

Differential expression analysis in EndoC- β H1 beta cells after IFN- α treatment

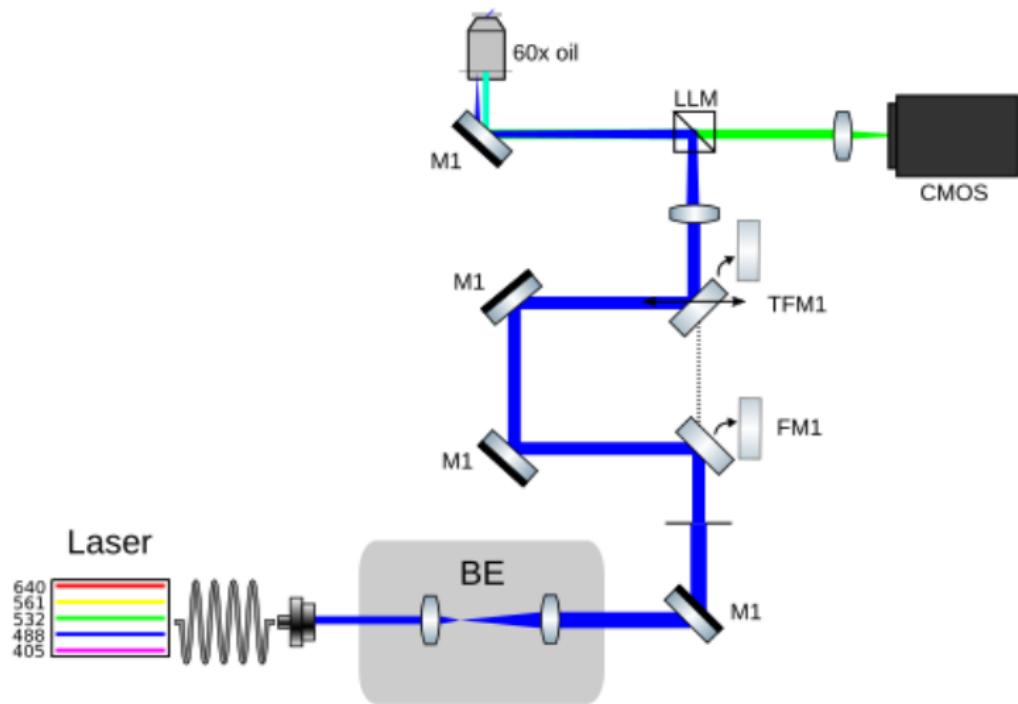
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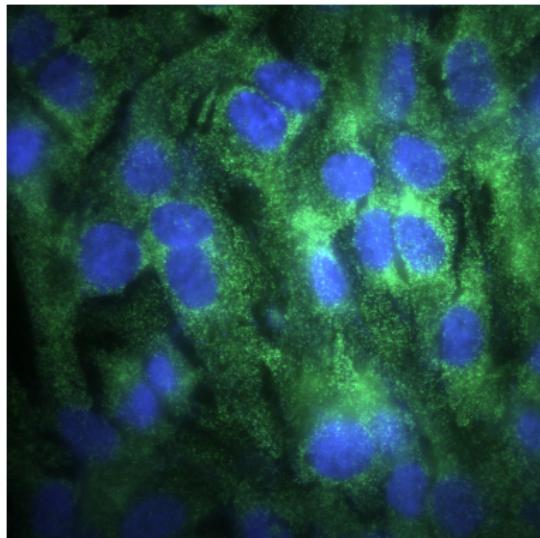
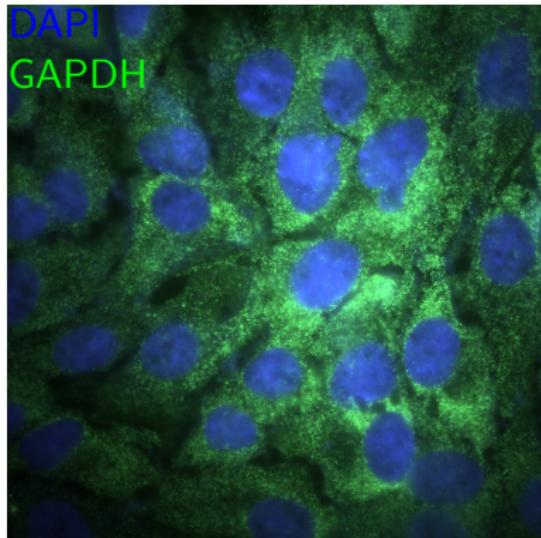
Overview

