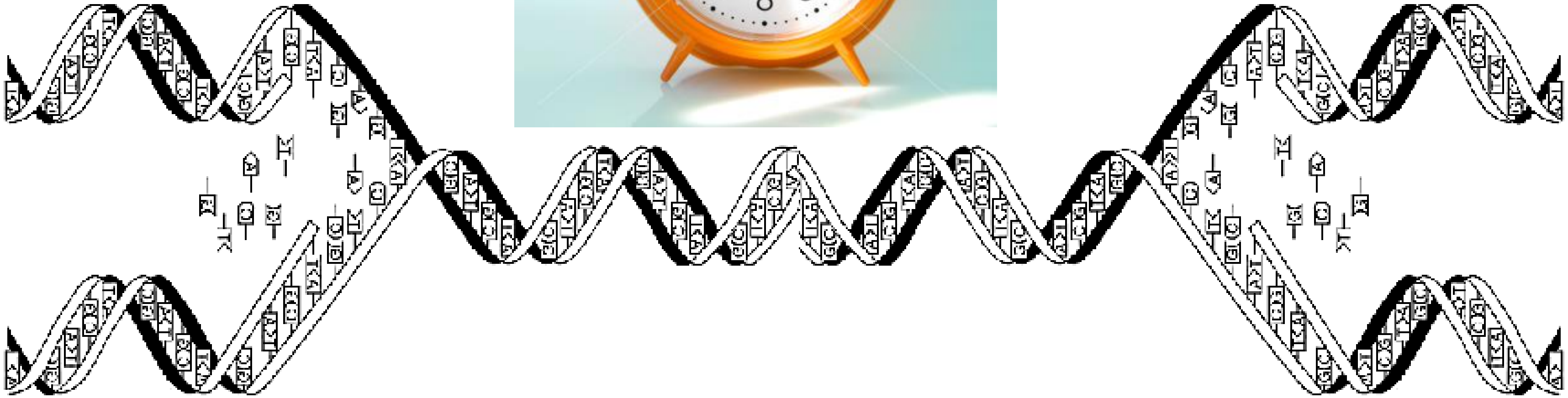
How *Xenopus* embryos Complete DNA replication reliably: Solution to the Random-Completion Problem



