Tuesday March 31st
12h15-13h30: Welcome and Lunch

Interactions with other GDRs
13h30-14h: Fabien Montel, director of GDR AQV (Approches Quantitatives du Vivant), *Transcriptional and Mechanical Plasticity of the Nuclear Pore Complex*

Modeling and visualizing DNA and the Chromatin fiber (chair: Cédric Vaillant)
14h-14h20: Elham Ghobadpour, *How Linker DNA Architecture and Nucleosome States Shape Chromatin Fiber Structure*
14h20-14h40: Amélie Leforestier, *Intermolecular interactions tune the DNA double helix conformation and the architecture of supramolecular assemblies*

3D Genome organization during development (chair: Cédric Vaillant)
14h40-15h: Marie Christou-Kent, *Defining the Interplay Between Transcription Factor-Driven Chromatin Rewiring and Histone H1-Mediated Restraint in B-cell Identity*
15h-15h20: Aline Probst, *Chromatin dynamics during the seed-to-seedling transition*

15h20-16h20: Coffee break + posters

DNA repair (chair: Aurèle Piazza)
16h20-16h40: Pierre-Alexandre Vidi, *RAD51 regulates eukaryotic chromatin motions in the absence of DNA damage*
16h40-17h: Nicolas Mendiboure, *Quantitative model of homology search during DNA repair by homologous recombination*

New technologies for 3D Genomics (chair: Aurèle Piazza)
17h-17h20: Axel Delamarre, *Chromatin architecture mapping by multiplex proximity tagging*
17h20-17h40: Léo Tarbouriech, *Revealing 3D contacts with time resolution in vivo using a new enzymatic technique*

18h-20h: Free time [possibility to go for a drink]
20h: Social Diner at Brasserie Georges - 30 Cours de Verdun – 69002 LYON

Wednesday April 1st
8h30-9h: Welcome and Coffee

Investigating SMC-mediated loop extrusion (chair: Ivan Junier)
9h-9h20: Nicolas Pellet, *Biophysics of condensin-mediated loop extrusion on chromatin*
9h20-9h40: Samuele Lipani, *Chromosome mechanics and relaxation from ensembles of polymer conformations*
9h40-10h: Flavia Corsi, *Modeling the 3D organization of centromeres: from holocentric to monocentric chromosomes*
10h-10h20: Timothy Foldes, *How cohesin and CTCF regulate enhancer-promoter communication*
10h20-10h40: Pascal Bernard, *Nucleosomes act as barriers to Condensin-driven mitotic genome folding*

10h40-11h20: Coffee break + posters

Chromatin and gene regulation (chair: Aline Probst)
11h20-11h40: Yad Ghavi-Helm, *Promoter-proximal elements restrict pleiotropic enhancer inputs to achieve tissue specificity*
11h40-12h: Julien Mozziconacci, *Expliquer les dépendances entre tracks génomiques grâce à l'IA*
12h-12h20: Jacques Serizay, *TBA*
12h20-12h40: Judith Lopes, *Interrogating the functional roles of H3K9me3 at pericentromeres*
12h40-13h: Gautham Ganesh, *Capturing motifs of folding from single-cell chromatin tracing data using unsupervised topic modelling*

13h: Farewell + Lunch Bag

ID de résumé : **9**

How Linker DNA Architecture and Nucleosome States Shape Chromatin Fiber Structure

Contenu

In this work, we investigate how linker DNA length and chromatin state shape the physical properties of chromatin fibers using physics-based polymer models. To this end, we have developed an open-source simulation framework that models DNA at 10.5 bp resolution and represents nucleosomes explicitly as 14–15 DNA segments wrapped around a histone core.

We compare chromatin fibers in open states that mimic histone acetylation, and closed states enriched in linker histone H1. For each chromatin state, we systematically explore integer,and half-integer linker lengths, corresponding to in-phase and out-of-phase nucleosome orientations. By quantifying observables such as the radius of gyration, mean-square internal distance, and persistence length, we show how variations in linker architecture and chromatin state strongly affect the mechanical and structural properties of chromatin fibers.

