Why are single cell data so special? The bursty nature of gene expression when seen at the single cell level.

Olivier Gandrillon

Let’s make a thought experiment.

Let us imagine the erythroid differentiation process:

During erythropoiesis, (mean) beta-globin gene expression increases.

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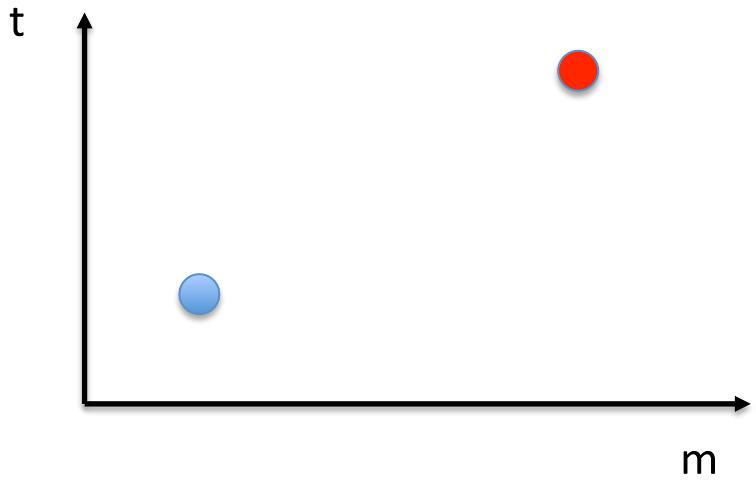
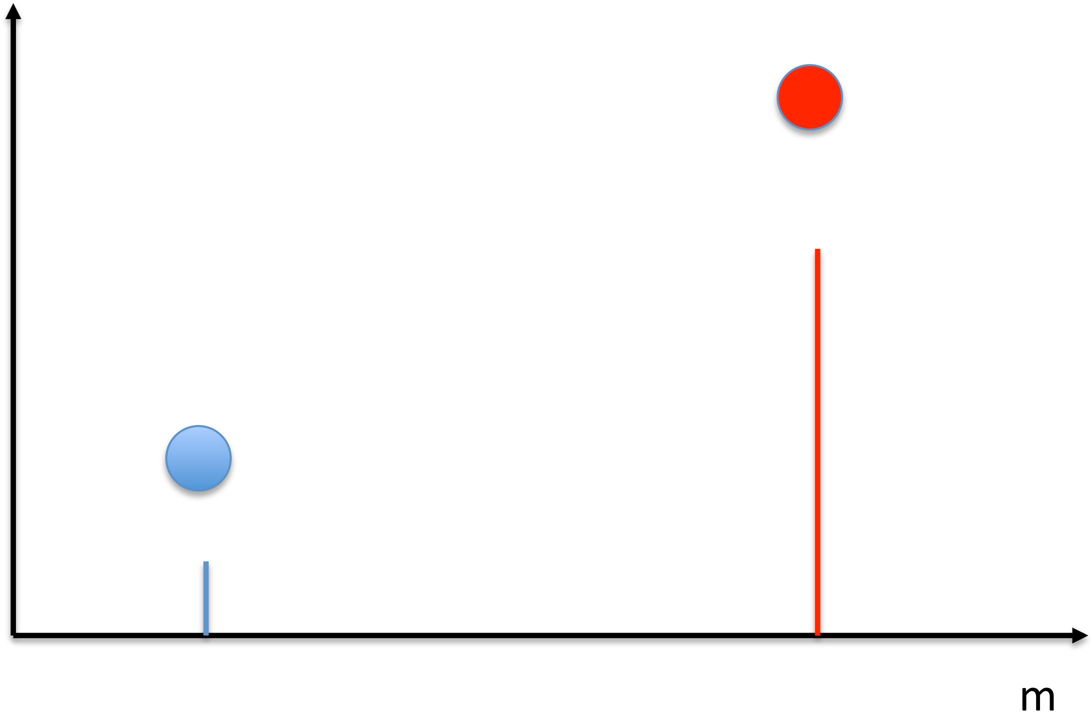
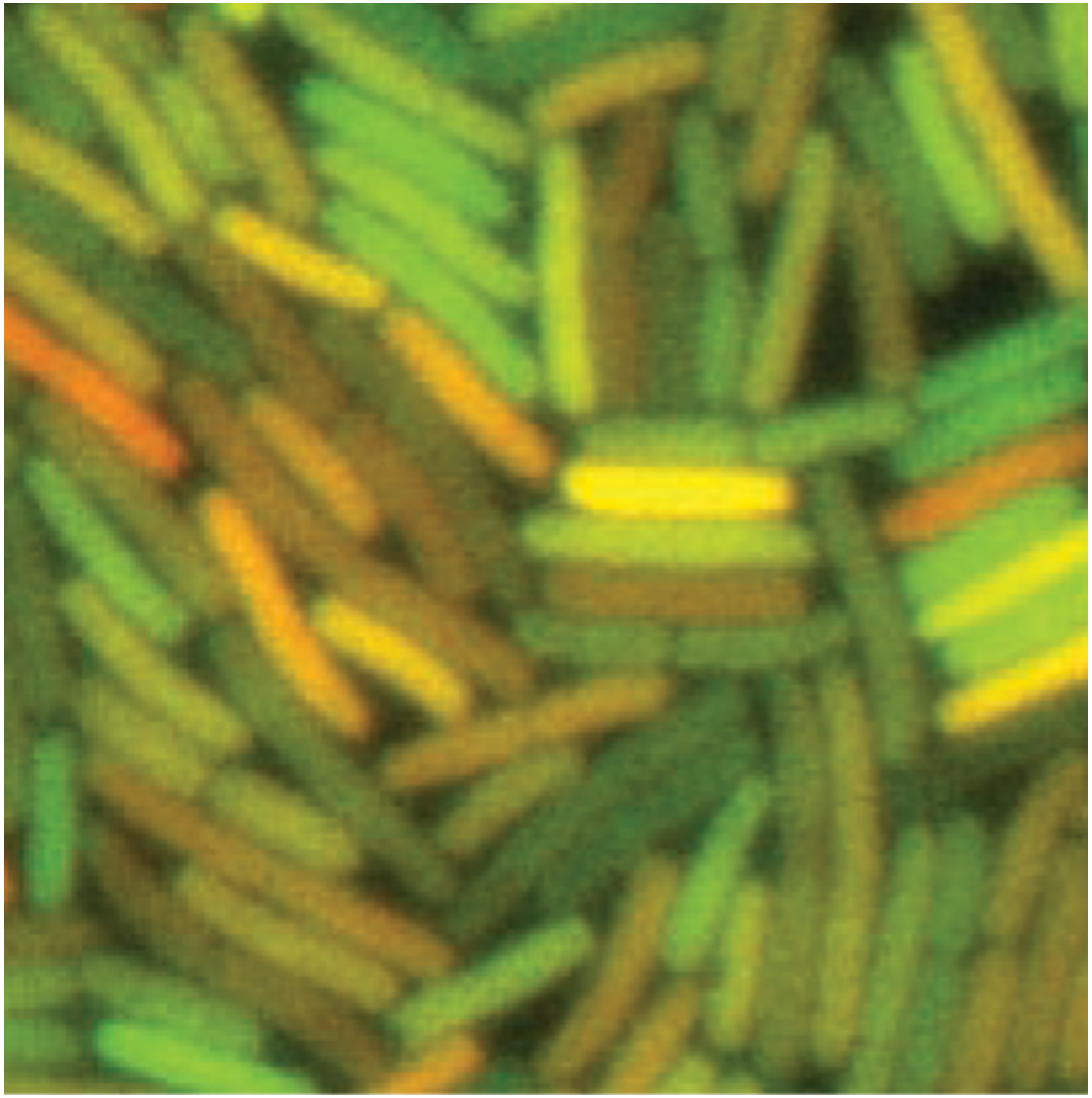