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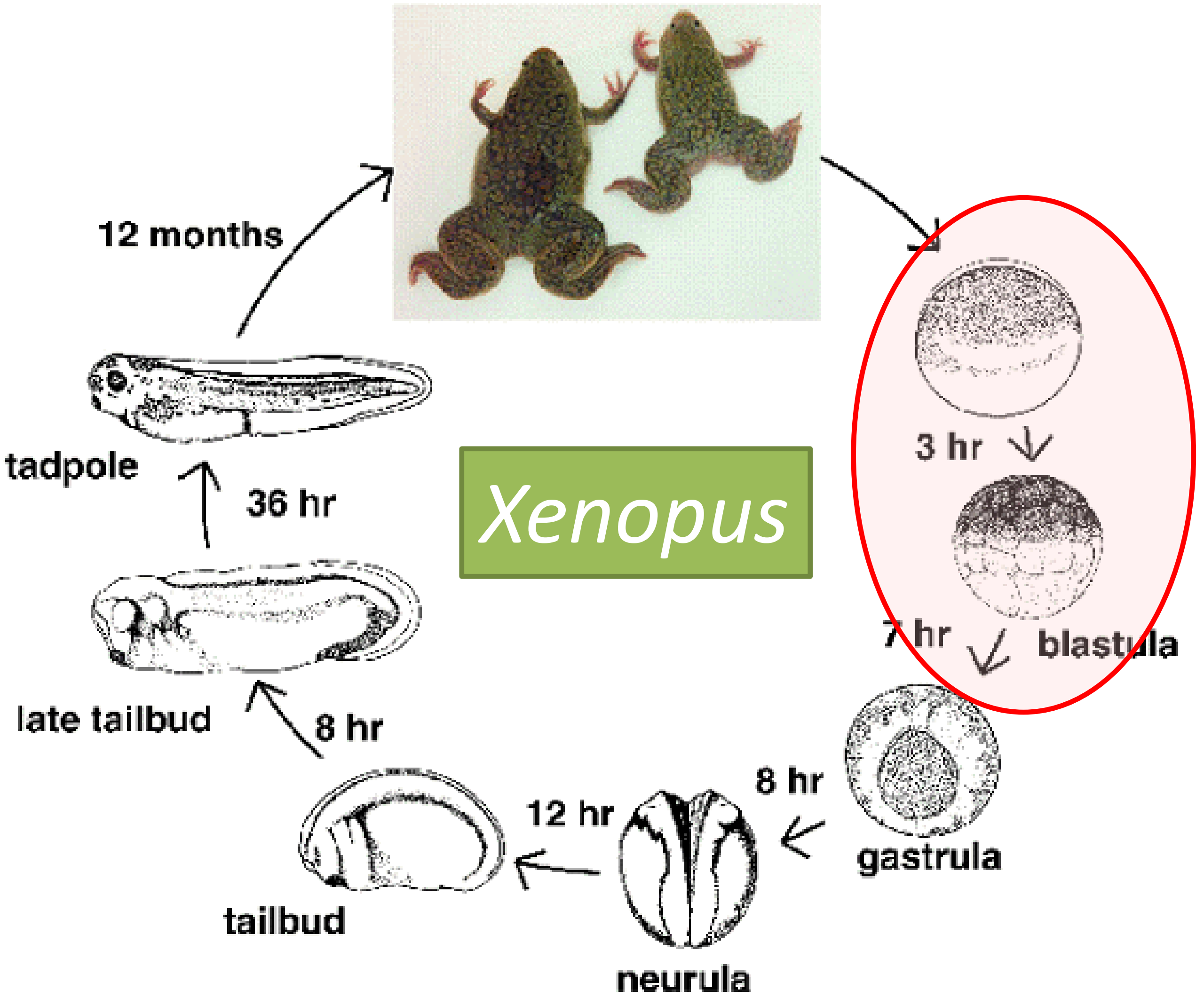
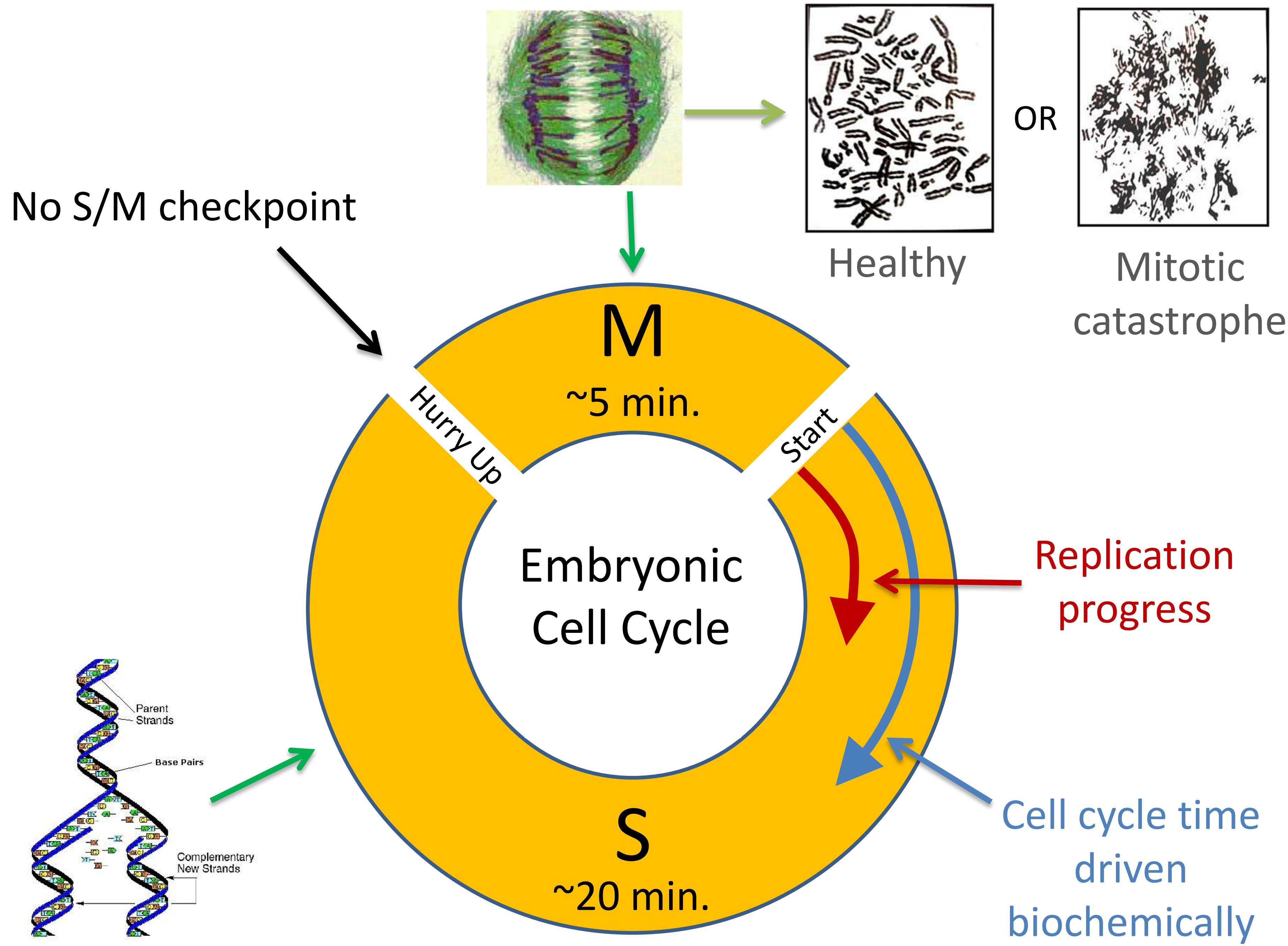
Outline