Auteurs: GHOBADPOUR, Elham (TIMC-Grenoble university/ ENS-lyon); Dr JOST, Daniel (Laboratory of Biology and Modeling of the Cell CNRS and Ecole Normale Superieure de Lyon); VAILLANT, Cedric (Laboratory of Physics École Normale Supérieure de Lyon (ENS Lyon))

Co-auteur: Dr CARRIVAIN, Pascal

Orateur: GHOBADPOUR, Elham (TIMC-Grenoble university/ ENS-lyon)

Déposé par **GHOBADPOUR, Elham** <elham.ghobadpour@ens-lyon.fr> le **mardi 17 mars 2026**

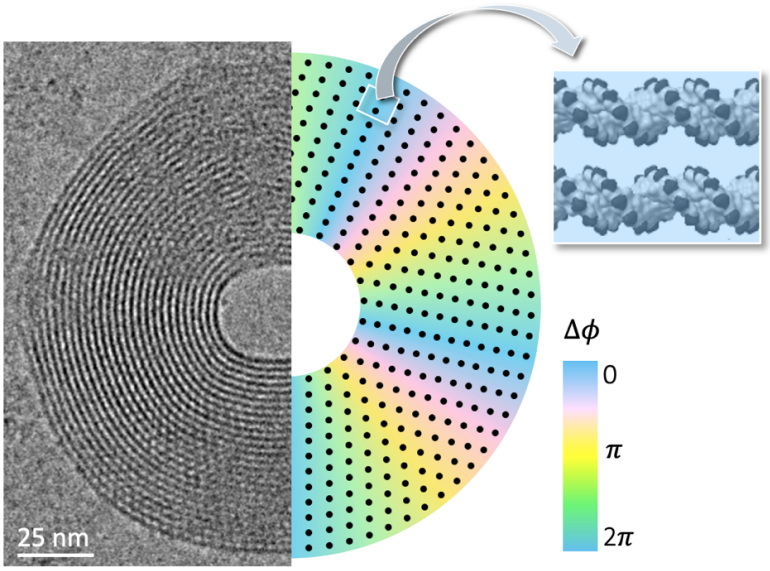
Intermolecular interactions tune the DNA double helix conformation and the architecture of supramolecular assemblies

By Amélie Leforestier

Shape matters in the interactions at work in chromosome shaping or sequence recognition, which take place in dense and confined environments: the close approach of helices such as DNA is expected to result in helically-modulated interactions, as charge (and condensed counterions) distribution as well as surrounding water structuration follow the helical symmetry of the molecule. Helices in compact assemblies are thus predicted correlated by theoretical works and simulations. However, this phenomenon is poorly documented experimentally. In addition, theory does not take into account curvature, which is not compatible with correlations but is a general feature of DNA dense states, both *in vitro* and *in vivo*.

Using cryo electron microscopy of DNA toroids self-assembled upon DNA condensation *in vitro*, we analyze this phenomenon. We find that in-phase helical correlations are preferred over a wide range of experimental conditions. This preferred interaction leads to nucleation of radial phasing, that propagate and reshape the toroid into pentagons and tetragons, with curvature concentrated within narrow sectors. There, we report a decrease of the helical pitch of the DNA molecule, which could correspond to a B to A transition, so far detected only in dehydrated assemblies.

Altogether, this work reveals how intermolecular interactions, through preferred phasing of helices, tunes both the shape of the assembly - at the mesoscale - and the conformation of the double helix - at the nanoscale. These phenomena can be expected at work within a broad range of biological and nanoengineering contexts, from DNA architectures in viral capids, toroidal bacterial nucleoids, or cylindrical spermatozoa, and more generally upon the close approach of doubles helices, at work in most DNA processes including molecular recognition.



Defining the Interplay Between Transcription Factor-Driven Chromatin Rewiring and Histone H1-Mediated Restraint in B-cell Identity

Marie Christou-Kent[1], Mahmood Mohammed-Ali[1], Anouk Emadali[1,2], Sylvain Carras[1,2], Guillermo Orsi[1]

[1]Institut pour l'Avancée des Biosciences, Grenoble
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Cellular identity is defined by the selective activation of lineage-specific gene programs and the robust silencing of inappropriate ones. While pioneering transcription factors (TFs) can override topological constraints to drive fate transitions, the structural mechanisms that maintain chromatin state stability to prevent malignant remodeling remain poorly defined. In B-cell malignancies, this stability is often compromised, frequently coinciding with the aberrant expression of lineage-inappropriate TFs and the subsequent rewiring of the 3D genome. Here, we investigate the interplay between TF-mediated plasticity and the role of Linker Histone H1 in stabilizing the B-cell cistrome.

