Modelling of Microtubule Dynamics

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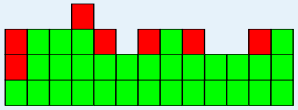

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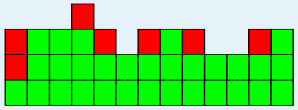
Introduction



BSI

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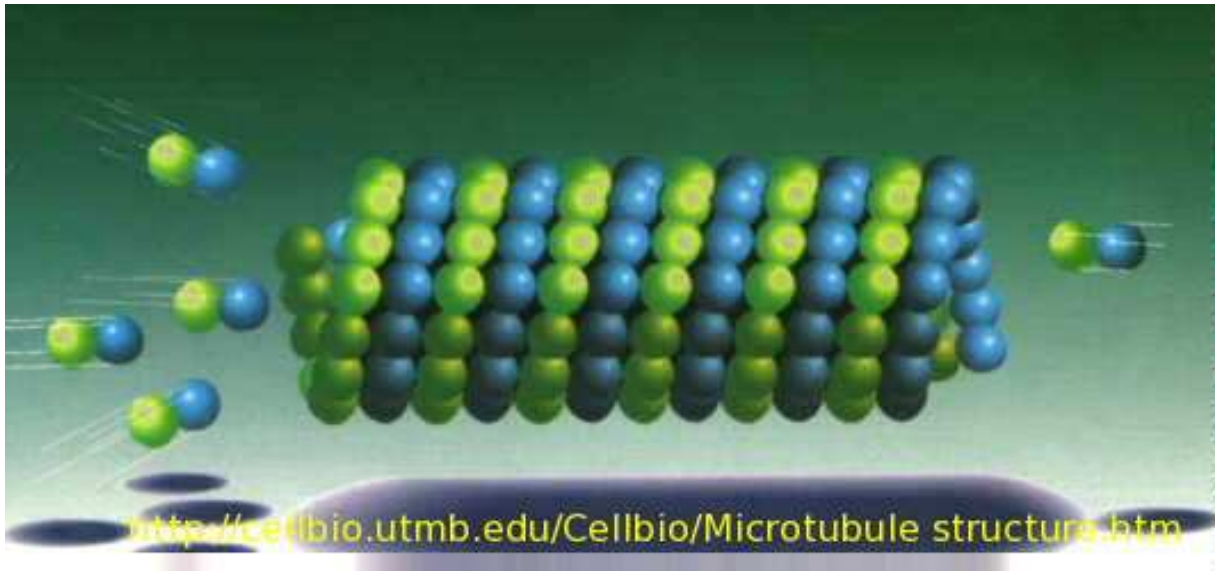
- 2007 : creation of Biophysical Science Institute in Durham
- After BSI 1 day meeting (Dec 2006), regular meetings between some Biologists and Mathematicians
- Topic: Modelling of Microtubules Dynamics

Mathematics: Kasper Peeters, Bernard Piette, Wojtek Zakrzewski

Biology: Michael Deeks, Tim Hawkins, Patrick Hussey, Junli Liu, Roy Quinlan, Andrei Smertenko.

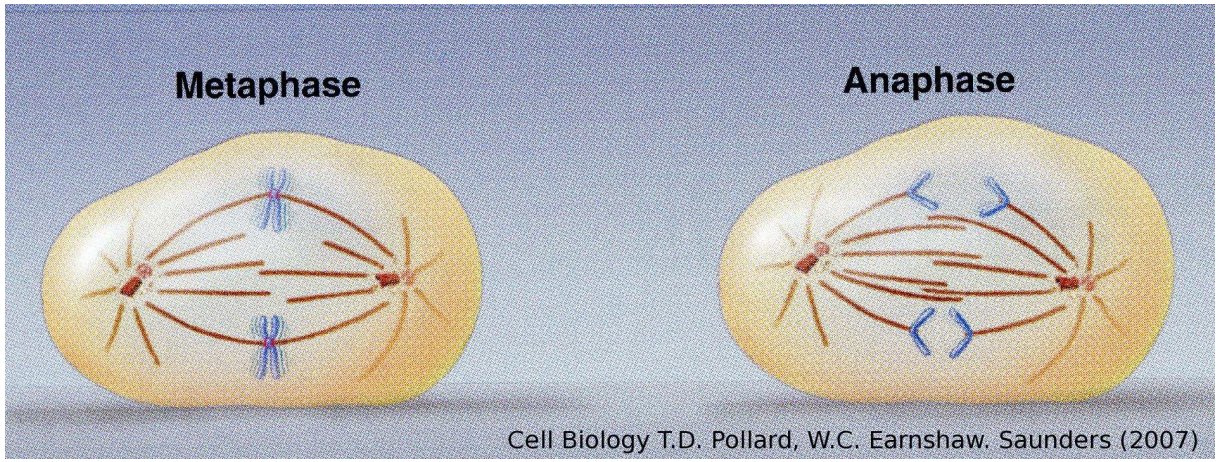
Microtubules

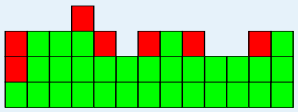
- Tiny tubes that are part of the cytoskeleton.
- Diameter : 25 nm
- Asymmetric (+ and - end).
- Assembly of tubulin protein dimers.
- 12 - 14 protofilaments.