- DNA replication in frog embryos
- Our model
- Results



http://embryology.med.unsw.edu.au/OtherEmb/frog1.htm



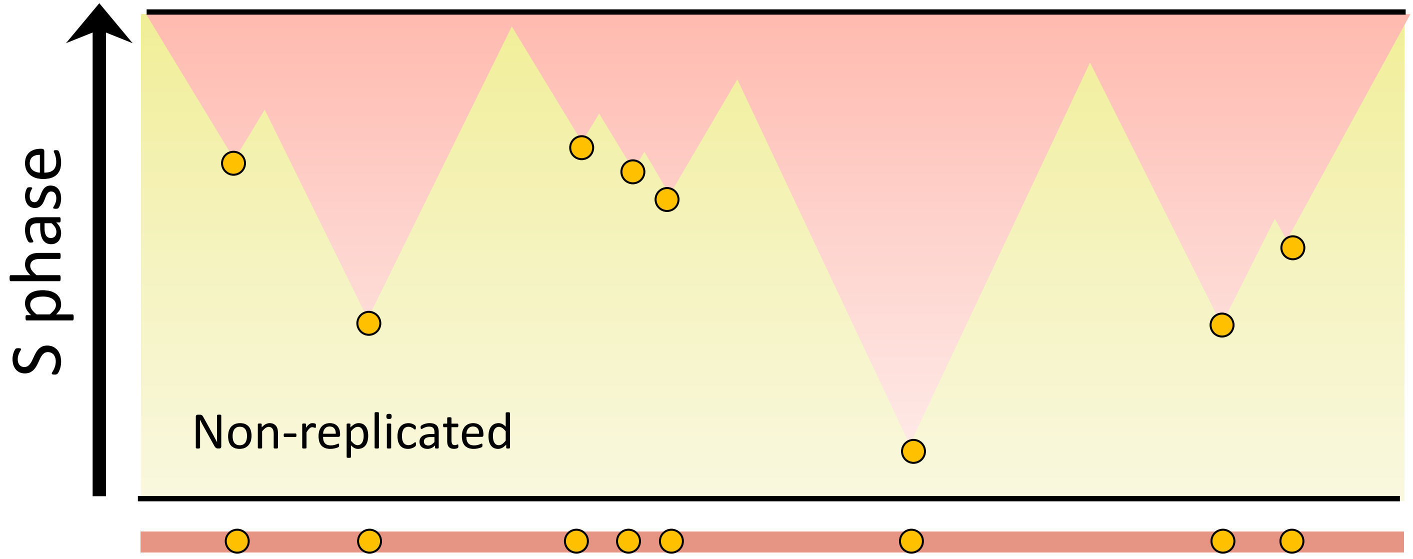
No S/M checkpoint
OR
Healthy
Mitotic catastrophe
M
~5 min.
Hurry Up
Start
Embryonic Cell Cycle
Replication progress
Parent Strands
Base Pairs
Complementary New Strands
S
~20 min.
Cell cycle time driven biochemically

The Random Completion Problem

- Initiations are stochastic
- Typical replication time ≈ 20 min.
- Dead if > 25 min.
- Occurs only 1 in 250 times!
- How is this possible?

