# Modeling double strand breaks in irradiated DNA

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# Irradiation of DNA with $\gamma$ rays.

- Experiments performed by Baverstock, Cundall [1,2,3,4] and others consisting of $\gamma$ irradiation of DNA. The result consists of double strands breaks (dsbs) of the DNA helix with the yield of shorter fragments.
- Attempts to fit the distribution of lengths of the fragments, based in a random breakage distribution, are successful only if the shorter fragments are excluded.
- This suggest that there are two different types of breaks, **primary breaks** caused directly by the radiation, with a random distribution and **secondary breaks**.

# Hypothesis

Energy propagates along the DNA molecule and produces a break in another point far away, in terms of number of base pairs, from the primary break, but close, compared to the length of the DNA helix.

**Questions**

How energy propagates?

Why does it stop and produces a break?

# Details for two types of DNA

1. T7 DNA
   - Length: 12.5 $\mu$m, 40.000 bp aprox.
   - Typical length of the shorter fragments in excess: 1–2 $\mu$m or 3000 to 6000 bp
   - Energy threshold for secondary breaks: 90 eV

2. Plasmid DNA (circular)
   - Easier to count the breaks
   - Length: 1.65 $\mu$m, 5.000 bp aprox.
   - Tipical length of the shorter fragments in excess: 0.15 $\mu$m or about 450 bp
   - Energy threshold for secondary breaks: 75 eV

This suggest that energy can travel several hundreds or thousands of bp before encountering a weak point.

# What can be a weak point?

1. A place where a primary single strand break (ssb) has previously taken place.
2. *Hot spots*, points close to local openings or denaturation bubbles of the DNA
3. Specific sequences of base pairs,
   (a) Rich A-T regions with lower energy.
   (b) Some specific code.

# Looking for a model

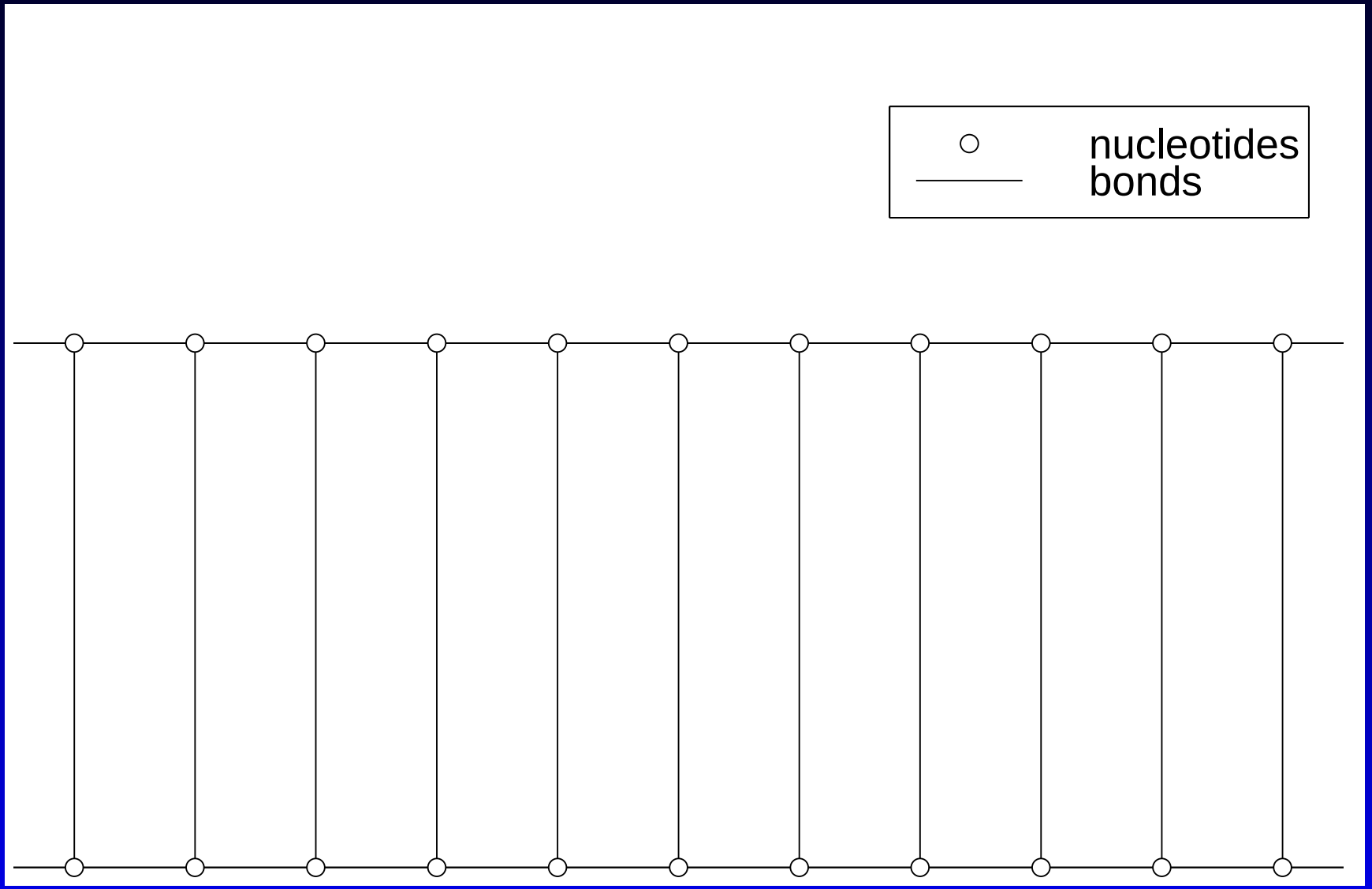
A suitable model for reproducing this phenomena need to have the following properties:

1. Two strands, to allow for the possibility of ssb and dsbs
2. A potential that becomes flat once the strands are broken
3. Inhomogeneity

# A starting point for a model

The simplest model with these properties seems to be the one used by Muto el al. [5], which corresponds to two parallel strands of point masses, to model the bases, coupled with next neighbours in the same strand (longitudinal direction) and to the opposite base in the other strand (transversal direction), the bases being able to move only in two dimensions. In the reference cited the potential used were Toda potentials for the coupling along the helix axis and Lennard-Jones potentials for the coupling with the bases.

# The Muto model



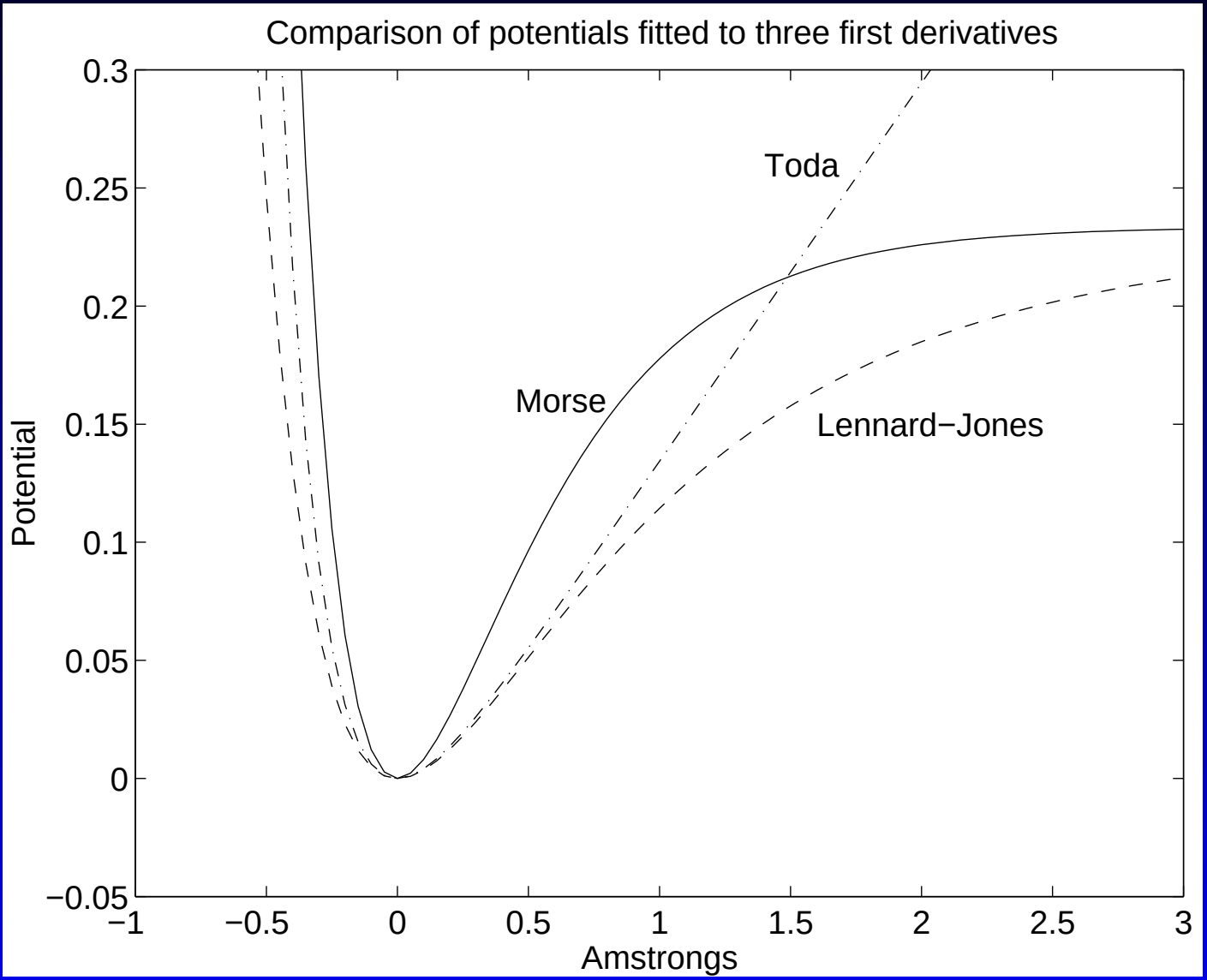
# Which potential to use?

**Toda** Used in the Muto model for analytic convenience to count solitons.

**Lennard Jones** Considered the most realistic for the Hydrogen bonds.

**Morse** Analytically simpler than Lennard Jones. Widely used when modeling DNA denaturation.

# Potentials


Comparison of potentials fitted to three first derivatives
Toda
Morse
Lennard−Jones
Potential
Amstrongs
0.3
0.25
0.2
0.15
0.1
0.05
0
−0.05
−1
−0.5
0
0.5
1
1.5
2
2.5
3

# A first model

- Morse potential everywhere.
  - We need everywhere a potential that becomes flat to simulate double breaks
  - Mathematically simpler than Lennard-Jones
- Energies and elastic constants according to Yakushevich [6].
- Random sequences of two sets of values for different base pairs.

# Problems

- Incoherence of the parameters found in the literature with the physical characteristics of the bonds.
- Traveling waves for low energies
- Chaotic breaks with high energies
- We choose new parameters according to the threshold energies in [1].About 4 eV for each phosphodiester bridge.

# Other problems

- The elastic constant is too large, giving oscillations smaller (tenths of ps) than the expected ( ps);
- Traveling kinks within the longitudinal direction.
- Uncoupled oscillations within the transversal direction.

