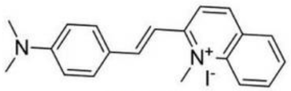
J. Org. Chem. 2018, 83, 3, 1185–1195.



ACS Appl. Mater. Interfaces 2017, 9, 31424−31432.

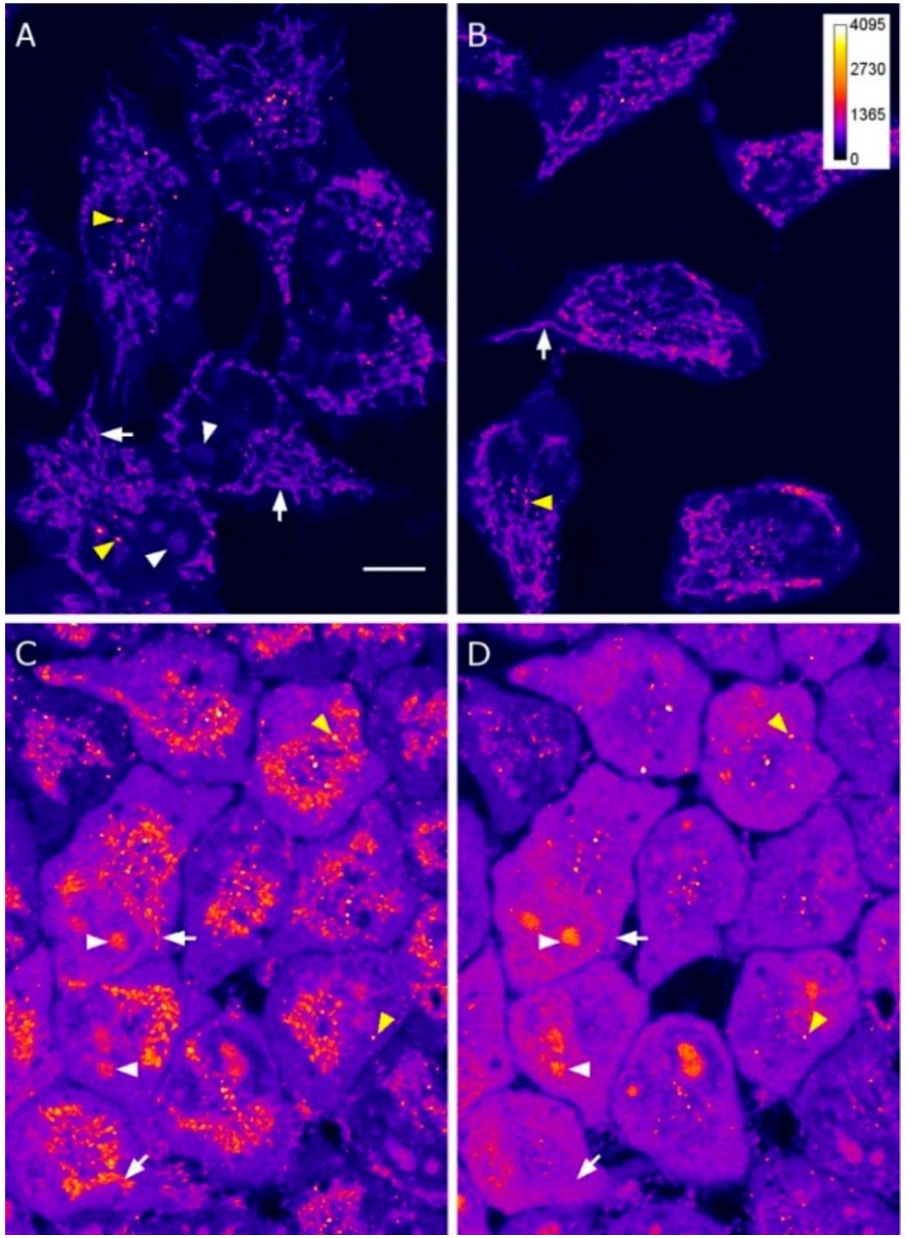
Nucleolus (rRNA) fluorescent imaging





MR-3

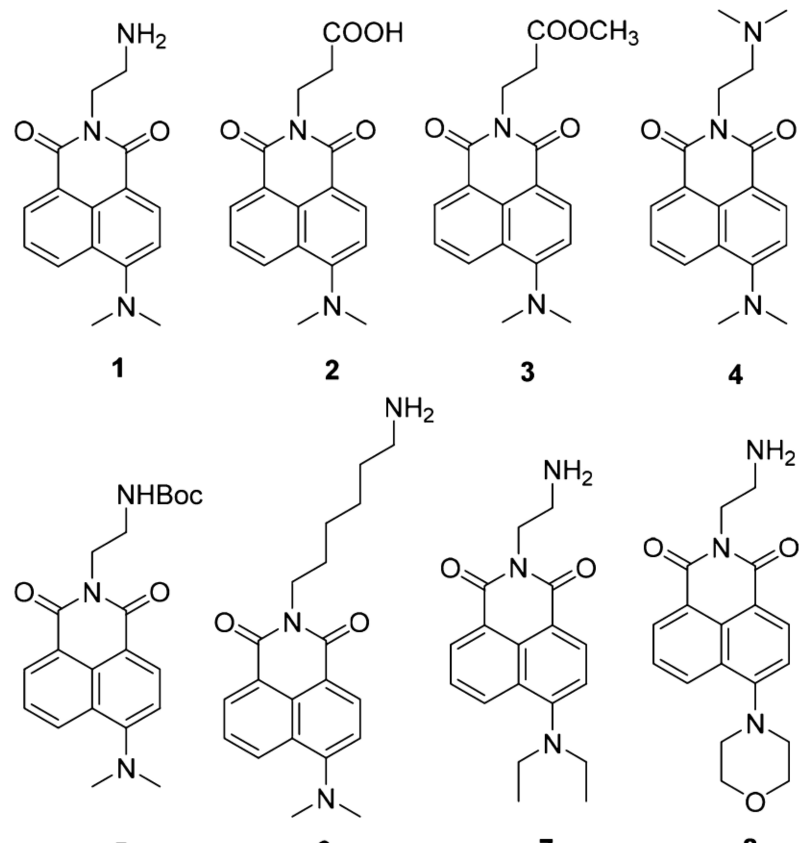
Sensors & Actuators: B. Chemical 2019, 292, 16-23.