Prior investigations utilizing the BLaER1 transdifferentiation model demonstrated that the pioneering factor CEBPA utilizes its intrinsically disordered region (IDR) to facilitate phase separation and the formation of higher-order chromatin hubs. These findings suggest that instructive TFs act as biophysical organizers that actively reshape the 3D genome. We now propose, however, that such plasticity is normally restrained by H1-mediated structural barriers.

Supporting this hypothesis, our recent CUT&Tag profiling of H1 in Diffuse Large B-cell Lymphoma (DLBCL) and K562 cell lines reveals a striking and non-canonical enrichment at ATAC-seq-positive active enhancers. This localization suggests that H1 is not merely a global repressor but serves as a localized regulator of enhancer activity. Given that H1 is frequently co-mutated with enhancer-modulating enzymes (p300, CBP, KMT2D) in DLBCL, we hypothesize that H1 loss lowers the threshold for chromatin rewiring. This permissive epigenetic state may facilitate the aberrant recruitment or activity of TFs at regulatory elements, contributing to the transcriptional instability and malignant plasticity characteristic of lymphoma. Together, these data suggest a framework where H1 acts as an essential guardian of identity by modulating the physical and biochemical accessibility of the active genome.

ID de résumé : **5**

Chromatin dynamics during the seed-to-seedling transition

Contenu

The transition from seed to seedling involves major changes in nuclear organization and gene expression. However, the extent to which this developmental transition requires chromatin reprogramming - particularly changes in the histone variant repertoire - remains largely unexplored.
To dissect the molecular mechanisms that drive these chromatin reprogramming events we are combining chromatin conformation capture methods, microscopy imaging coupled with deep-learning-driven analysis tools, genetics, and epigenomics. I will present recent evidence that, in dry seeds, a specific histone H2B variant termed H2B.8 contributes to higher-order chromatin organization by forming spatial clusters that structure the 3D nuclear space. In dry seed embryos, the H2B.8 variant forms heterotypic nucleosomes at euchromatic transposons and lowly expressed genes and, during imbibition, modulates the transcriptional activation of a subset of these genes. We found that imbibition triggers a decrease in H2B.8 transcripts and the eviction of H2B.8 proteins in a process that operates independently of DNA replication. The observed histone eviction is not limited to H2B.8 as imbibition also induces the turnover of the H3.3 histone variant, thereby initiating a broad, replication-independent chromatin reprogramming process.
Our findings highlight a fundamental mechanism of epigenetic regulation during early plant development.

Auteurs: PROBST, Aline (GReD); Dr SIMON, Lauriane (Institute of Genetics, Reproduction and Development)

Orateur: PROBST, Aline (GReD)

Déposé par **PROBST, Aline** <aline.probst@uca.fr> le **jeudi 12 mars 2026**

ID de résumé : **6**

RAD51 regulates eukaryotic chromatin motions in the absence of DNA damage

Contenu

In yeasts and higher eukaryotes, chromatin motions may be tuned to genomic functions, with transcriptional activation and the DNA damage response both leading to profound changes in chromatin dynamics. The RAD51 recombinase is a key mediator of chromatin mobility following DNA damage. As functions of RAD51 beyond DNA repair are being discovered, we asked if RAD51 modulates chromatin dynamics in the absence of DNA damage and found that inhibition or depletion of RAD51 alters chromatin motions in undamaged cells. Inhibition of RAD51 increased nucleosome clustering. Predictions from polymer models are that chromatin clusters reduce chain mobility and, indeed, we measured reduced motion of individual chromatin loci in cells treated with a RAD51 inhibitor. This effect was conserved in mammalian cells, yeasts, and plant cells. In contrast, RAD51 depletion or inhibition increased global chromatin motions at the microscale. The results uncover a role for RAD51 in regulating local and global chromatin dynamics independently from DNA damage and highlight the importance of considering different physical scales when studying chromatin dynamics.