Our Model

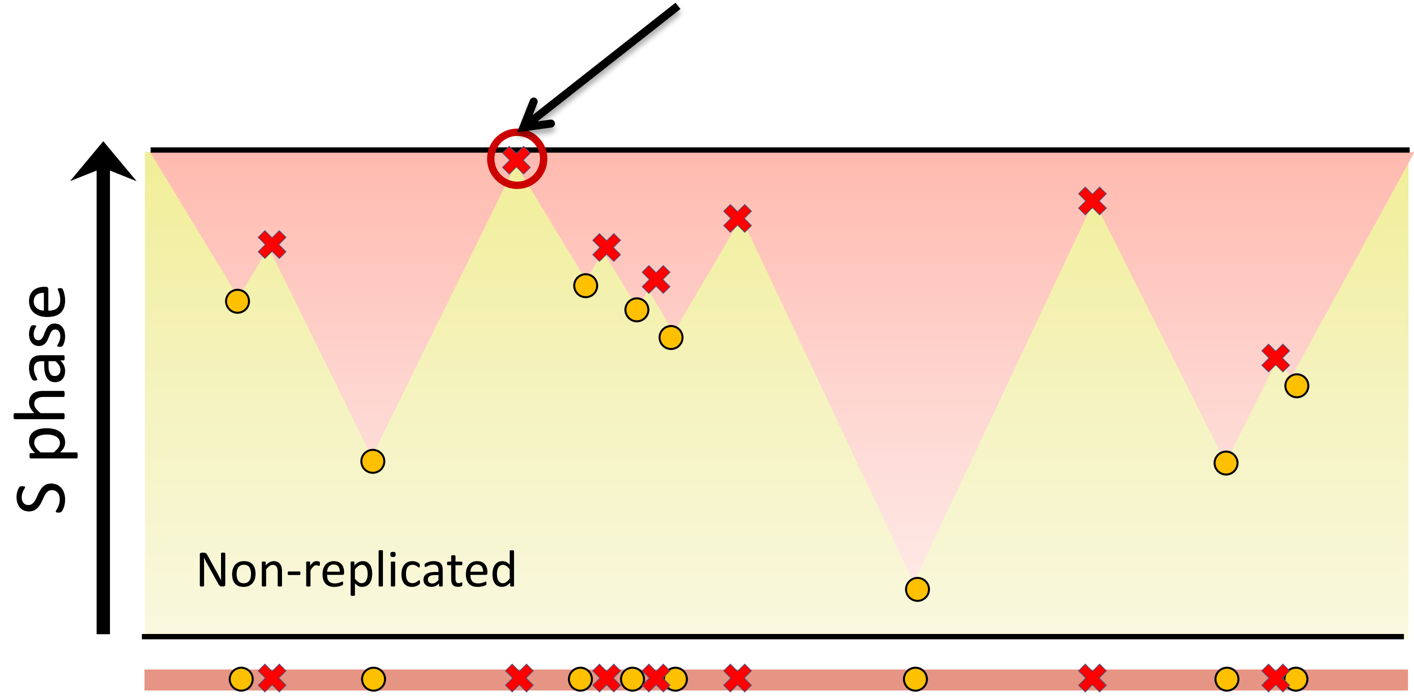
$I(t)$ = number of initiations / non-replicated length / time