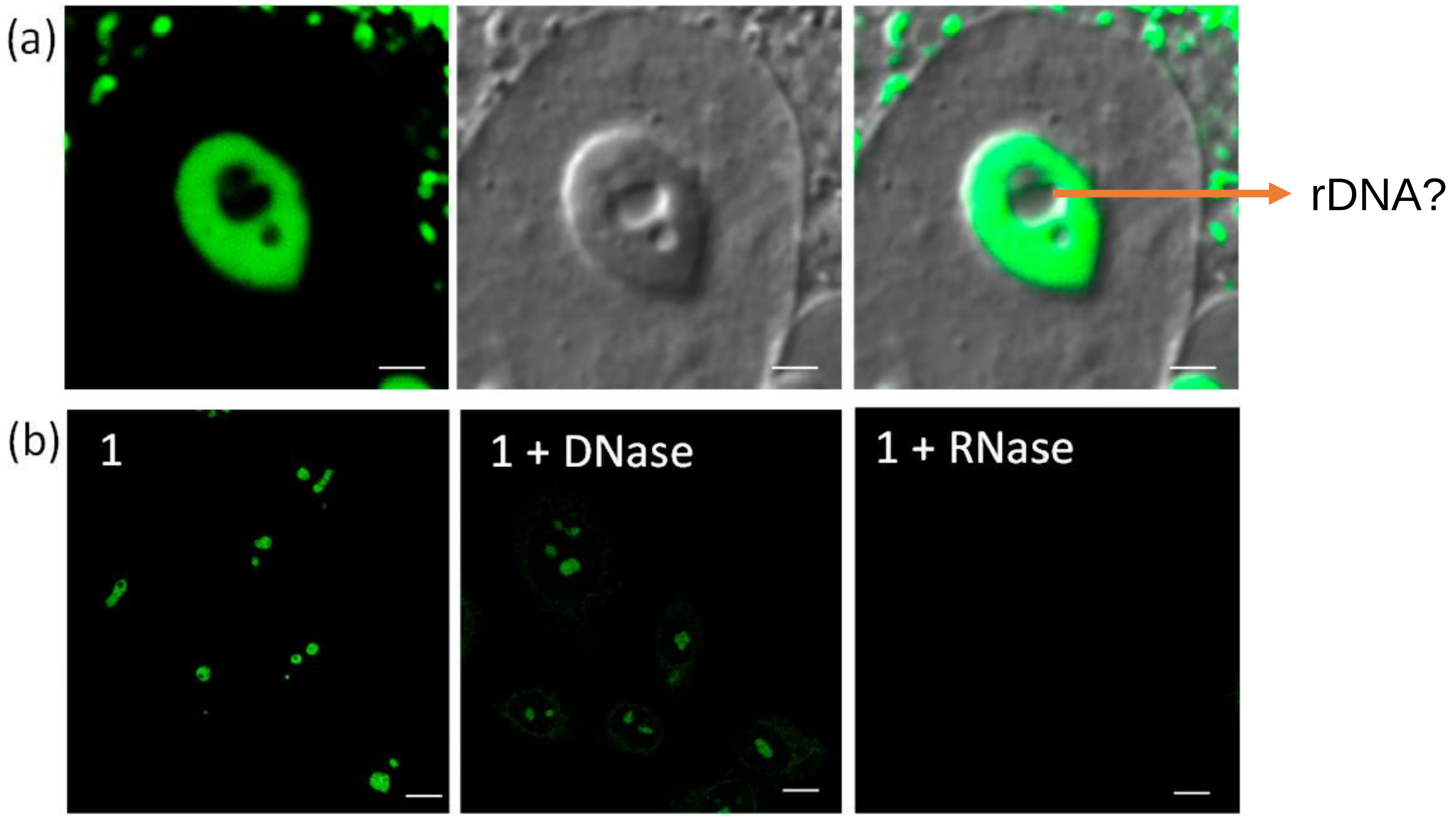


J. Org. Chem. 2018, 83, 3, 1185–1195.

Nucleolus (rRNA) fluorescent imaging

- naphthalimide