Auteur: VIDI, Pierre-Alexandre (Institut de Cancérologie de l'Ouest)

Co-auteurs: ATANASIU, Andrew; BLOOM, Kerry; BONIN, Keith; HOMMAIS, Chloé; IQBAL, Fadil; KOLBIN, Daniel; LIU, Jing; LOCATELLI, Maëlle; MAAROUF, Amine; MÜHLEMANN, Joëlle; SANAULLAH, Sarvath

Orateur: VIDI, Pierre-Alexandre (Institut de Cancérologie de l'Ouest)

Déposé par **VIDI, Pierre-Alexandre** <pierre.vidi@ico.unicancer.fr> le **vendredi 13 mars 2026**

ID de résumé : **2**

A quantitative and predictive computational model of homology search during DNA repair by homologous recombination

Contenu

Homologous recombination (HR) is a conserved DNA repair mechanism that uses an intact DNA molecule as a template to mend double-strand breaks (DSBs) and single-stranded gaps, ensuring genomic stability. The accurate search and choice of an homologous donor is of prime importance for HR fidelity, as repairing using non-allelic repetitive sequences can lead to structural variations. Multiple mechanisms involved in the homology search mitigate this risk, but they remain incompletely characterized.

My PhD project aims to elucidate the molecular controls governing donor selection during HR. To this end, I developed a computational model of the HR pathway in S. cerevisiae that integrates stochastic parameters for complex formation, disruption rates, protein binding on single-stranded DNA, and chromatin accessibility. Guided by quantitative experimental data, the model simulates thousands of virtual cells, each generating metrics such as first passage times for the homology search, numbers of D-loops formed or disrupted, and high-resolution two-dimensional chromatin contact maps.

By aggregating these outputs, the framework provides robust population-level insights, correlates input parameters with HR outcomes, and facilitates direct comparisons with experimental data. Ultimately, this predictive model will help quantify the roles of specific factors in ensuring HR efficiency and fidelity, with ongoing experimental validations further refining our understanding of homologous donor selection.

Auteur: MENDIBOURE, Nicolas (CNRS)

Co-auteur: M. PIAZZA, Aurèle

Orateur: MENDIBOURE, Nicolas (CNRS)

Déposé par **MENDIBOURE, Nicolas** <nicolas.mendiboure@ens-lyon.fr> le **lundi 23 février 2026**

ID de résumé : **1**

Chromatin architecture mapping by multiplex proximity tagging

Contenu

Chromatin plays a pivotal role in genome expression, maintenance, and replication. To better understand chromatin organization, we developed a proximity-tagging method to map molecules that associate in 3D space. Using this method - PCP (proximity copy paste) - we mapped the positioning and connectivity of individual nucleosomes in *Saccharomyces cerevisiae*. We show that chromatin is predominantly organized into regularly spaced nucleosome arrays that can be positioned or delocalized. PCP can also map long-range, multi-way interactions, and we provide direct evidence supporting a model that metaphase chromosomes are compacted by cohesin loop clustering. Analyzing single-molecule nuclease footprinting data, we define distinct chromatin states within a mixed population to show that non-canonical overlapping di-nucleosomes are a stable feature of chromatin. PCP is a versatile method, allowing the detection of the connectivity of individual molecules locally and over large distances to be mapped at high resolution in a single experiment.

Auteurs: BAILEY, Benton; DELAMARRE, Axel; KOCHE, Richard; MOHIBULLAH, Neeman; WHITEHOUSE, Iestyn; YAVID, Jennifer

Orateur: DELAMARRE, Axel

Déposé par **DELAMARRE, Axel** <axel.delamarre@ens-lyon.fr> le **vendredi 13 février 2026**

ID de résumé : **11**

Revealing 3D contacts with time resolution in vivo using a new enzymatic technique

Contenu

In the nucleus of eukaryotic cells, the DNA is folded in a structure called chromatin1. It has been shown that there is a strong connection between the three-dimensional organisation of the genome and its expression. The domain of 3D genomics and physics of the genome is now moving forward to find fundamental principles of genome organisation. Many methods exist in the domain to reveal the three-dimensional contacts inside DNA. I think they can be classified in two types.

Firstly, the method that rely on crosslinking (HiC, 3C, 4C$\cdots$). These methods are the most used and the most developed. Despite being very useful in revealing the structure of the genome at different scales, they measure the contact after performing a fixation and crosslinking. This chemistry might have a strong impact on genome organisation at small scale2.

Secondly, there are methods relying on enzyme reaction on the genome. The later has the advantage that the contacts are marked in vivo. DamId and Dam-C3–5 are examples of techniques of this class. Both rely in a bacterial enzyme called DNA Adenine Methylase that binds on GATC quadruplets and catalyses methyl group transfer from S-adenosyl-methionine (AdoMet) to the nitrogen atom at the sixth position of adenine (m6A). In DamId technique, DAM enzyme is bound to a protein of interest, forming a X-DAM protein (for example rTetR-DAM). Then, the m6A positions in the genome reveal the preferential binding position of X. This technique has been shown to be efficient for rTetR and LexA protein binding3. The Dam-C technique relies on the same logic. But Dam is bound to a protein whose binding sites are known and the methylation signal is used to identify trans-contacts between the addressing loci and distant loci in the genome. DamId and DamC are useful in eukaryotes because they do not have constitutive m6A methylation.