Averaged upon 10 million cells



Averaged upon 10 million cells

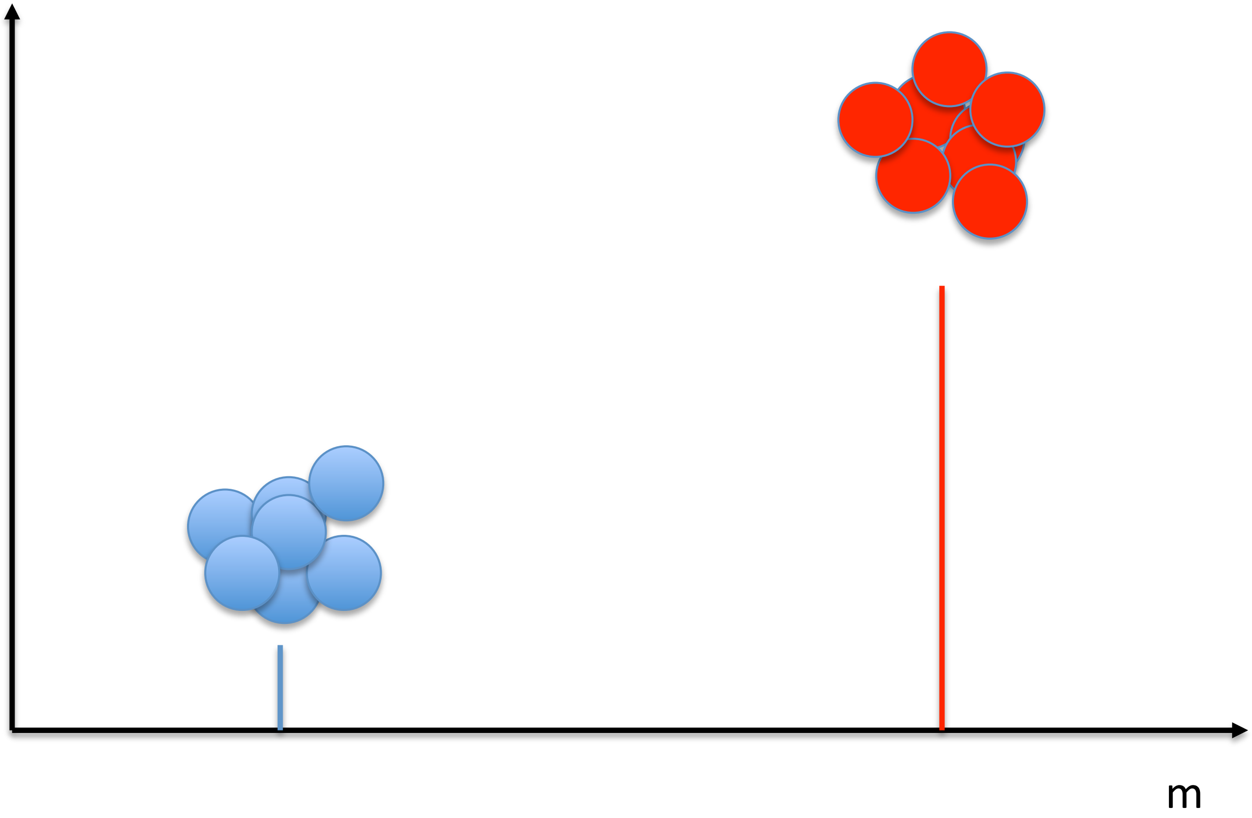


Stochastic Gene
Expression in a
Single Cell

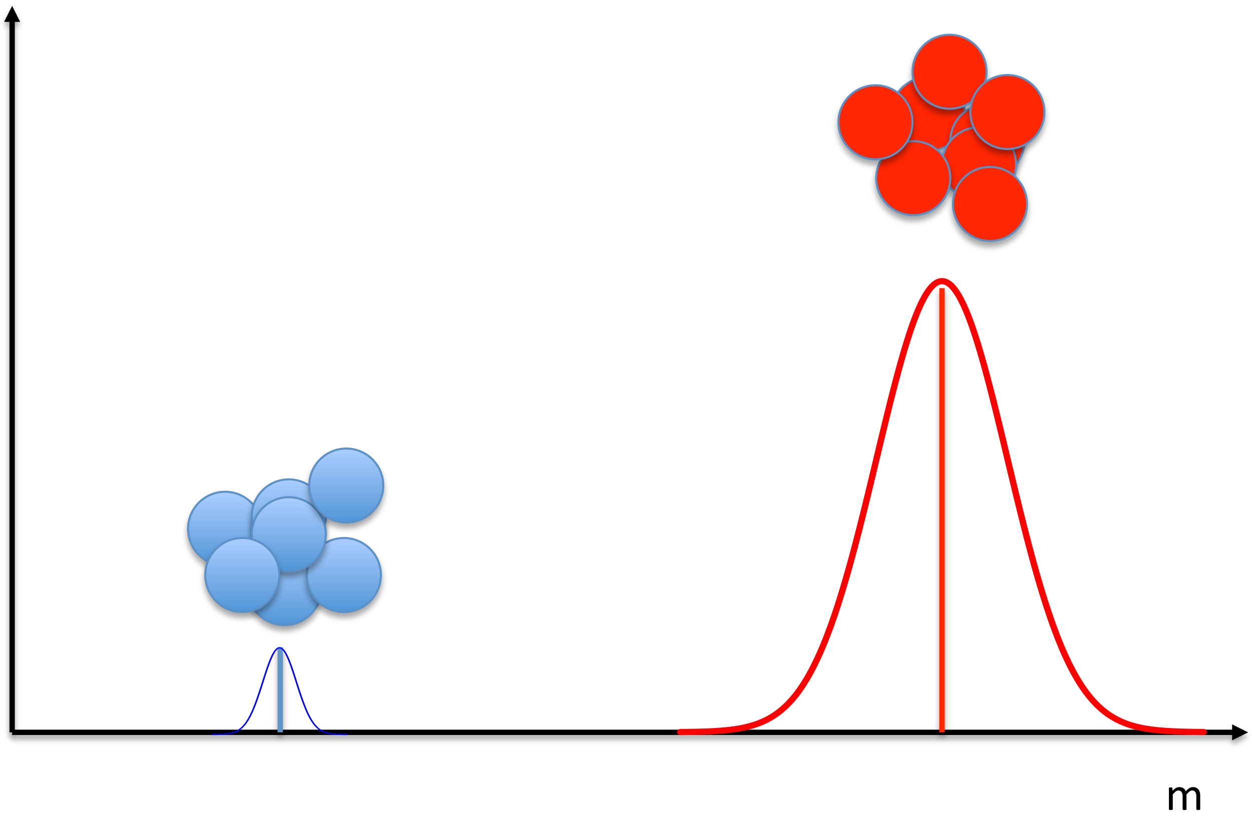
Michael B.Elowitz,
Arnold J. Levine,
Eric D. Siggia and
Peter S. Swain