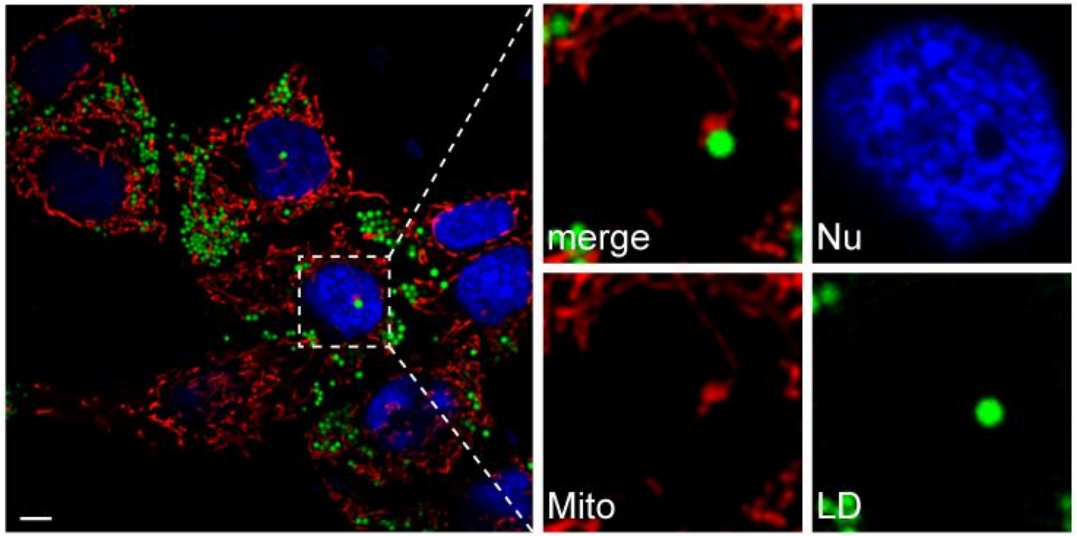


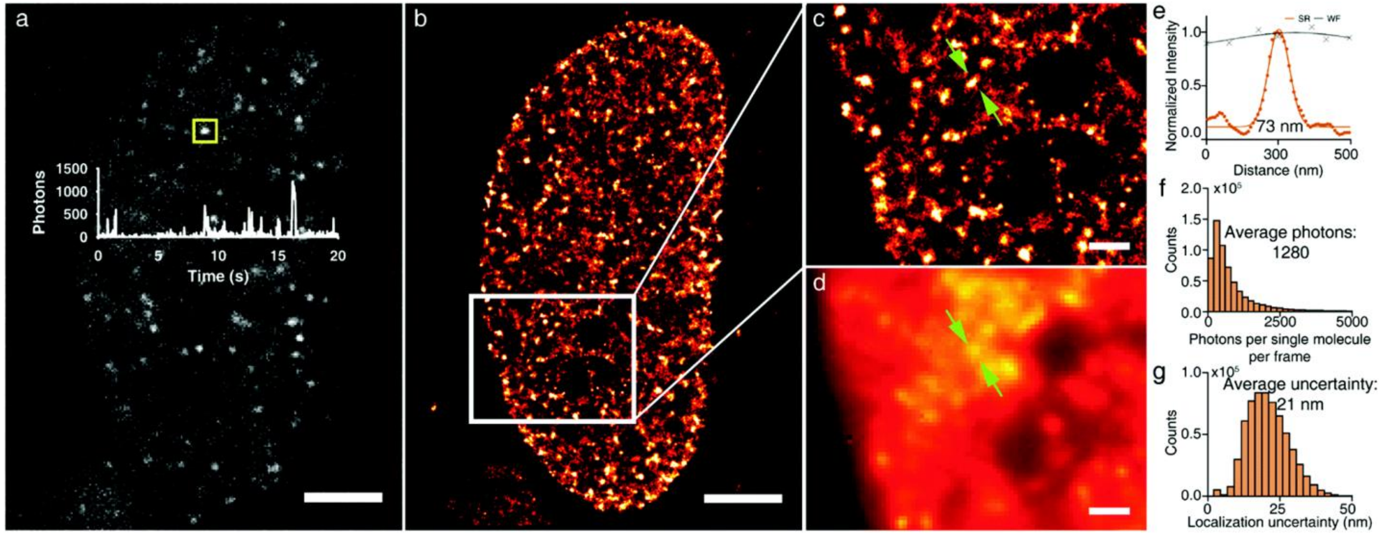
ACS Sens. 2019, 4, 5, 1409-1416.

- metallodrug complexes

Chem. Soc. Rev., 2019, 48, 971-988.

