Reconstructing and visualising cell lineages

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UAB Seminars Recerca

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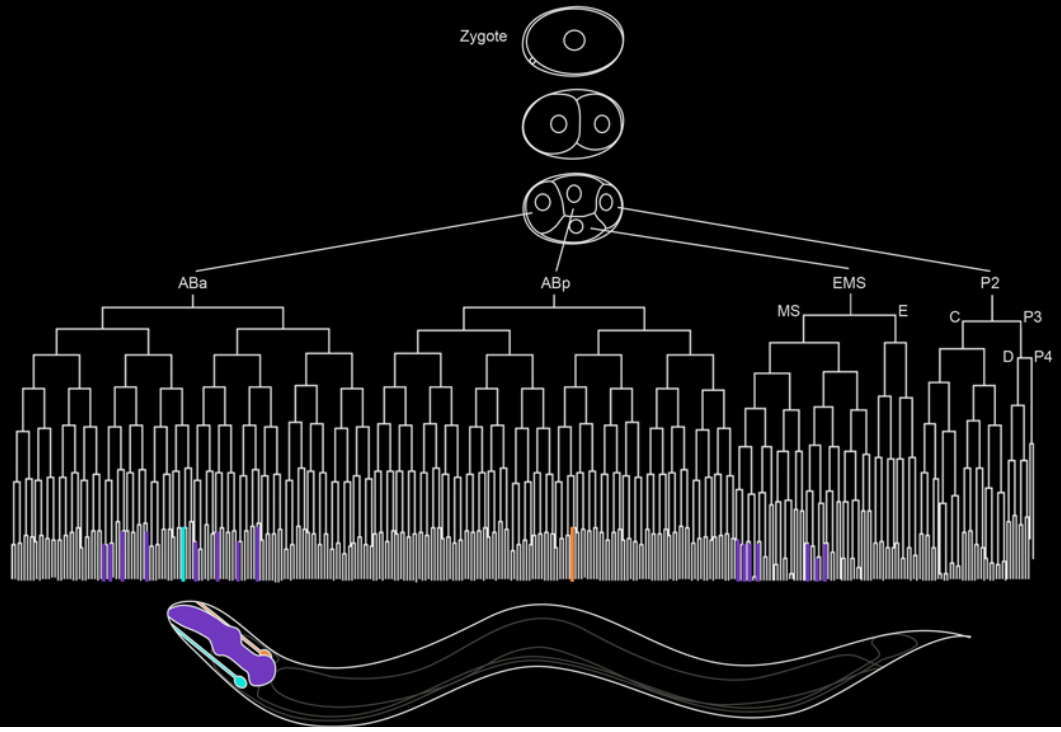
Cell lineage

Key concept in Dev. Biol.

- Developmental history of a cell traced back to the zygote
- Poorly known in most animals



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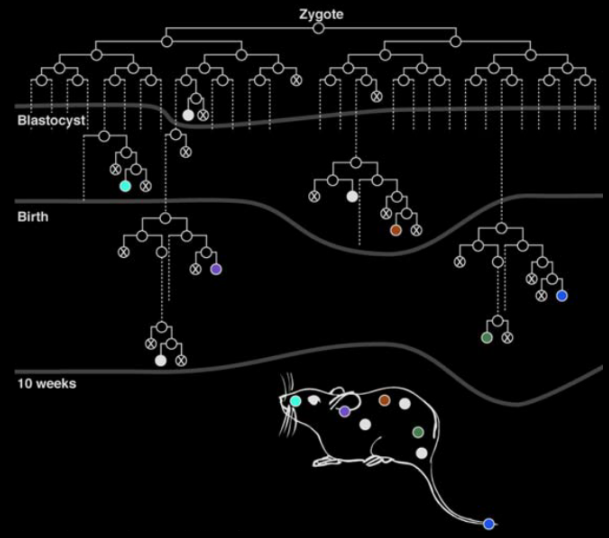
How can it be determined?