The team of Gael Yvert at LBMC is developing a modified version of Dam-C technique that we called Light Inducible DAM (LiDAM) which rely on a Dam enzyme on which asLov site has been appended to. The asLov-Dam (a.k.a. LiDam) is built such that the reactive site of DAM is blocked by the asLov protein in closed conformation. When the sample is exposed to light in the visible spectrum, the asLov conformation changes to an open state, letting the reactive site of Dam accessible and allowing the binding and methylation to take place at GATC loci. In the current setting, a plasmid expressing rTetR-LiDam is used. We are using saccharomyces cerevisiae (yeast) cells that have been engineered to contain a docker of TetO sites on chromosome 10. TetO is the known binding site of rTetR. This system is the same as in the original Dam-C and we are currently in the track of reproducing the original DamC study with this system.

The originality of our study relies (1) on the use of nanopore sequencing which allow for a big simplification of the experimental protocol, (2) on the use light induction. The light induction allows to gain time resolution. One can control when the reaction of methylation can occur. This leads us to imagine a scenario where the cells are cultured in the dark. Then the cell might be synchronized in a given state. At time after synchronization a perturbation is made to the cells (for instance inducing a double strand break, DSB). The cells evolve for a time and then they are illuminated during . We would obtain a recording of all the contacts that occurs during the duration . To make the analogy with a photography, plays the role of exposure time while plays the role of a delay between a pump (the trigger of the DSB) and a probe which measure the contacts. Scanning pump-probe delay would give access to a "film"of the repair of the double strand break. The method is still under development and we are not yet there.

In my talk I will present the current status of this project. I will first talk about the experimental setup that have been developed by Mohammed Baddaze in the team of Gael Yvert. Secondly, I will explain which data analysis strategy I settled. Finally, I will present conclusion we are able to draw now. Especially I will show comparison of methylation patterns we observed in different conditions and HiC data and accessibility data in yeast genome.

Auteur: TARBOURIECH, Leo (LBMC, ENS de Lyon)

Co-auteurs: Dr JOST, Daniel (LBMC, ENS de Lyon); Dr YVERT, Gaël (LBMC, ENS de Lyon); M. BADDAZE, Mohammed (LBMC, ENS de Lyon); Dr MODOLO, Laurent (LBMC, ENS de Lyon)

Orateur: TARBOURIECH, Leo (LBMC, ENS de Lyon)

Déposé par **TARBOURIECH, Leo** <leo.tarbouriech@ens-lyon.fr> le **mercredi 18 mars 2026**

ID de résumé : **10**

Biophysics of condensin-mediated loop extrusion on chromatin

Contenu

Inside the cellular nucleus, DNA is compacted into a highly dynamic polymer-like structure known as chromatin. This organization enables the storage of genetic information while still allowing regulated access for processes such as transcription, replication, and repair. The self-organization of chromatin into functional domains, facilitated by a combination of physical interactions and biochemical processes, remains one of the most fundamental and unresolved challenges in molecular biology. Recent studies suggest that chromatin organization is not purely random but rather orchestrated by specialized proteins and molecular motors that dynamically reshape its structure over time.

Our research is centered on modelling the loop extrusion process, a key mechanism thought to drive the formation of topologically associating domains (TADs) and other large-scale chromatin structures. Loop extrusion is mediated by condensin, a complex of proteins that actively translocates along DNA while anchoring and extruding loops. In vitro assays have demonstrated that condensin binds preferentially to free DNA, exhibiting a remarkable ability to extrude loops at rates measurable in real time. However, the in vivo behavior of this mechanism remains less understood, as the chromatin landscape is densely populated with obstacles such as nucleosomes, transcription factors, and other chromatin-associated proteins. These obstacles are believed to influence loop extrusion efficiency and dynamics significantly, but their exact roles are still debated.

To address these questions, we have developed a one-dimensional (1D) computational model that captures the interplay between loop extrusion machinery, nucleosome positioning, and the mechanical properties of the chromatin fiber. This model employs just two tunable parameters, yet it successfully recapitulates key metrics observed experimentally, including loop extrusion processivity and first passage times. By systematically varying these parameters, we aim to disentangle the individual contributions of chromatin-bound obstacles and DNA mechanics to the overall dynamics of loop extrusion.