1. Hybrid microscope setup
2. Motivation for studying transcriptional bursting
3. Gene selection

Widefield-HILO hybrid microscope schematic



Example images



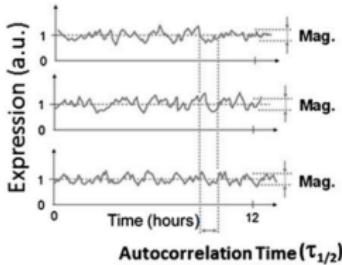
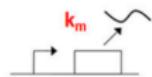
U2OS cells stained for DAPI and human GAPDH (housekeeping gene) using in-situ hybridization

100ms and 750ms exposure respectively

Gene expression is stochastic and non-constitutive

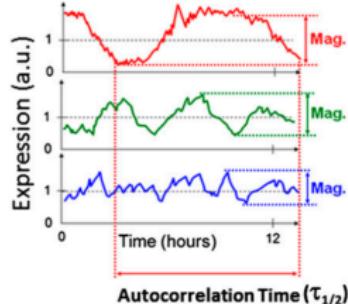
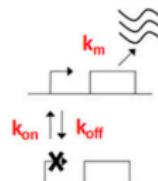
A

Constitutive gene expression



B

Episodic 'bursty' gene expression



Single-state models

- ▶ RNAs are 'born' at a fixed rate
- ▶ RNA counts are Poisson

Multi-state models

- ▶ Promoter can be in multiple states
- ▶ RNA counts are not Poissonian

Single-state models tend to underestimate variance in RNA counts

EndoC- β H1 treated with IFN- α

Studies of IFN- α induced expression in cultured cells often lack:

- ▶ Single cell resolution of RNA counts and locations
- ▶ Sub-hour time resolution of transcript counts and locations
- ▶ Rigorous statistical models of gene expression

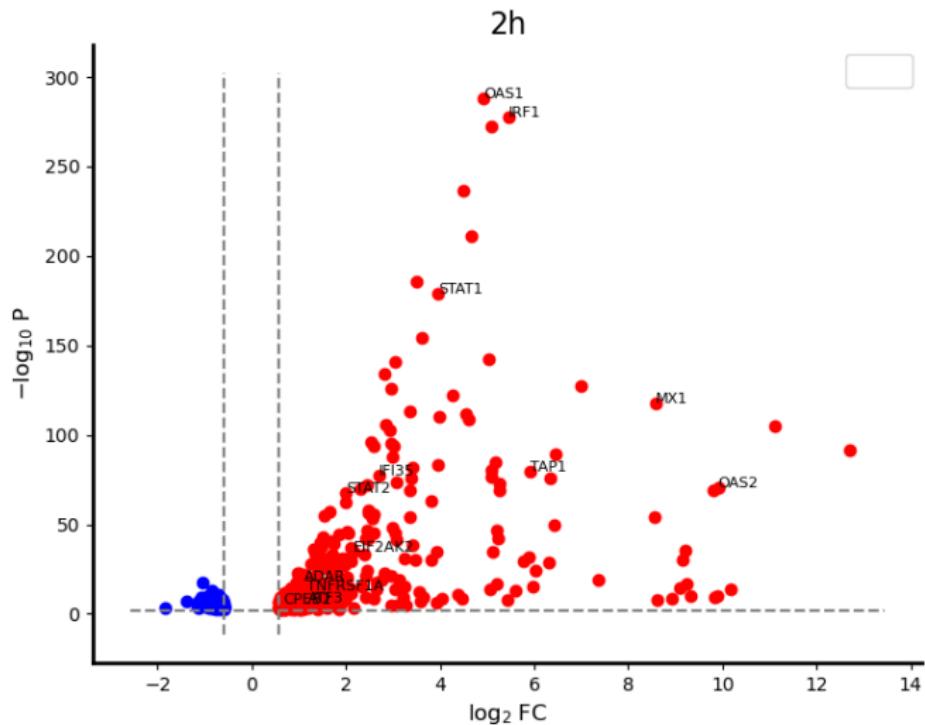
Starting point:

Colli, M.L., et al. *An integrated multi-omics approach identifies the landscape of interferon- α -mediated responses of human pancreatic beta cells.* Nat Commun 11, 2584 (2020)

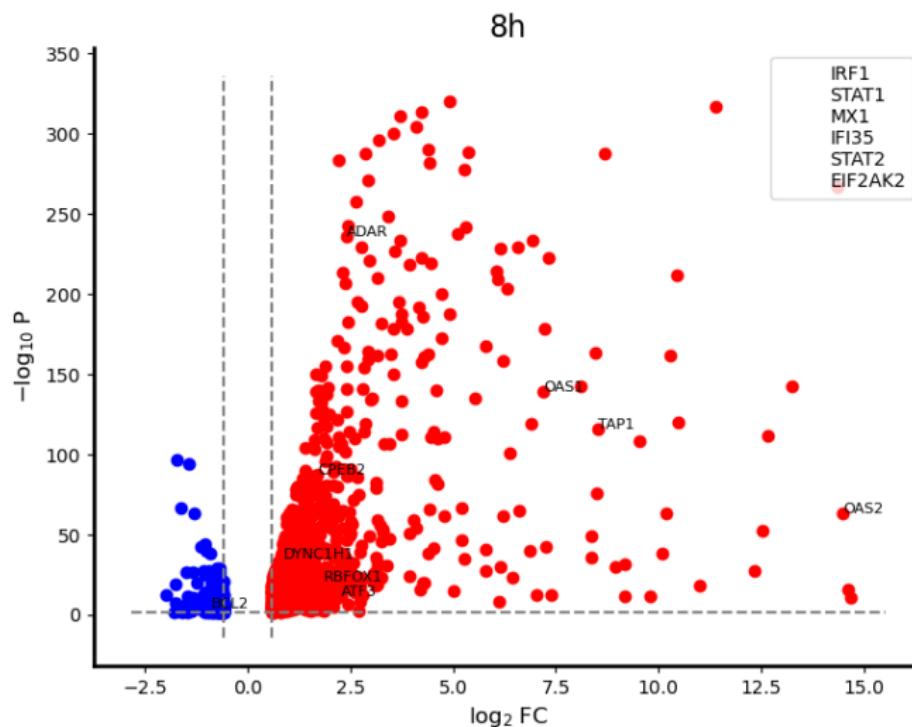
Identifying genes: EndoC- β H1 treated with IFN- α

	2h	8h	24h
OAS1	4.93168069	7.191862952	7.092263724
IRF1	5.46178697	4.32295656	3.205810071
STAT1	3.94861523	5.162369756	4.590065144
MX1	8.57733885	12.02247715	11.59157855
TAP1	5.9090454	8.531763128	7.948687457
IFI35	2.71568439	6.035546104	5.436688198
OAS2	9.9090287	14.49331111	14.26822957
STAT2	1.99879019	3.960535201	2.82738251
EIF2AK2	2.17343926	1.11018016	2.795287863
ADAR	1.11018016	2.4180559	2.247901832
TNFRSF1A	1.16892149	x	x
ATF3	1.20153286	2.27198949	2.543452183
CPEB2	0.6736743	1.69981822	1.219628141
DYNC1H1	x	0.8724557679	x
RBFOX1	x	1.844265408	1.2661383
BCL2	x	-0.870219720	x

Identifying genes: EndoC- β H1 treated with IFN- α at 2h



Identifying genes: EndoC- β H1 treated with IFN- α : 8h



Identifying genes: EndoC- β H1 treated with IFN- α : 24h