- Direct observation
- Labelling techniques
- **Somatic** mutations

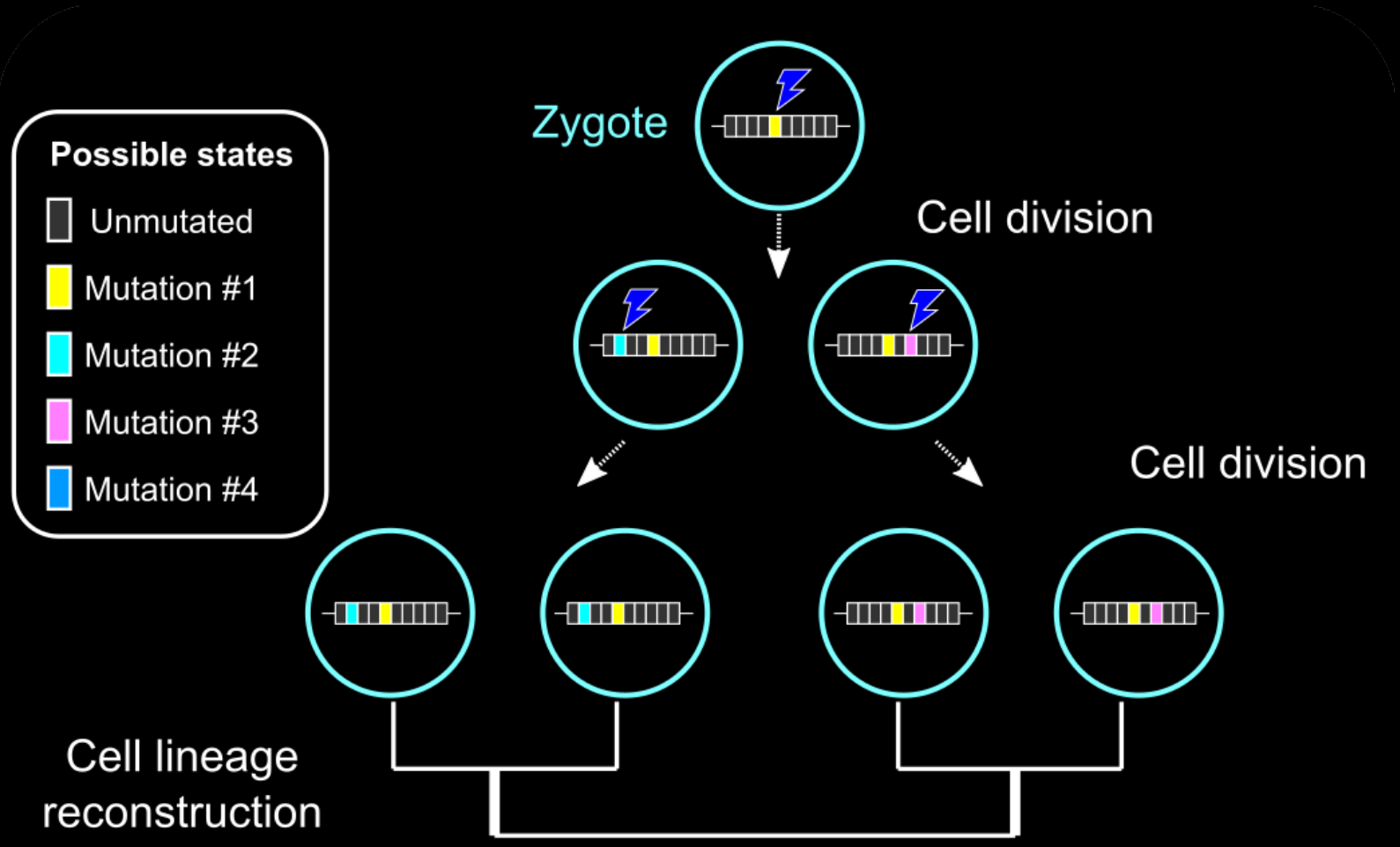


Wasserstrom et al., 2008

GREAT IDEA!!