In addition to quantifying the effects of these factors, our model provides a framework for exploring the emergent properties of loop extrusion under biologically realistic conditions. For example, it predicts how variations in nucleosome density or the presence of sequence-specific DNA-binding proteins can alter the rate and extent of loop formation. The insights gained from this 1D model serve as a foundation for more complex three-dimensional (3D) simulations, which will incorporate higher-order chromatin folding and interactions between multiple extrusion complexes. Such extensions will allow us to compare our findings directly with experimental imaging data and Hi-C contact maps, bridging the gap between theoretical predictions and empirical observations.

Looking forward, the next steps in our work include adapting the model to capture the dynamic interplay between condensin and other architectural proteins, such as cohesin and CTCF, which are known to play complementary roles in chromatin organization. By combining our theoretical approach with high-resolution experimental data, we hope to uncover the principles governing chromatin self-organization and elucidate how disruptions to these processes contribute to disease states such as cancer and developmental disorders.

Auteur: PELLET, Nicolas (ENS LYON - Laboratoire de Biologie et Modélisation de la Cellule)

Orateur: PELLET, Nicolas (ENS LYON - Laboratoire de Biologie et Modélisation de la Cellule)

Déposé par **PELLET, Nicolas** <nicolas.pellet@ens-lyon.fr> le **mardi 17 mars 2026**

ID de résumé : **3**

Chromosome mechanics and relaxation from ensembles of polymer conformations

Contenu

DNA in the nucleus is not randomly packed: it folds into 3D structures that help regulate genes and must be reestablished each time the cell divides. This folding is controlled by molecular motors that consume energy. For example, cohesin and condensin can actively pull DNA to form loops (“loop extrusion”). Because these processes use energy, they push chromosomes away from equilibrium conformations and create structures that can persist over time before relaxing. For example, during mitotic exit, the constraints established by condensins disappear and chromosomes undergo a major structural transition as interphase organization is rebuilt.

My project is to build a physical model of chromatin as a chain of connected segments and to introduce a way to quantify the internal “tension”along the polymer chain. This tension reflects two effects: random thermal motion that tends to expand the chain (osmotic), and constraints due to the bonds that resist deformation (elastic). By following how tension spreads along the chain and decays over time, the model explains how chromosomes gradually lose the “memory”of imposed loops or compaction.

Auteur: LIPANI, Samuele (Insitut Curie)

Orateur: LIPANI, Samuele (Insitut Curie)

Déposé par **LIPANI, Samuele** <samuele.lipani@curie.fr> le **jeudi 5 mars 2026**

ID de résumé : **13**

Modeling the 3D organization of centromeres

Contenu

Centromeres are essential for accurate chromosome segregation, yet their 3D organization remains largely unknown. Holocentric chromosomes distribute centromeric activity along their entire length, while monocentric chromosomes, like those in humans and chickens, localize it to a single region. Despite this morphological difference, both systems rely on conserved biophysical mechanisms, including condensin-mediated loop extrusion and sister chromatid cohesion, to create a functional centromeric structure capable of withstanding spindle forces and enabling proper kinetochore attachment.

To investigate these mechanisms, we employed polymer simulations to model the 3D organization of mitotic holocentric chromosomes, incorporating loop extrusion by condensin and cohesin, nucleosome interactions, and cohesion. Our model predicts a robust architecture consisting of two cohesed chains of consecutively linked condensin-mediated loops. In this conformation, condensins form two peripheral axes that align with kinetochore locations and provide mechanical rigidity, consistent with experimental data in holocentric species.

We then generalized this folding principle to monocentric chromosomes by introducing a gradient of loop sizes and a cohesion gap at the core centromere, where CENP-A nucleosomes reside. This adaptation recreates the exposed bipartite CENP-A structure observed in chicken centromeres, which remains stable under spindle tension.

Notably, both our holocentric and monocentric models remain robust under variations in loop size and partial cohesin depletion.

By integrating polymer simulations with Hi-C data and imaging, we provide a predictive framework to model centromere folding across eukaryotes. It generates testable hypotheses on the effects of cohesin or condensin depletion and offers new insights into the physical basis of centromere function and chromosome missegregation.

