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The Editors  
*Nature*

Dear Editors,

I submit **“A scaling law of periodic radial geometry organises eukaryotic chromosomes”** for consideration as an Article.

We report a conserved periodic radial fold that organises eukaryotic chromosomes above the level of A/B compartments, following an empirical scaling law  $T \propto L^{0.83}$  across 71 chromosomes in human, mouse, chicken, and *Drosophila*. Each chromosome traces approximately five radial excursions between nuclear speckles and the lamina, regardless of length, so chromosomes of widely different sizes achieve proportional access to nuclear environments.

The fold is revealed by a coordinate change: indexing chromosomes on the ordered sequence of accessible chromatin peaks rather than on base pairs eliminates the autocorrelation that masks it in standard analyses. Three signatures separate the fold from compartment identity. (i) The cross-species scaling law itself, of biophysical interest. (ii) Wavelet phase predicts radial nuclear position by TSA-seq ( $R^2 = 0.90$ ), reproduced at single-cell resolution in 14/14 GM12878 nuclei by Dip-C, in 240/240 mouse cortical neurons (P7–P28; Dip-C), and by orthogonal seqFISH+ and MERFISH imaging. (iii) Two perturbations dissociate wavelength from coherence: mitotic compartment dissolution collapses the signal  $\sim 426$ -fold, while RIF1 loss abolishes interchromosomal coherence without shifting the wavelength. Cross-cell-type validation across 74 ENCODE human lines spanning pluripotent, immune, neural, epithelial, and cancer lineages confirms universality (pooled  $\hat{b} = 0.91$  [0.83, 0.98]).

The fold links chromosome geometry to biology and to disease. Transcription-factor occupancy, super-enhancer activity (H3K27ac,  $3.96\times$  enrichment at wave crests), pan-cancer mutation density, retroviral integration, and translocation breakpoints co-register on the wave coordinate; an in-patient verification on the ICGC PCAWG consensus structural-variant call set (1,487 aliquots, 35,975 inter-chromosomal autosomal TRA pairs) reproduces the wave-aligned translocation finding (mean  $\cos(\Delta\varphi) = +0.066$ , cluster-robust  $t = 10.03$  over 2,159 donor clusters) and stratifies it across 19/20 solid tumour cohorts. The wave coordinate further predicts the chromosomal distribution of pathogenic copy-number variation in held-out clinical and population catalogs: across five v38-pipeline phase maps, the cumulative distribution of  $\cos(\varphi)$  at 9,800 ClinVar pathogenic CNV breakpoints differs from genome-wide null in every cell line ( $p$  ranging  $9.9 \times 10^{-15}$  to  $1.8 \times 10^{-53}$ ), with  $2.30\times$  A-leaning enrichment specifically in the 200 kb–3 Mb non-allelic homologous recombination band, replication in gnomAD-SV ( $p = 1.2 \times 10^{-42}$ ), and 7/11 canonical recurrent CNV syndromes at extreme phase positions ( $|\cos(\varphi)| > 0.7$ ). The wave is therefore a structural coordinate that links chromosome geometry, nuclear access, gene regulation, and the distribution of disease-causing chromosome rearrangements in human patients.

**Affiliation and provenance.** This work was developed without institutional sponsorship over a nine-year period, beginning with an initial observation made during my postdoctoral research at the Institute of Molecular Biology, Mainz (2011–2016), and crystallised into the present cross-species framework through the analysis described here. My membership application at Ronin Institute (Montclair, NJ; an established research home for independent scholars) is currently under review, and I would update affiliation accordingly should it confirm during your editorial process. I have included an Acknowledgment to Anjana Rao (La Jolla Institute for Immunology), with whom I have discussed the work and exchanged drafts throughout its development.

**Suggested reviewers.** For breadth across the cell-biology and genomics readership, plausible reviewers include Job Dekker (UMass Chan Medical School; chromosome conformation, Hi-C), Erez Lieberman Aiden (Baylor College of Medicine; Hi-C, 3D genome), Wendy Bickmore (MRC Human Genetics Unit, Edinburgh; nuclear position, microscopy), Bing Ren (UCSD / Ludwig Institute; chromatin organisation), and either Anders Sejr Hansen (MIT; single-molecule live imaging) or Kyle Eagen (Baylor College of Medicine; chromatin biophysics).

**Reproducibility.** A complete reproducibility bundle accompanies the submission: the chrompe-riod analysis pipeline, all per-cell-line phase maps, the cross-species scaling-law table, and 80+ pre-registered BIOMNI experimental protocols with binding disposition rules. Every honest negative result is reported transparently in Methods footnotes alongside its positive companion.

**Competing interests.** None declared. **Funding.** Independent research; no external funding.

Sincerely,

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