CRISPR-Cas9 mutations can be used as lineage markers!

- Irreversible mutations accumulate in Development



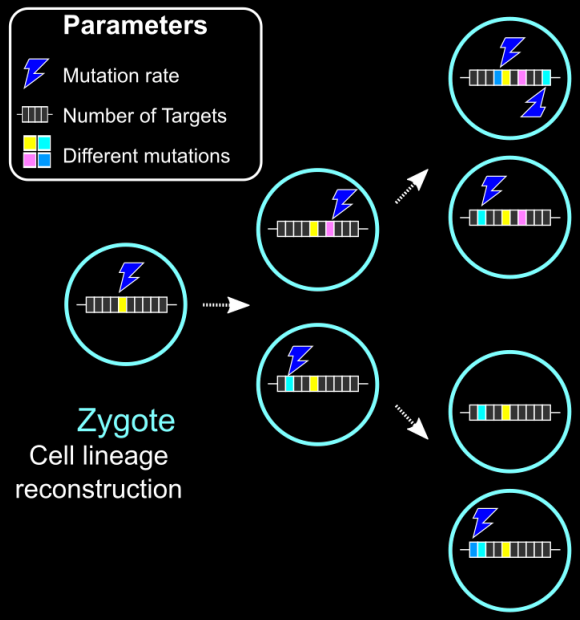
Several published recorders in past 2 years

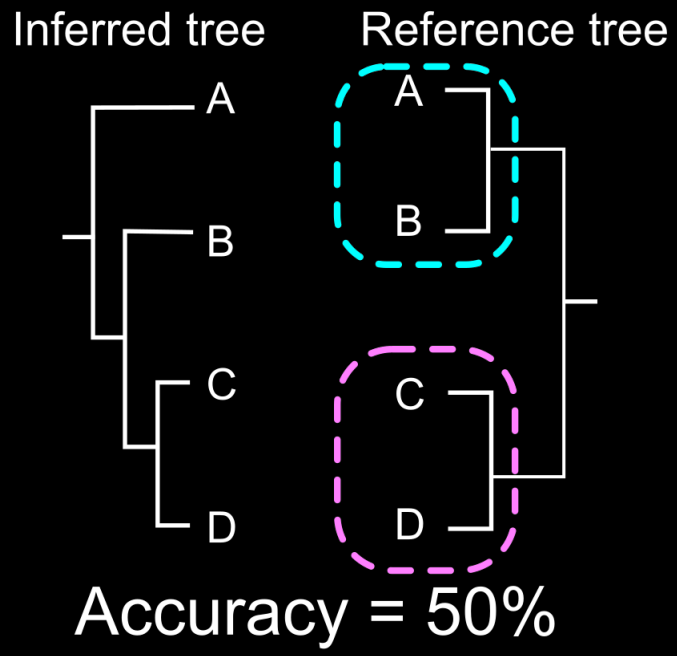
But... HOW ACCURATE ARE THESE TREES?

Bring on the simulations!

Aim:

A lineage of 16 cell divisions (65K cells $\simeq$ *Drosophila* larva)