Auteurs: CORSI, Flavia; MIRNY, Leonid

Orateur: CORSI, Flavia

Déposé par **CORSI, Flavia** <flavia.corsi@curie.fr> le **vendredi 20 mars 2026**

ID de résumé : **12**

Nucleosomes act as barriers to Condensin-driven mitotic genome folding

Contenu

Nucleosomes and DNA-loop extruding SMC protein-complexes such as condensin and cohesin shape the 3D genome in eukaryotes, but their mutual functional relationships remain largely unclear. Using the fission yeast Schizosaccharomyces pombe as model, we investigated the interplays between nucleosomes and condensin-mediated mitotic chromosome assembly. We found that purified condensin fails to bind DNA wrapped into nucleosomes, regardless of whether they contain canonical or variant histones, whereas subnucleosomal particles permit condensin binding. In vivo, we found that condensin associates with the histone chaperone FACT and the nucleosome remodeler Chd1/Hrp1, both key players in transcription-coupled nucleosome dynamics. Acute depletion of FACT subunit Spt16 in metaphase-arrested cells causes an extensive loss of nucleosomes, likely due to the role played by FACT in restoring nucleosome architecture in the wake of mitotic transcription. This nucleosome loss increases the frequency of mitotic DNA loops and enhances mitotic chromosome condensation in a condensin-dependent manner, yet without increasing condensin occupancy. Lack of Chd1/Hrp1 or reduced histone gene dosage similarly facilitates condensin activity. Depleting RNA Pol II further revealed that condensin does not merely benefit from transcription-mediated nucleosome remodeling. Our results suggest that nucleosomes act as barriers to condensin-mediated loop extrusion in vivo and that condensin relies on dedicated nucleosome remodelling to bypass this obstruction.

Auteurs: Mme TOSELLI, Esther (LBMC, CNRS & ENS-Lyon); Mme EL MEOUCH, Dana (LBMC, CNRS & ENS-Lyon); Dr COLIN, Léonard (LBMC, CNRS & ENS-Lyon); Dr BOOPATHI, Ramachandran (LBMC, CNRS & ENS-Lyon); Prof. HAERING, Christian H. (University of Würzburg); Dr BERNARD, Pascal (LBMC, CNRS & ENS-Lyon)

Orateur: Dr BERNARD, Pascal (LBMC, CNRS & ENS-Lyon)

Déposé par **Dr BERNARD, Pascal** <pascal.bernard@ens-lyon.fr> le **vendredi 20 mars 2026**

ID de résumé : **8**

Promoter-proximal elements restrict pleiotropic enhancer inputs to achieve tissue specificity

Contenu

Developmental enhancers are regulatory elements that establish precise spatio-temporal patterns of gene expression, yet how they selectively regulate one gene over its neighbors remains unclear. Current hypotheses suggest that such specificity arises from the 3D organization of the genome or from the sequence of the core promoter. Here, we provide evidence that the core promoter acts in concert with sequences directly upstream to it to provide such specificity.

To reach this conclusion, we first dissected the activity of the E3 enhancer of twist in Drosophila melanogaster. Although E3 was previously characterized as an embryonic mesodermal enhancer, our reporter assays revealed its surprisingly complex activity profile. E3 is active in tissues and developmental stages where twist is not expressed, including in non-mesodermal tissues derived from other germ layers, indicating that E3 is a pleiotropic enhancer. We further discovered that E3 drives the expression of at least three more unrelated (non-paralogous or not in the same pathway) genes, each in a different spatial and temporal context.

While E3 drives a broad and complex expression pattern, each of its target genes is only expressed in a particular spatio-temporal window. How is this achieved? We showed that these differences cannot be due to context-dependent chromatin looping or selective promoter accessibility. Instead, they arise from the action of each gene's core promoter and promoter-proximal sequences. These sequences act as "gatekeepers"to restrict enhancer input into precise tissue- and stage-specific transcription, thus functioning as active interpreters rather than passive recipients of enhancer signals. We propose that promoter-proximal gatekeepers belong to an emerging class of non-canonical regulatory elements that provide a critical but under-appreciated layer of regulatory specificity within complex gene expression programs.