*The good parameters question is yet unsolved.*

# Parallelization method: PVODE

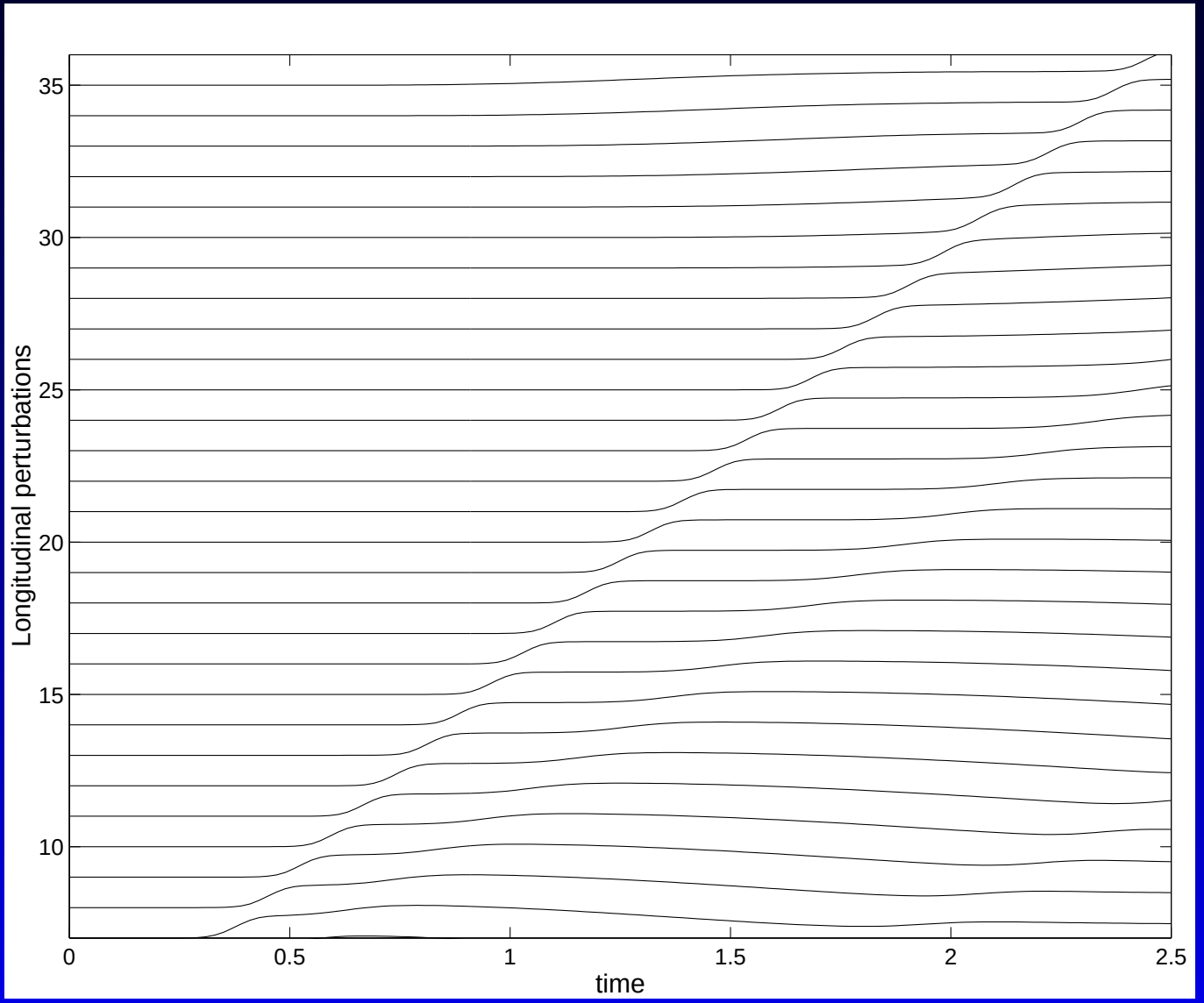
PVODE is a portable solver for ordinary differential equation systems. It is based on robust mathematical algorithms, and targeted at large systems on parallel machines.

Single Program, Multiple Data programming model, with message-passing communication.

The message passing calls are made through MPI.

http://acts.nersc.gov/PVODE/

# A traveling kink



# Model variants

1. Better parameters. Where?
2. Zig–zag model to provide rigidity to the double strand.
3. Helicity, with bonds with nucleotides several bases apart.
4. Directionality of the phosphodiester bonds, with angular coupling.

*The good and simple model question is yet unsolved.*

# Conclusions

- There exist traveling kinks in this model
- They propagates large distances along the DNA double strand
- The model is not yet suitable to model DNA breaks

# References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5. V Muto, PS Lomdahl, and PL Christiansen. Two–dimensional discrete model for DNA dynamics: longitudinal wave propagation and denaturation. *Physical Review A*, 42(12):7452–7458, 1990.
6. LV Yakushevich. *Nonlinear physics of DNA*. Springer-Verlag, 1998.

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