Cell division

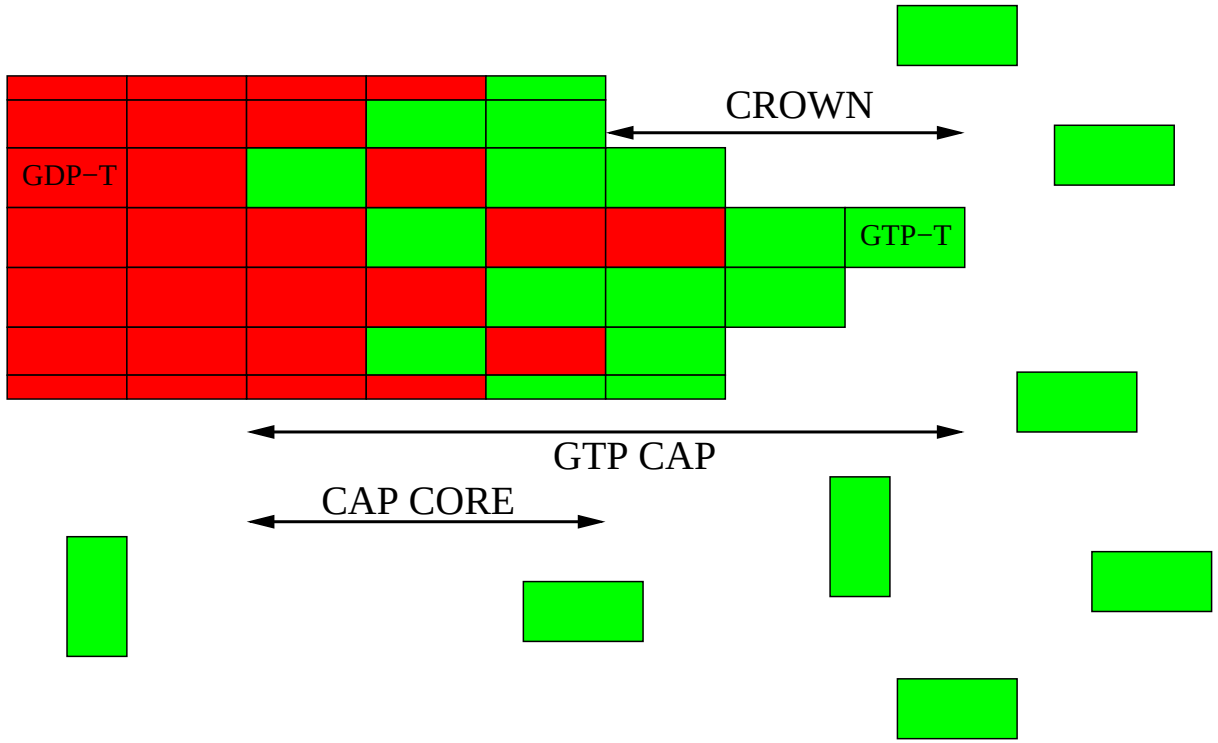
- Form spindles to split chromosomes during cell division.
- Taxol: anti-cancer drug. Stabilises MT grows and stop cell division.