Nucleolus (rRNA) fluorescent imaging

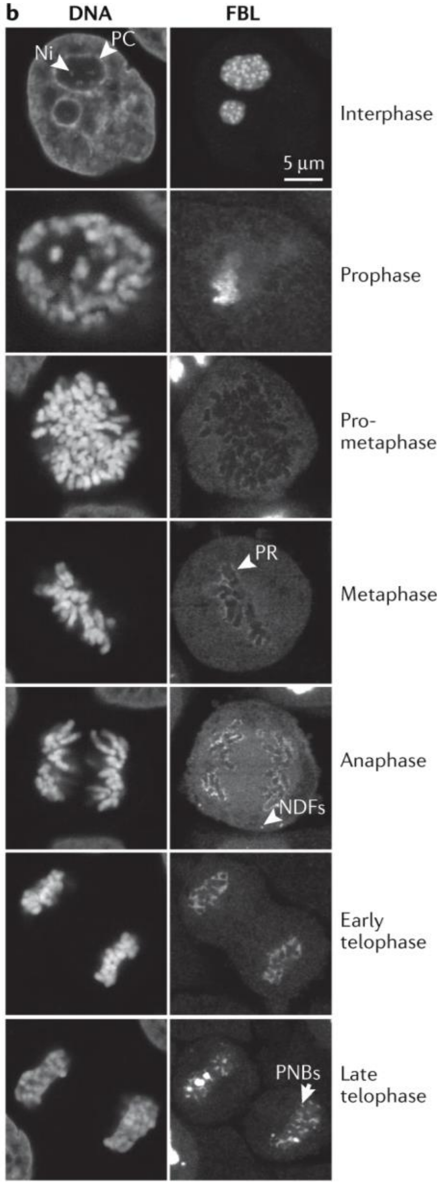




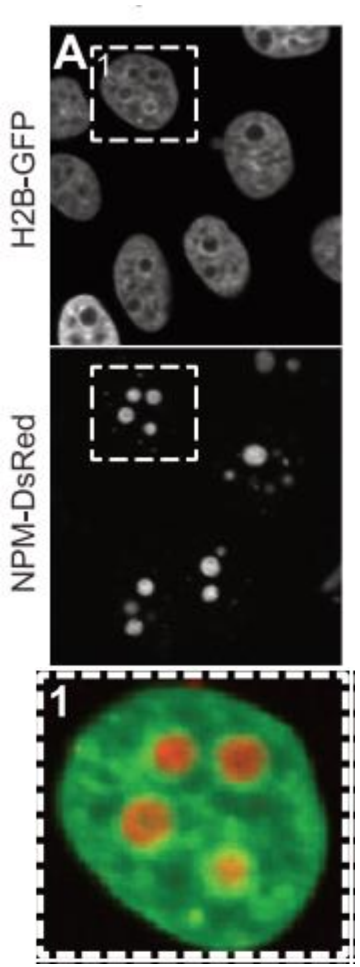
Chem. Commun., 2019, 55, 1951-1954.

Chromatin around nucleolus

- DNA stained by DAPI and fluorescent protein



Nat Rev Mol Cell Biol, 2021, 22, 165-182.



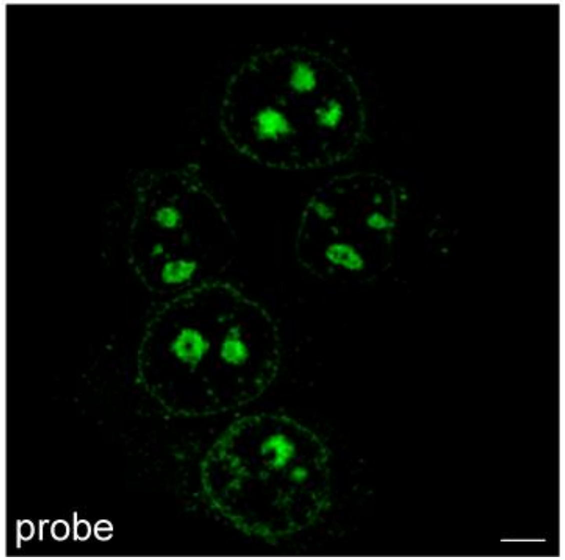
功能：稳定核仁

- 核周染色体的堆积致密程度影响核仁形态，并且参与调控核仁融合过程

eLife 2019, 8, e47533.

- 有的会插入核仁中心，有特定结构域

Nat Rev Mol Cell Biol, 2021, 22, 165-182.