SCIENCE (2002)
VOL 297, pp
1183-1186

Let’s assume we are now looking at single cells, and assume some cell-to-cell variation



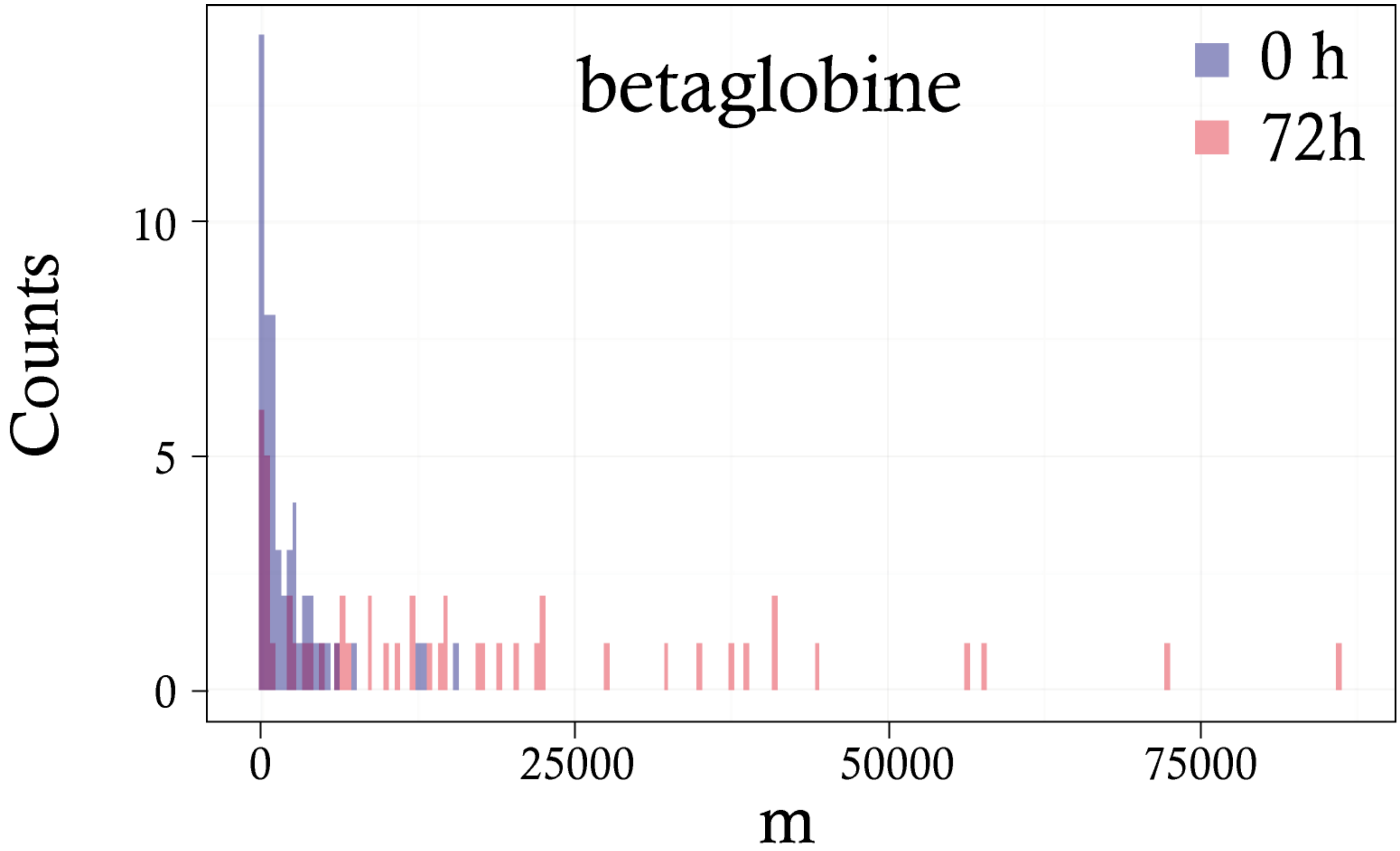
Let’s assume we are now looking at single cells, and assume some cell-to-cell variation



Let’s assume we are now looking at single cells, and assume some cell-to-cell variation

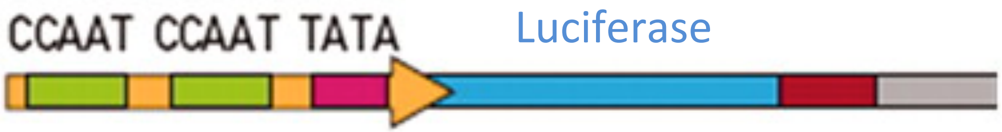
Is this true?