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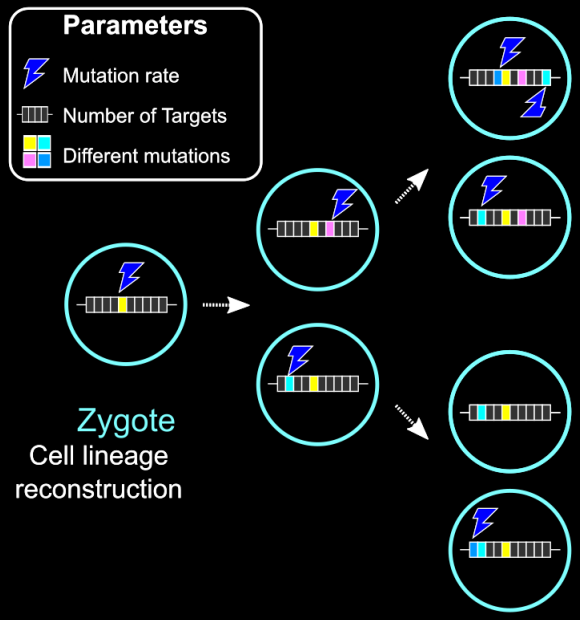
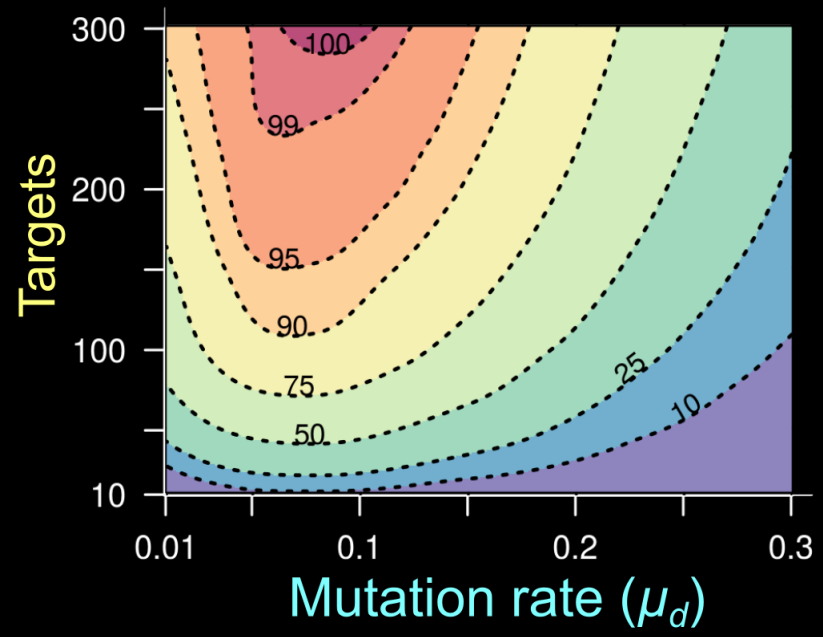
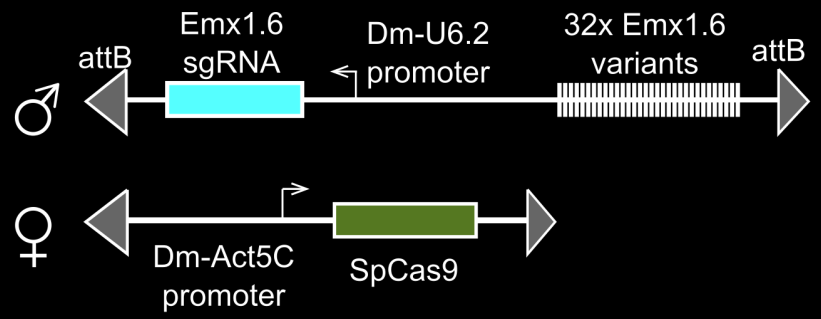