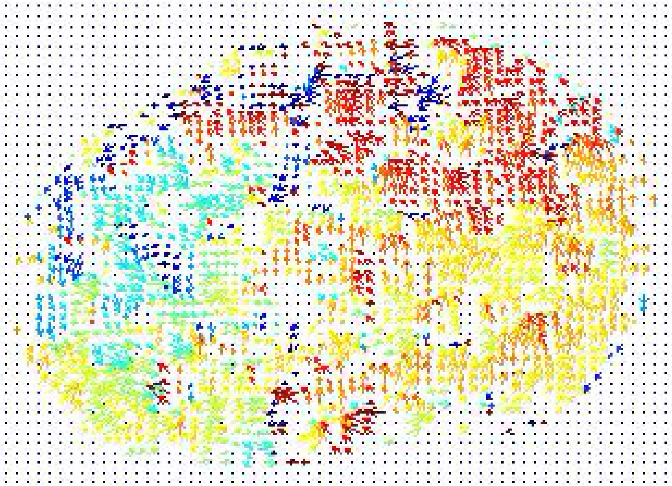


- 核周染色体影响核仁运动速度（显著降低）

Nat. Phys. 2021, 10.1038/s41567-020-01125-8

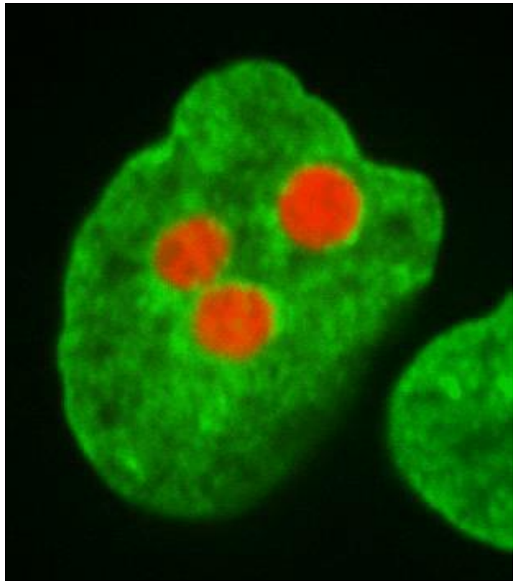
Alexandra Zidovska Lab

- Chromatin Organization and Dynamics

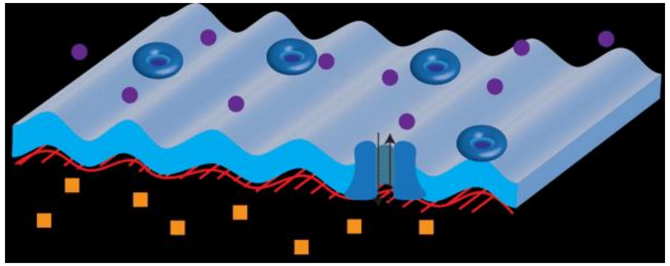


- Physics of Chromosomes

- Liquid Condensates in the Nucleus



- Nuclear Envelope Dynamics

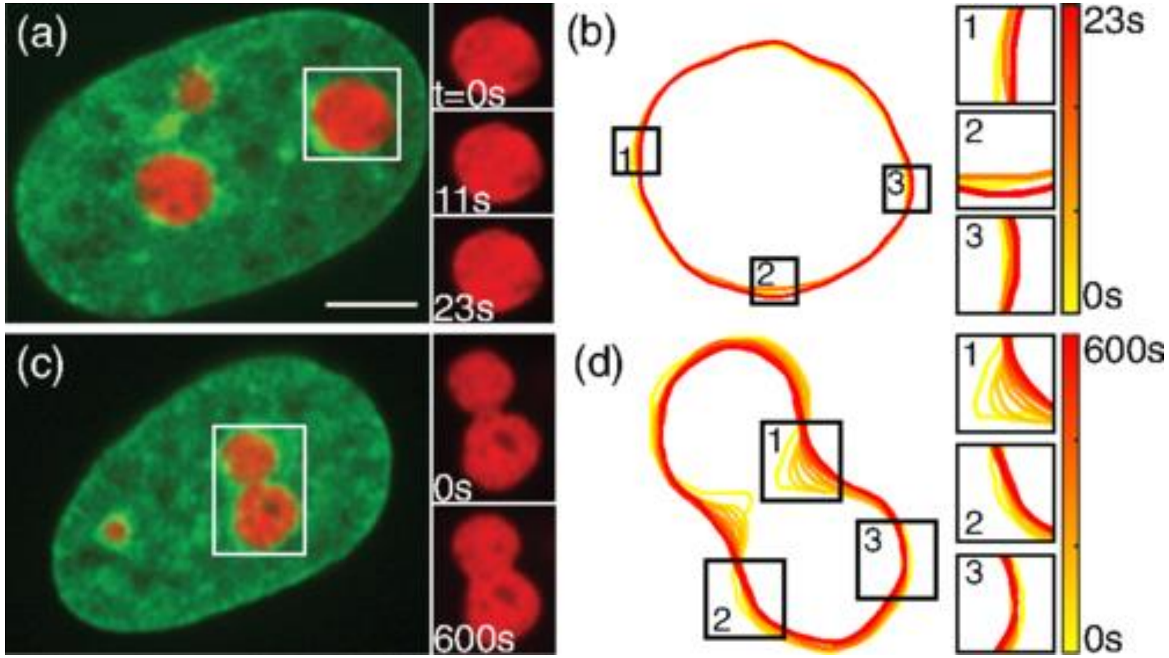


Imaging and analytical techniques

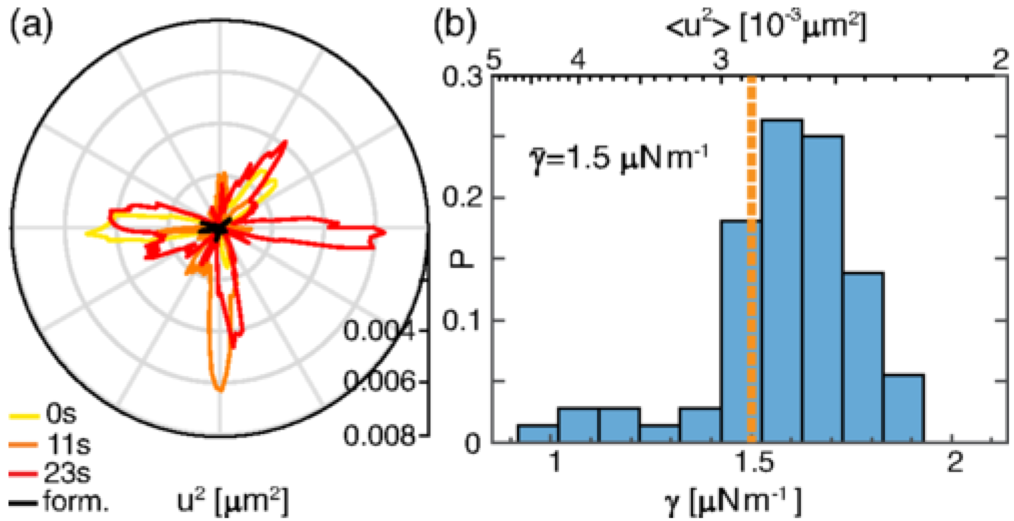
https://physics.nyu.edu/zidovskalab/

Surface Fluctuations and Coalescence of Nucleolar Droplets in the Human Cell Nucleus