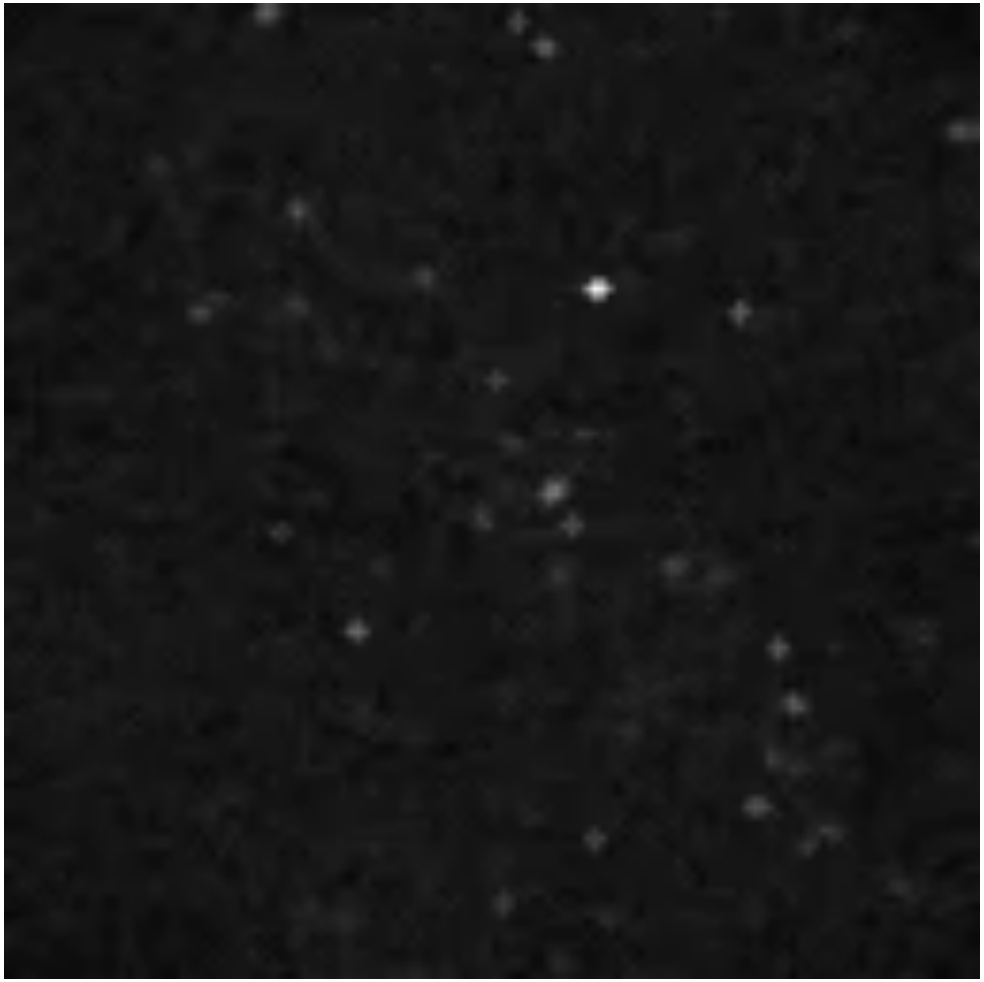
Not really…



Why isn’t it true?