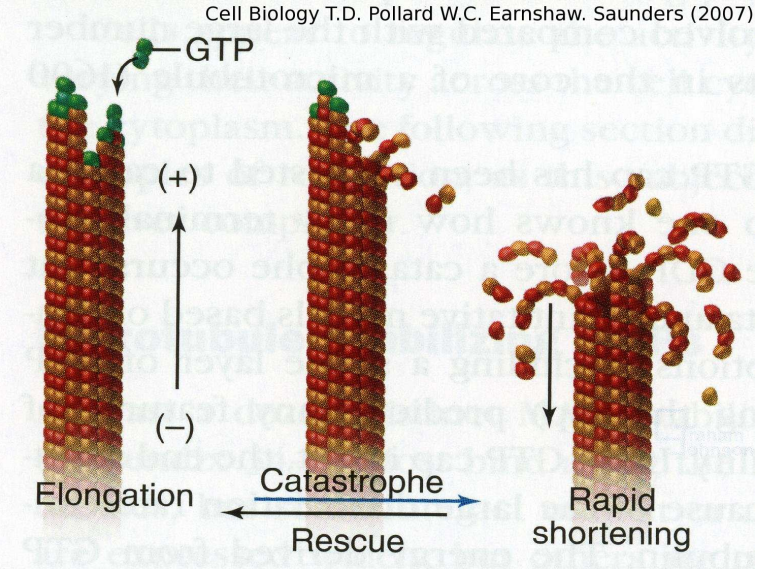
Tubulin Dimer

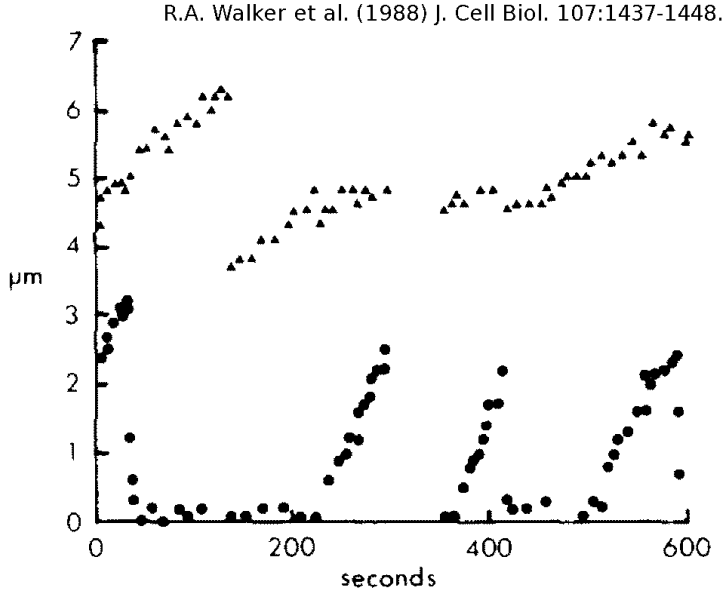
- Two type of dimers : GDP-Tubulin and GTP-Tubulin
- In microtubules GTP-Tubulin hydrolyses to GDP-Tubulin (rate $\approx 0.2/s$).
- GDP-Tubulin does not polymerise.
- GDP-Tubulin depolymerise 15 times faster than GTP-Tubulin .

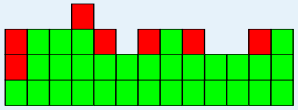


Microtubules Dynamics

- Microtubules grow and decay constantly.

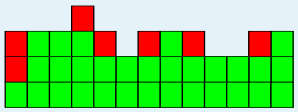






Open Questions

- Can we model/explain microtubule dynamics?
- Can we extract microtubule structural information from polymerisation data?



Biologists and Applied Mathematicians

Biologists:

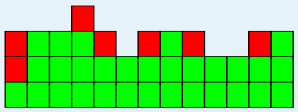
- Analyse complex systems.
- Use qualitative descriptions.
- Most results described in sentences or images.

Applied Mathematicians:

- Prefer simple systems.
- Use quantitative descriptions.
- Most results described in equations or numbers.

Collaborations lead to:

- New approach to problems.
- Ask new questions.
- Biologists can extract more information from their experiments.
- Mathematicians can study more complex systems.