H2B-GFP & NPM-mApple



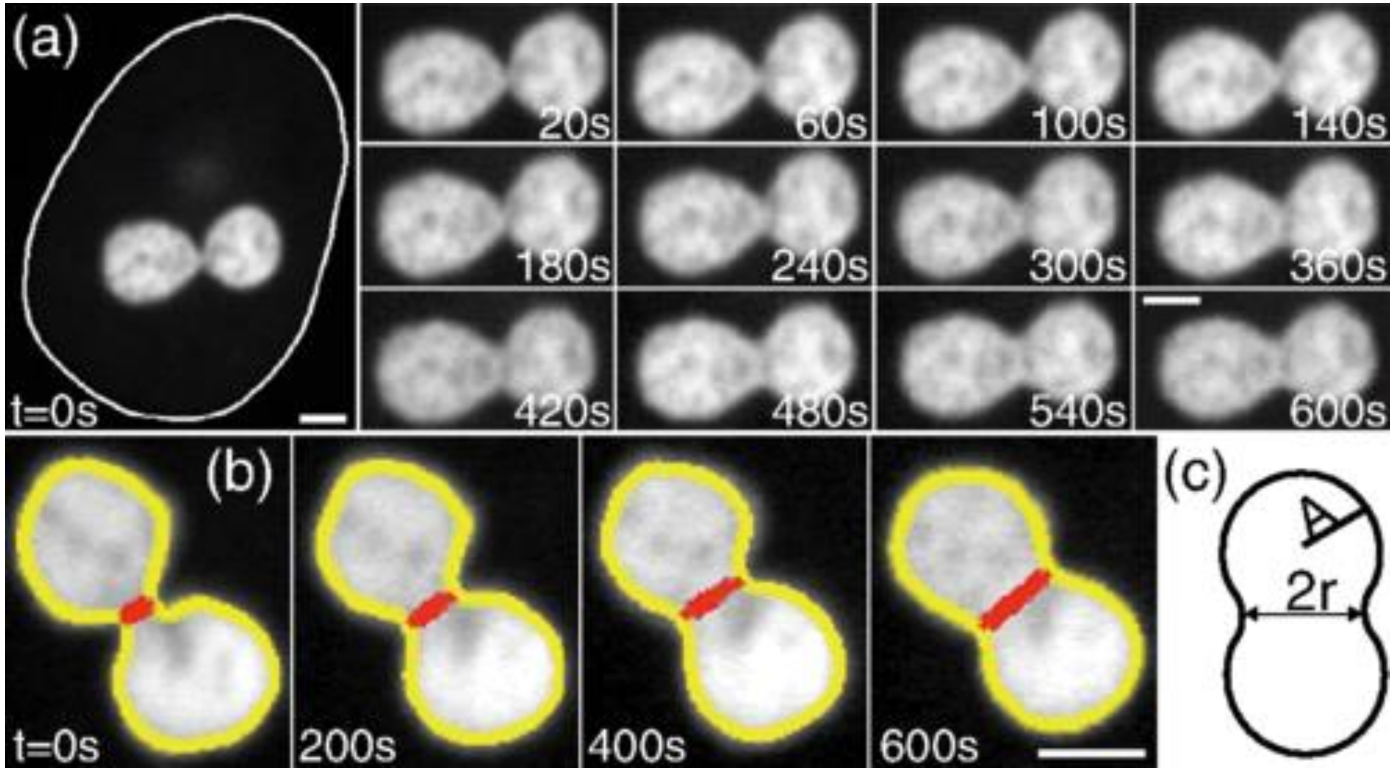
detect and monitor these rare events [Fig. 1(c)]. First, we have identified cells where nucleoli appeared to be located close to each other, thus more likely to fuse, and followed them for two hours imaging every 5 min. After we detected a fusion event, we recorded a time lapse for 10 min with a time step of 20 s, which was carefully chosen to minimize photobleaching and phototoxicity, while maximizing the time resolution with which we monitor the nucleolar shape. Moreover, we selected for fusion events happening