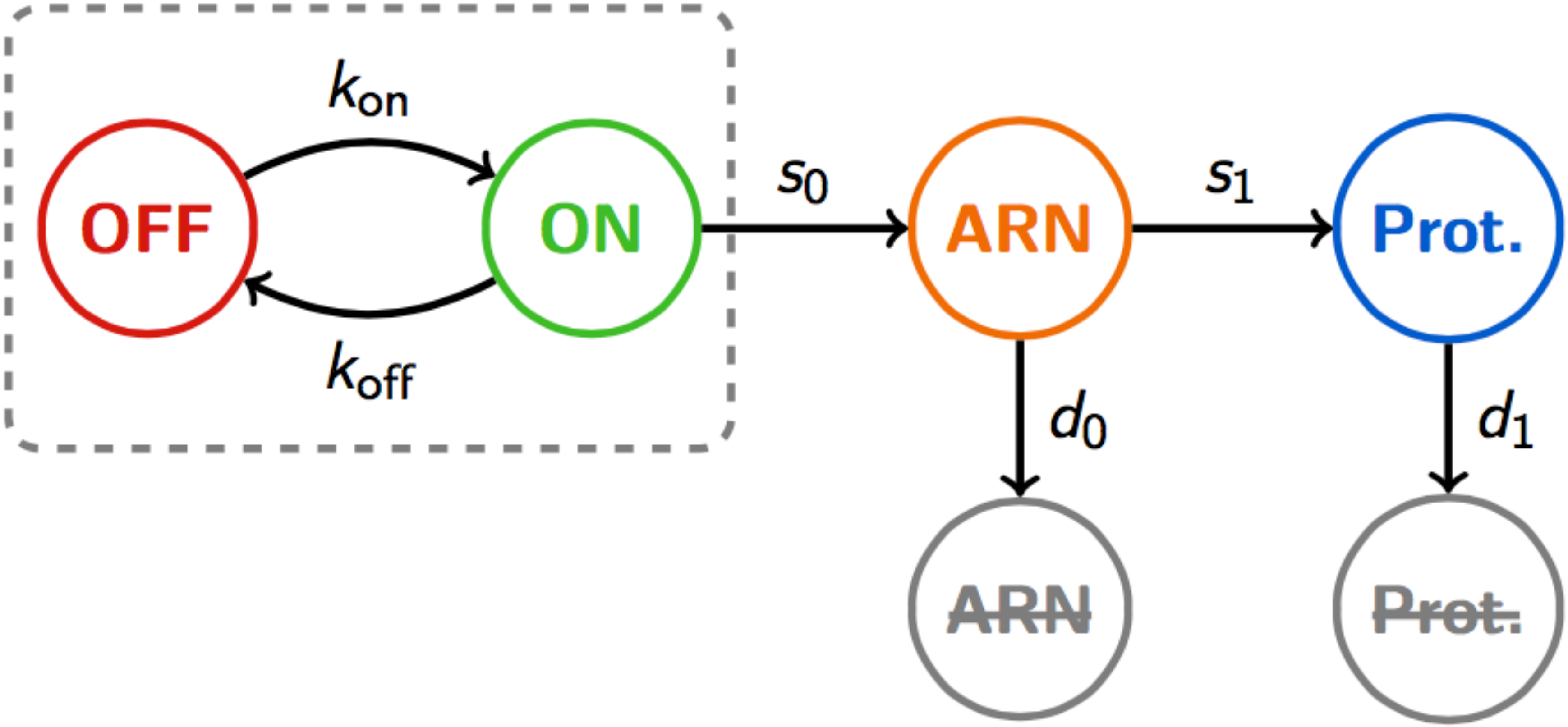
Gene expression is a bursty process



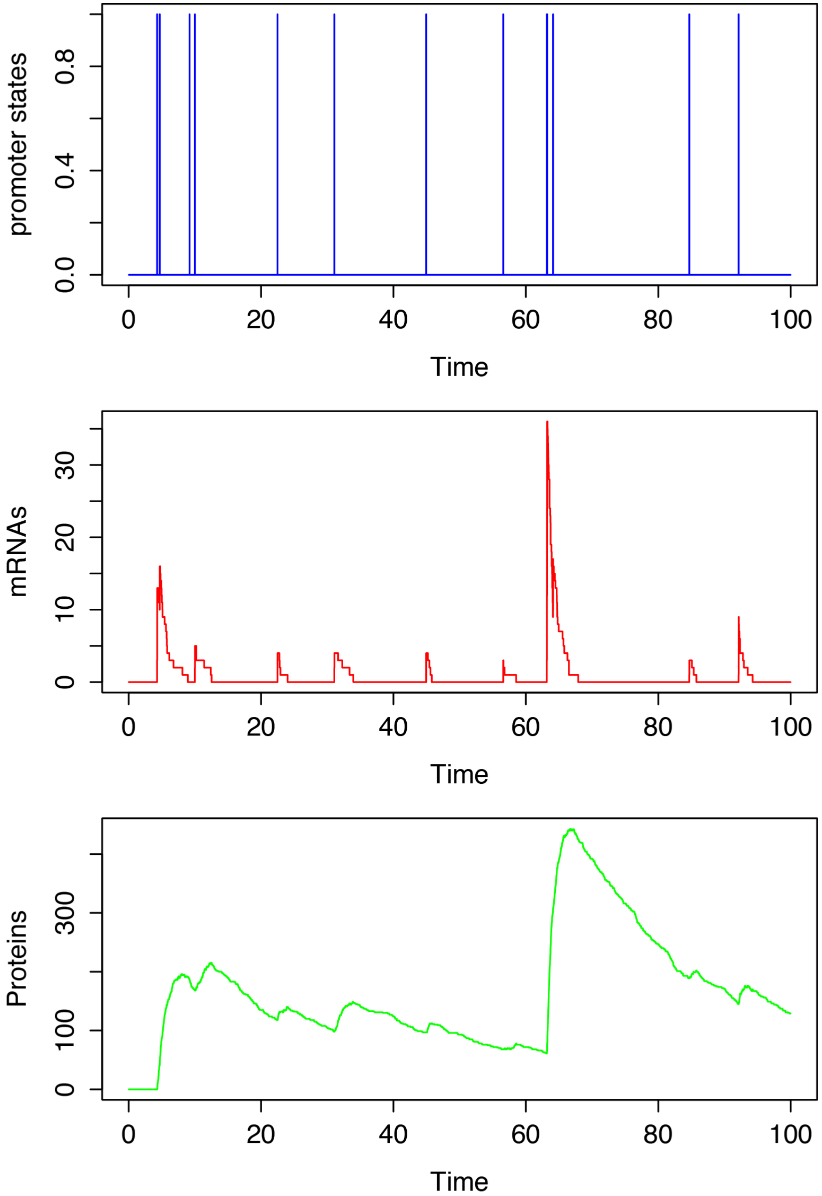


Suter et al.
(2011). Science
332, pp. 472-474
(2 days movie)