Auteur: GHAVI-HELM, Yad (CNRS)

Orateur: GHAVI-HELM, Yad (CNRS)

Déposé par **GHAVI-HELM, Yad** <yad.ghavi-helm@ens-lyon.fr> le **lundi 16 mars 2026**

ID de résumé : **4**

Expliquer les dépendances entre tracks génomiques grâce à l'IA

Contenu

Les modèles d'apprentissage profond en génomique ont fortement progressé : à partir de la séquence d'ADN, ils prédisent des cartes d'activité chromatinienne (marques d'histones, accessibilité) et l'expression les gènes. Reste toutefois une question centrale : comment ces modèles articulent-ils les différentes sorties, et que se passerait-il si l'on modifiait localement un signal ?

Nous présentons Back-Forward Propagation (BFP), une approche d'intervention virtuelle à l'intérieur du réseau. Concrètement, BFP applique au niveau d'un locus une perturbation contrôlée d'une représentation interne afin d'augmenter ou diminuer un signal épigénétique ciblé, puis propage cette modification à travers le modèle pour mesurer les réponses coordonnées sur l'ensemble des sorties. Cette procédure permet de caractériser où et comment l'effet se diffuse : demeure-t-il local, s'étend-il à des régions voisines, couple-t-il d'autres marques ou l'expression de gènes ?

Avec BFP, nous retrouvons des principes établis (p. ex. l'antagonisme entre marques activatrices et répressives), nous rejouons in silico des perturbations expérimentales publiées (répression d'enhancer, déplétion de CTCF) et nous quantifions des effets à distance cohérents avec l'organisation 3D du génome. BFP n'informe pas sur une causalité biochimique stricte ; il rend explicite la logique interne apprise par les modèles séquence-vers-fonction et fournit des hypothèses testables pour explorer les dépendances régulatrices au laboratoire.

Auteur: Prof. MOZZICONACCI, julien (string)

Co-auteur: M. OPSOMER, Thomas

Orateur: Prof. MOZZICONACCI, julien (string)

Déposé par **Prof. MOZZICONACCI, julien** <julien.mozziconacci@mnhn.fr> le **mercredi 11 mars 2026**

ID de résumé : **7**

Interrogating the functional roles of H3K9me3 at pericentromeres

Contenu

Centromeric regions of eukaryotic chromosomes contain large arrays of tandemly repeated DNA sequences, known as satellite DNA. In mouse NIH3T3 cells, pericentromeric satellite sequences from distinct chromosomes cluster into chromocenters. These structures consist of constitutive heterochromatin enriched in specific epigenetic modifications, including H3K9me3, and they recruit HP1 proteins—both of which are known to be required for chromocenter formation. However, their precise roles and their interplay with other heterochromatin domains remain unclear. To dissect their roles, we engineered a TALE-KDM4D tool that specifically demethylates H3K9me3 at major pericentromeric satellites. Using 3D imaging, we found that local loss of H3K9me3 reduces HP1 recruitment at chromocenters but leaves their overall 3D architecture largely intact, indicating that additional factors contribute to chromocenter formation. Moreover, by combining 3D microscopy with ChIP-seq, we show that removing H3K9me3 from pericentromeres triggers a redistribution of the mark: methyltransferases are redirected to other genomic regions, leading to increased H3K9me3 at sites already enriched, coinciding with the emergence of compact, heterochromatin-rich domains outside chromocenters. Hi-C analysis further reveals that this redistribution is accompanied by a reorganization of interactions between heterochromatin domains. Together, these results reveal a novel crosstalk between distinct heterochromatin regions and challenge the notion that H3K9me3/HP1 alone is sufficient to drive chromocenter formation.

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Capturing motifs of folding from single-cell chromatin tracing data using unsupervised topic modelling

Contenu

Over the past decade, imaging-based chromatin tracing has emerged as a reliable method to simultaneously visualise the spatial organisation of chromatin and transcription of specific genomic loci at single-cell resolution. However, extracting interpretable structural patterns from these datasets remains a major challenge. To address this, our lab recently developed *3DTopic*, a topic modelling framework that identifies recurrent chromatin folding motifs (CFMs) across single alleles in an unsupervised manner (Messina *et al.*, 2024, bioRxiv preprint). Here, we introduce the associated software package, which provides a well-documented and accessible pipeline for the analysis of chromatin tracing data. We then demonstrate the performance of the method on (1) simple *in silico* datasets generated using polymer simulations, and (2) experimental data from Bintu & Chen *et al.*, 2018, where it robustly recovers known structural features. Finally, we highlight the role of loop extrusion in the formation of such features by comparing data from wild-type and RAD21-depleted cells, uncovering distinct shifts in the folding motifs known to be associated with cohesin activity.

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