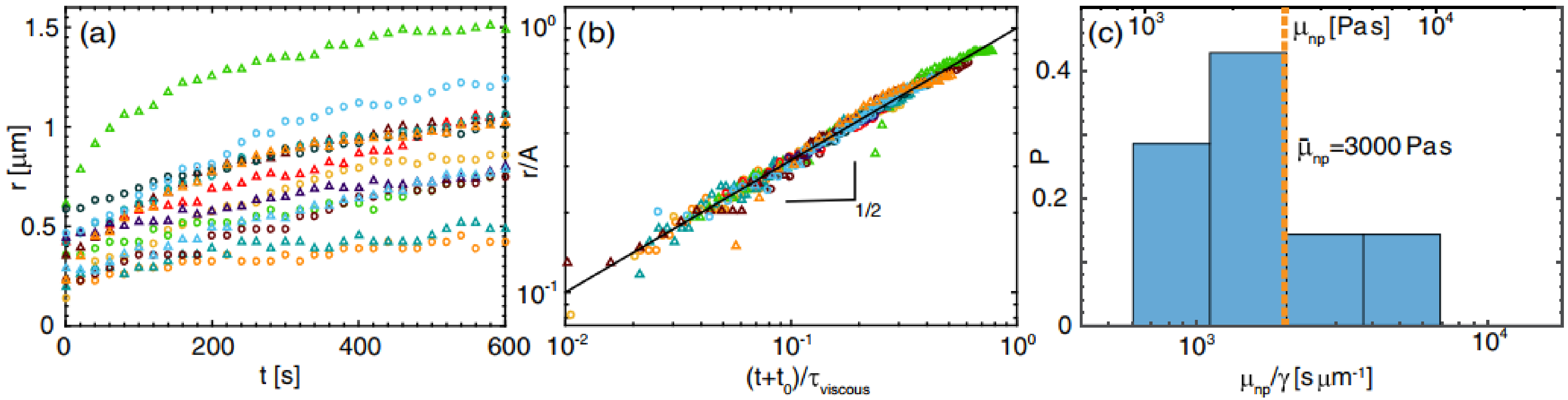


nucleolar signal. Our experiments scanned through $\sim 10^4$ cells, where we identified ~150 cells with nucleoli in close proximity in the *x*-*y* plane, which led to 14 nucleolar fusion events in total.

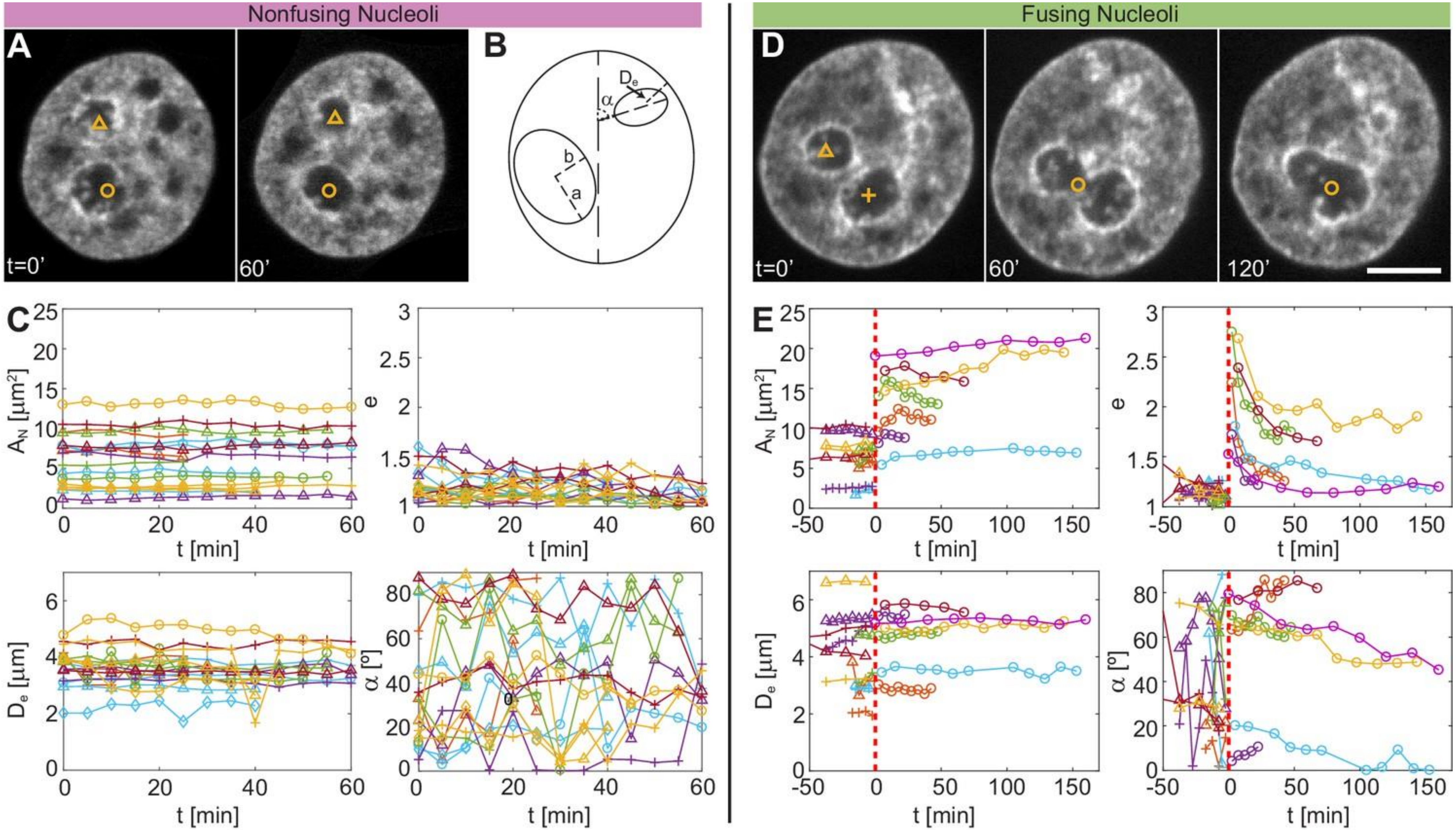
Phys. Rev. Lett. 2018, 121, 148101.