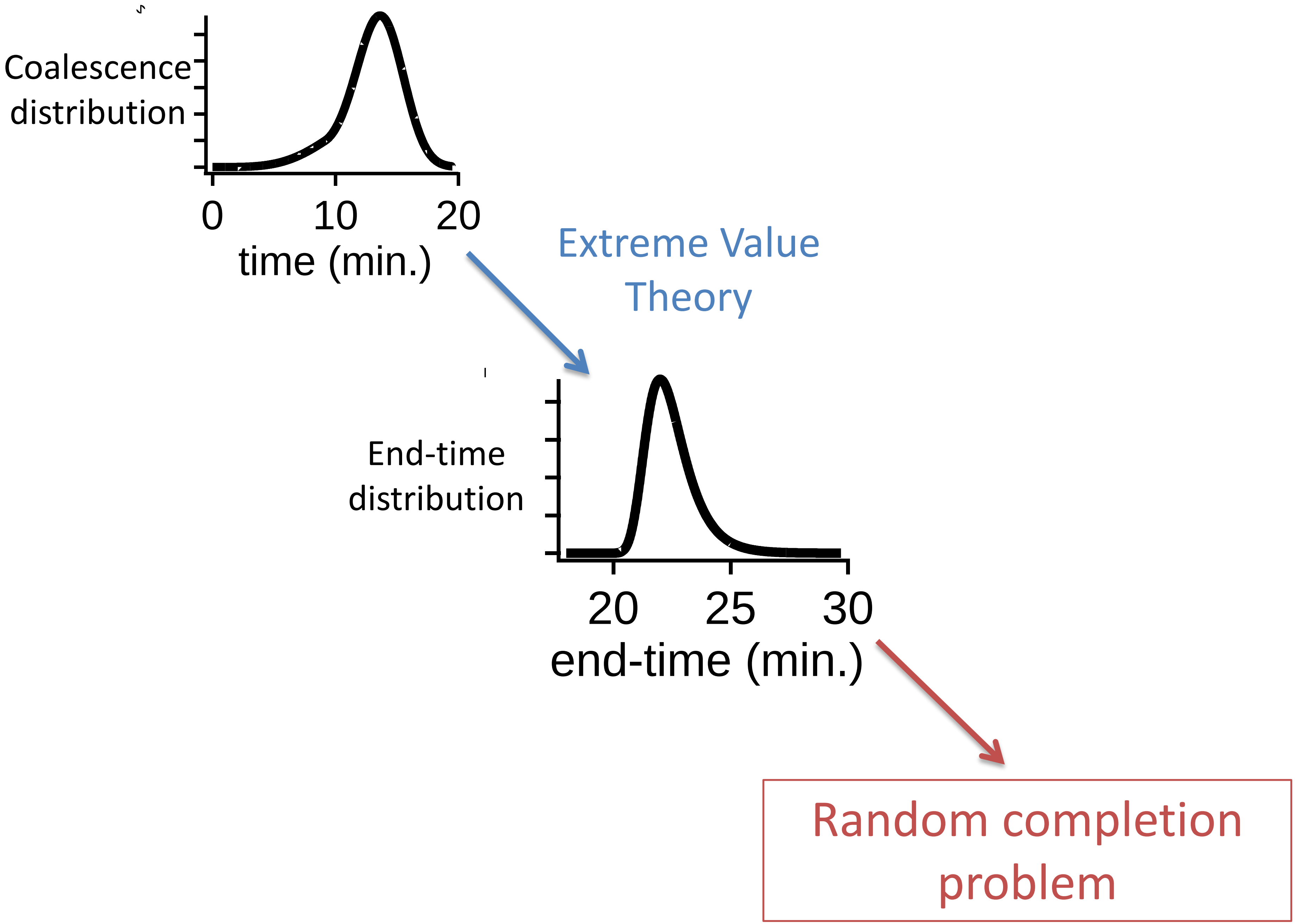
Spatially random origins

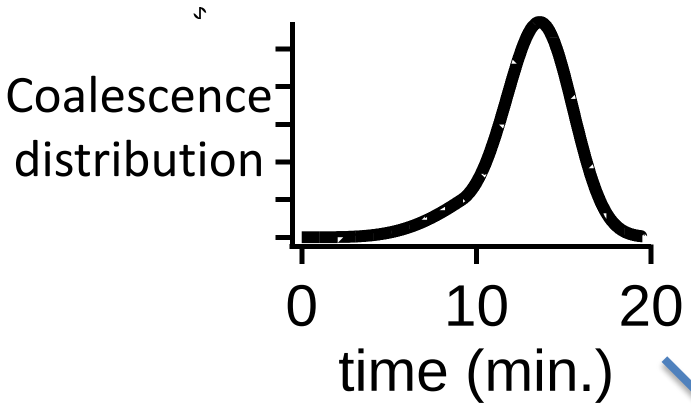
Our Model

Last Coalescence Event = Replication end-time

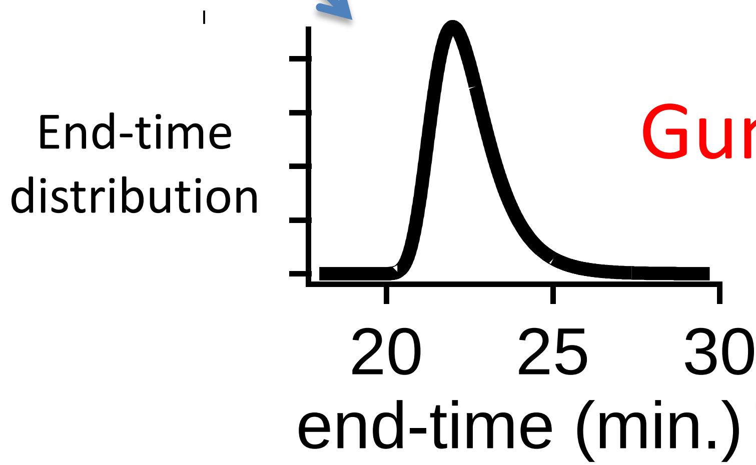


Spatially random origins


Coalescence distribution
0
10
20
time (min.)
Extreme Value Theory
End-time distribution
20
25
30
end-time (min.)
Random completion problem



