Research Stage (M2)

Title: Dissecting the impact of natural genetic variation on chromatin conformation and gene regulation
Where: Quantitative regulatory genomics team, LBMC
(http://www.ens-lyon.fr/LBMC/equipes/quantitative-regulatory-genomics)
ENS de Lyon, 46, allée d'Italie, 69364 LYON CEDEX 07, France
When: Beginning of 2021 (flexible)
Duration: 6 months (M2)
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Keywords: Big data, integrative genomics, machine learning, regulation of gene expression, chromosome conformation.

Description of the project:
In the "Quantitative Regulatory Genomics" (QRG) team we are interested in both genetic- and non-genetic influences gene regulation and phenotypes[1-4].
Chromosomes adopt a complex spatial conformation inside the nucleus, which plays an important role in gene regulation[5] and genetic changes in chromatin conformation can underly human genetic diseases[6]. Yet surprisingly very few studies have systematically explored the genetic architecture of chromosome conformation. To what extent natural genetic variation in chromosome conformation contributes to gene regulation and phenotypic variation in evolution and disease is still unknown.

We want to address this and specifically we ask: what is the relative contribution of *-cis* and *-trans* natural genetic variation in chromatin conformation and gene expression?
To answer this question, we have collected data comparing gene expression and chromatin conformation during embryogenesis between two fly lines with about a million of genetic differences. By integrating these data together with available functional genomics data, we aim at understanding how genetic variation impact chromatin conformation and gene expression.

You will learn how to manage, integrate and analyse big gene expression and genomic data using state-of-the-art machine learning tools, to address fundamental biological questions.
A good level of English is absolutely required, such as good computational and statistical skills and scripting skills in a programming language among R, Matlab or Python.

In short, if you have good computational and data analysis skills and you want to crack the secrets of the regulation of gene expression, join the QRG team at the LBMC!

Contact me at Mirko.francesconi@ens-lyon.fr to ask for further information and apply (CV and a motivation letter).

References

1. Francesconi, M. & Lehner, B. The effects of genetic variation on gene expression dynamics during development. *Nature* **505**, 208-211, doi:10.1038/nature12772. Epub 2013 Nov 24. (2013).[1]
2. Perez, M. F., Francesconi, M., Hidalgo-Carcedo, C. & Lehner, B. Maternal age generates phenotypic variation in Caenorhabditis elegans. *Nature* **552**, 106-109, doi:10.1038/nature25012 (2017).
3. Francesconi, M. *et al.* Single cell RNA-seq identifies the origins of heterogeneity in efficient cell transdifferentiation and reprogramming eLife 8:e41627 (2019).
4. Francesconi, M. & Lehner, B. Reconstructing and analysing cellular states, space and time from gene expression profiles of many cells and single cells. *Mol Biosyst* **11**, 2690-2698, doi:10.1039/c5mb00339c (2015).
5. Schoenfelder S. & Fraser P., Long-range enhancer–promoter contacts in gene expression control, Nature Reviews Genetics 20, 437–455 (2019)
6. Lodewijk Krijger PH & de Laat W., Regulation of disease-associated gene expression in the 3D genome, Nature Reviews Molecular Cell Biology 17, 771–782 (2016).