Surface Fluctuations and Coalescence of Nucleolar Droplets in the Human Cell Nucleus



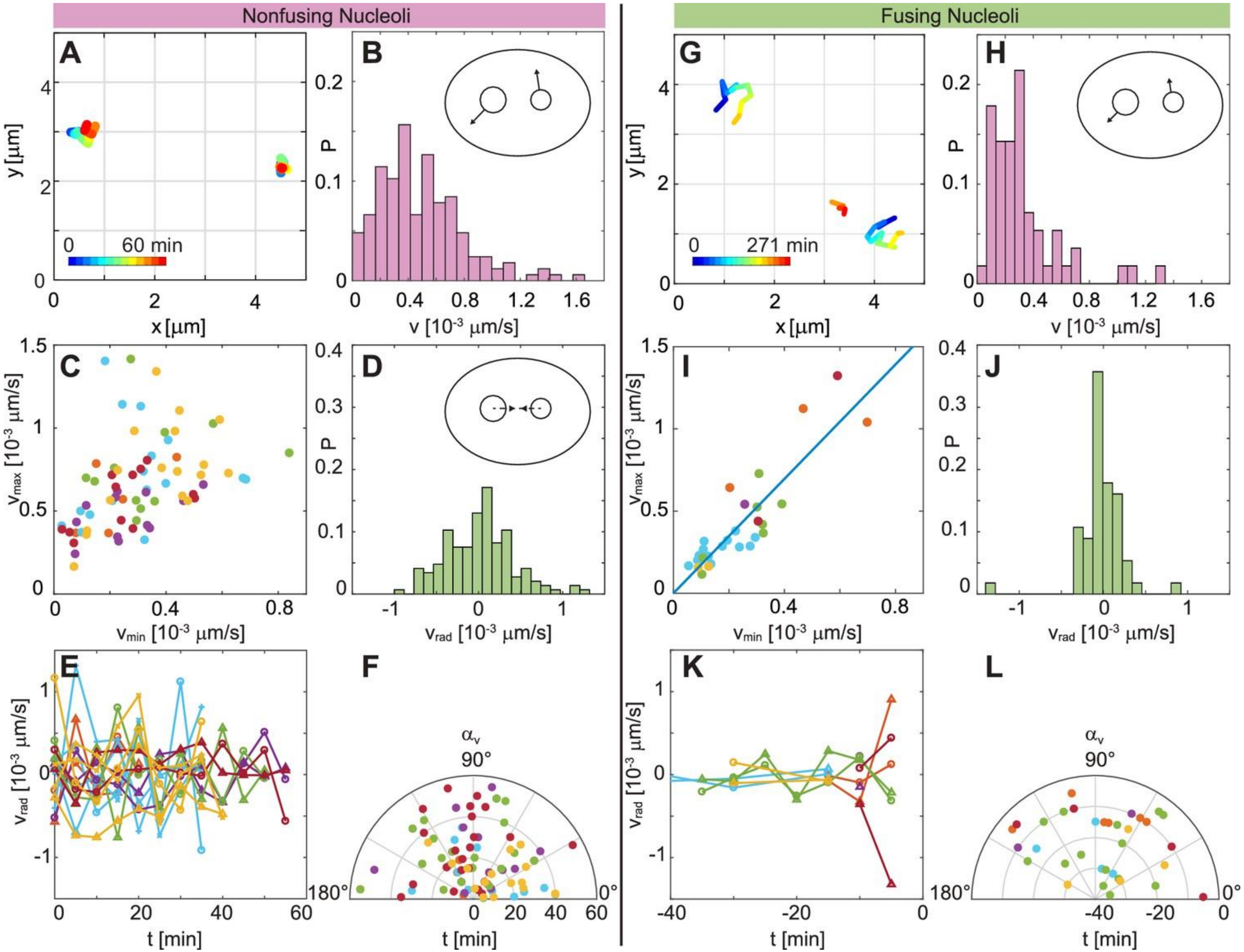


Fusing and non-fusing nucleoli



eLife 2019, 8, e47533.

Dynamics of fusing and non-fusing nucleoli



eLife 2019, 8, e47533.