Dialogue

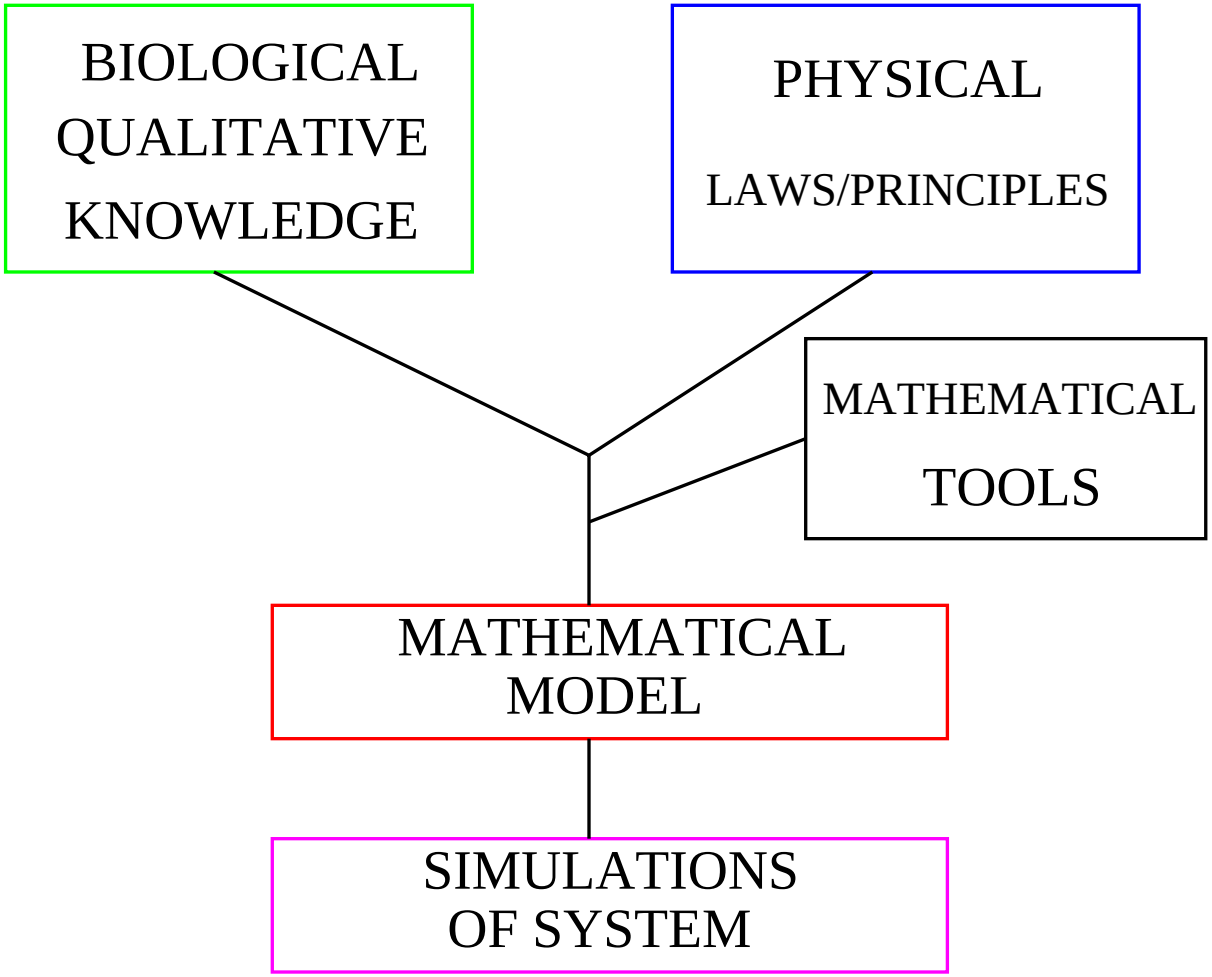
Example:

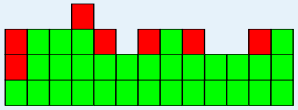
- Mathematicians: How fast do tubulin dimers diffuse in a cell?
- Biologists: Is this important?

Mathematicians explain why the diffusion is important.

- Biologists: This is interesting. We never thought about it that way. This gives us ideas of other experiments we can do.
- Mathematicians: Can you measure the effect of temparature on the microtubule polymerisation rate?
- Biologists: Yes we can but doing this can change everything in the cell.

Mathematical Modelling : an INTELLECTUAL MICROSCOPE.





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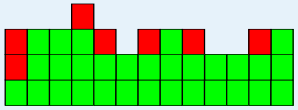

Model

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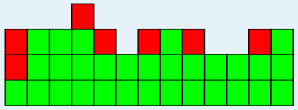
- Monte-Carlo model
- Use thermodynamics to reduce the number of parameters.

Our model is similar to model of Van Buren, Odde, Cassimeris but

- We consider the system as a perfect solution (not a gas).
- Implement the Monte Carlo algorithm correctly (Van Buren et al. had a bug in their code).
- Hydrolysis rate never set to zero.



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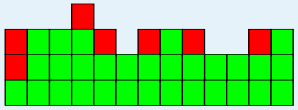
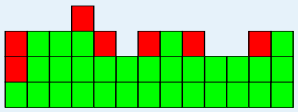


Washout experiment

- Good reproduction of experimental data.
- Washout experiment argues for large cap model.
- The amount of GTP-tubulin decreases exponentially as one moves away from the growing end of the MT.
- GTP cap length fluctuates in time.



Conclusions

- Collaboration between Biologists and Mathematicians allows to address more challenging problems.
- Mathematics: tools for physicists to describe nature and to get an insight into how the world works. Mathematics can do the same for biologists.
- Mathematical models: allow one to extract more information from experimental data.
- Lead to better understanding of biological systems.