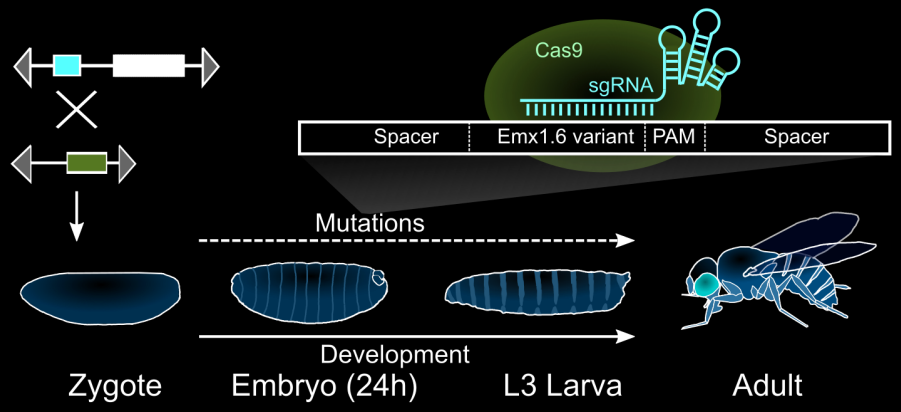


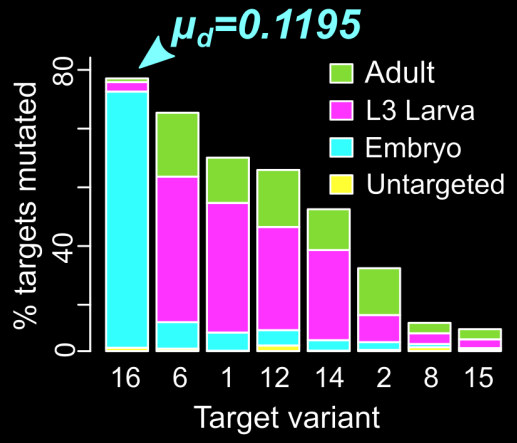
Fine-tuning the mutation rate

32 variants of *emx1.6* (Hsu et al. 2013)
Single-double mismatches; alternative PAM sequence



Marco Grillo & Michalis Averof
(IGFL, Lyon)

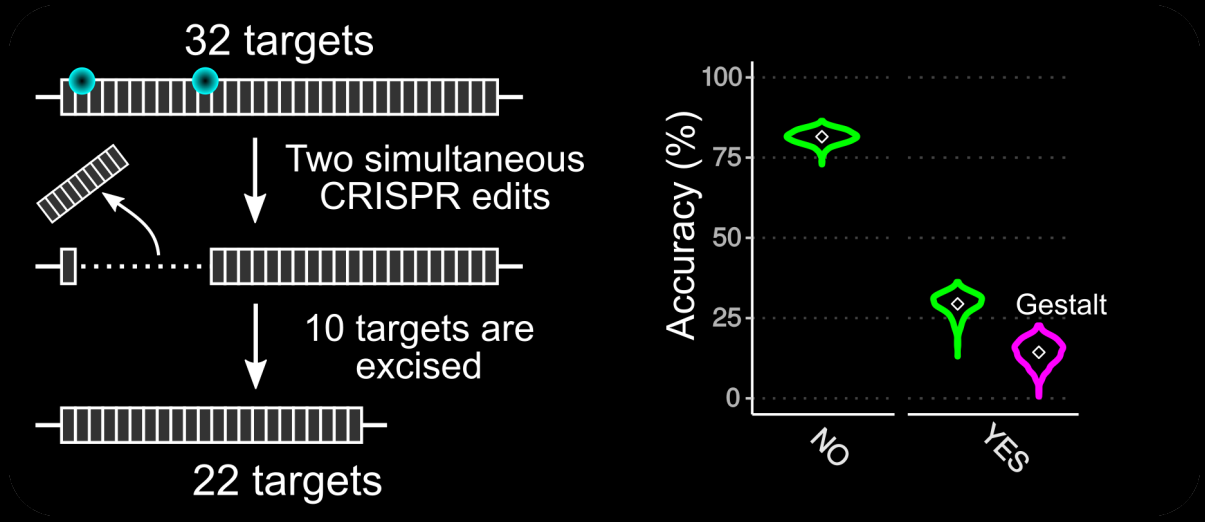




Salvador-Martínez*, Grillo* et al. *eLife* 2019

Test recorder under different scenarios!

Dropouts



Salvador-Martínez*, Grillo* et al. *eLife* 2019

Conclusions

- CRISPR recorders are an exciting technology
- Lots of room for improvement
- Simulations are useful!

If you want to know more..

Salvador-Martínez, I., Grillo, M., Averof, M., & Telford, M. J. **Is it possible to reconstruct an accurate cell lineage using CRISPR recorders?** (2019) *eLife*. https://doi.org/10.7554/eLife.40292

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