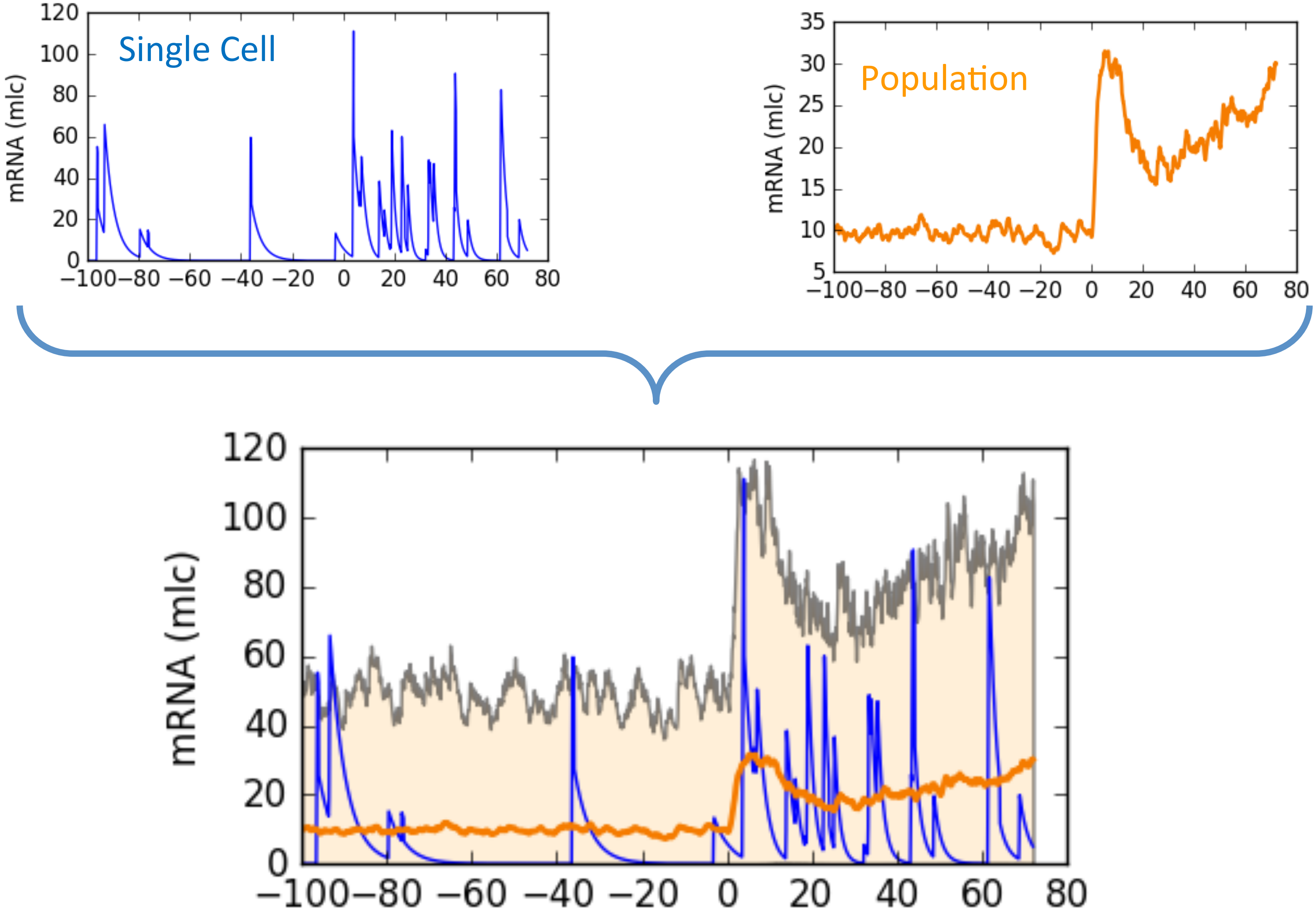
The 2-state model



A trajectory of the model



In another terms:

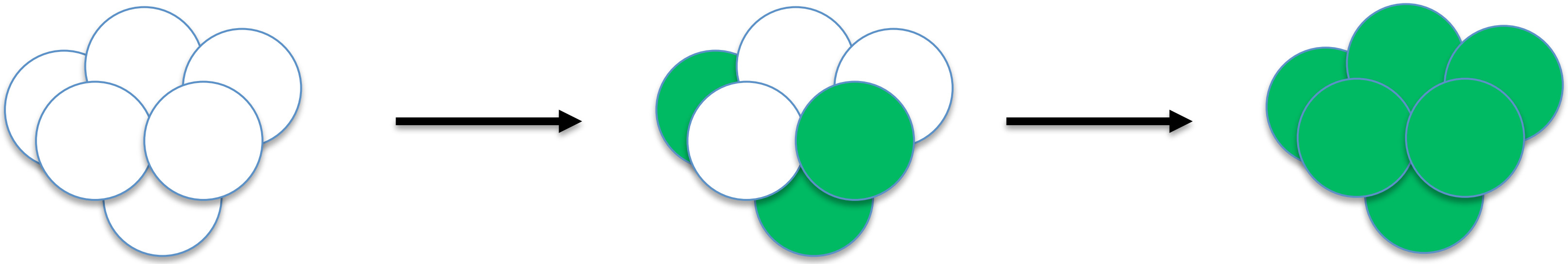

Single Cell
mRNA (mlc)
120
100
80
60
40
20
0
−100
−80
−60
−40
−20
0
20
40
60
80
Population
mRNA (mlc)
35
30
25
20
15
10
5
−100
−80
−60
−40
−20
0
20
40
60
80
mRNA (mlc)
120
100
80
60
40
20
0
−100
−80
−60
−40
−20
0
20
40
60
80

OK, but then why bother?

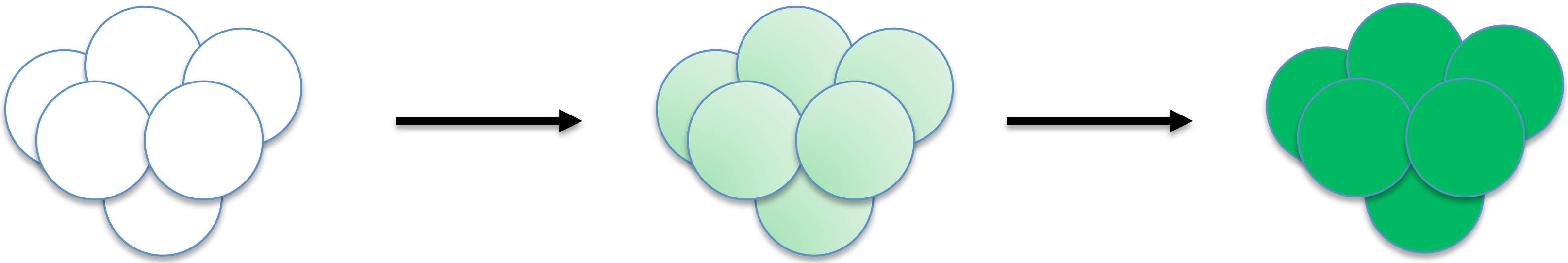
Questions linked to:

- The cellular composition of a tissue;
- The presence of small populations of cells in the middle of large amounts of other cells;
- The question as to whether a global increase is digital or gradual;
- HCA;
- GRN inference
- etc…

digital



gradual



Bottom line: if you want to make a reasoning at the cellular level, it is strongly advisable to acquire data at the single-cell level.

The program:

14h30 – 15h00: Arnaud Bonnaffoux (LBMC): A pipe-line for scRTqPCR analysis.

15h00 – 15h30: Coffee break

15h30 – 16h00: Laurent Modolo (LBMC): Analysing single cell RNAseq

16h00 - 16h30: Helena Todorov (CIRI; DAMBI): Trajectory inference from single cell data