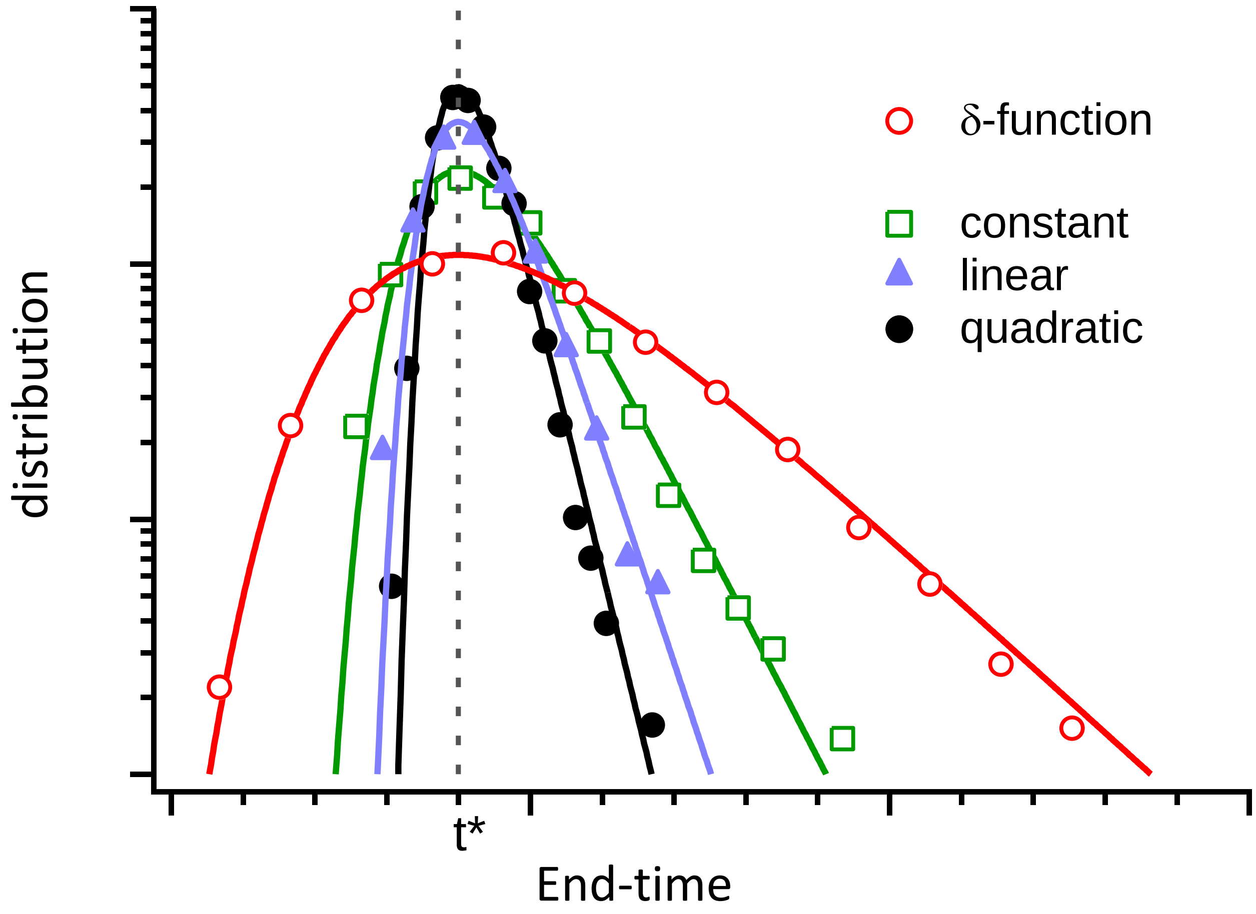
Extreme Value Theory



Gumbel

Random completion problem

Results



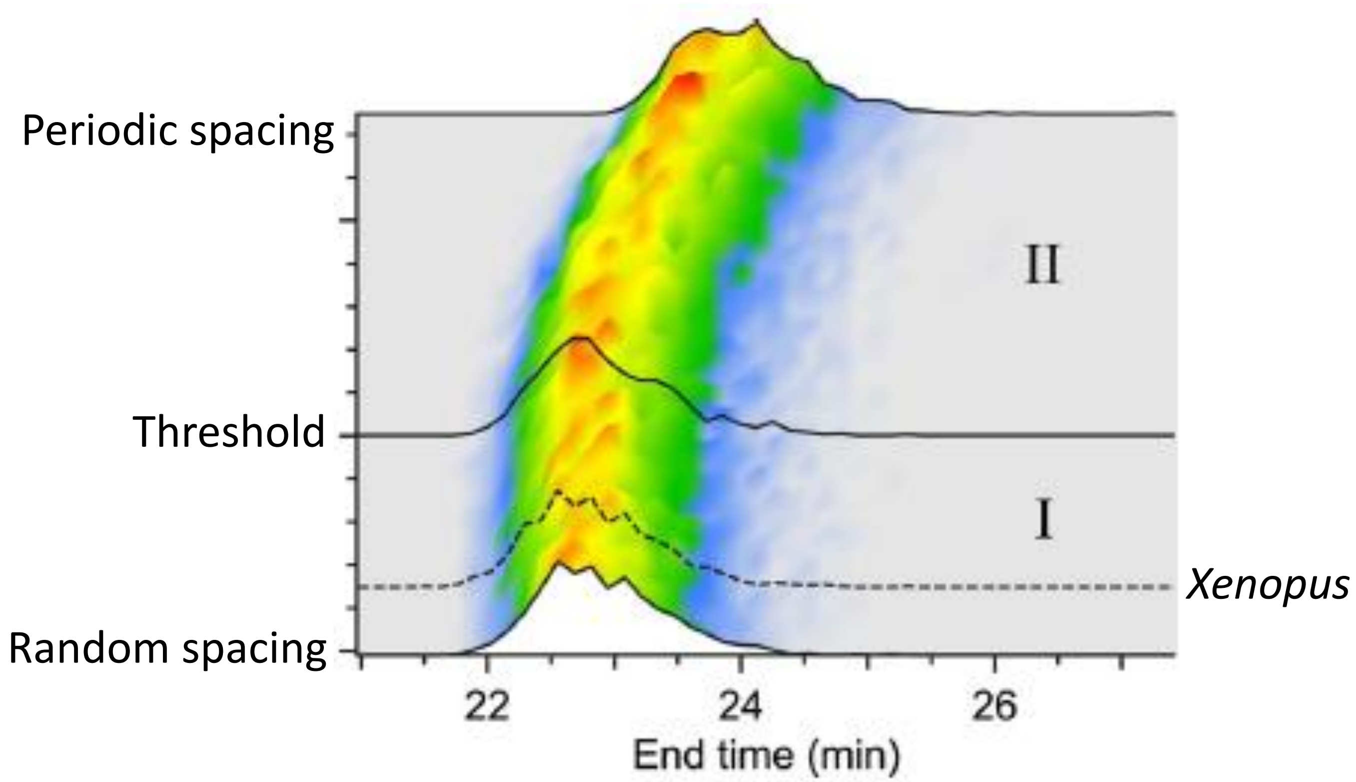
Increasing *I(t)* → narrows distribution

Controlling the end-time distribution

- Why increasing I(t) → narrow distribution?
  - δ-function case

  - mind the gap
  - End-time distr. meets constraints → v, I(t), # origins

Does spatial regularity matter?



Regularity only has a minor effect.

Conclusion

- Modelled replication
- EVT → random completion problem
- Increasing *I(t)* helps timing control
- Spatial regularity unimportant
- Does nature adopt an optimized *I(t)*?

Ref: S.C.-H. Yang & J. Bechhoefer, PRE **78**, 041917 (2008)

Commentary: S. Jun & N. Rhind, Physics **1**, 32 (2008)