Scaffold Assisted Chromosome Condensation:
Molecular Dynamics Simulations

Dong-Gil Shin
MIT PRIMES
May 21, 2011

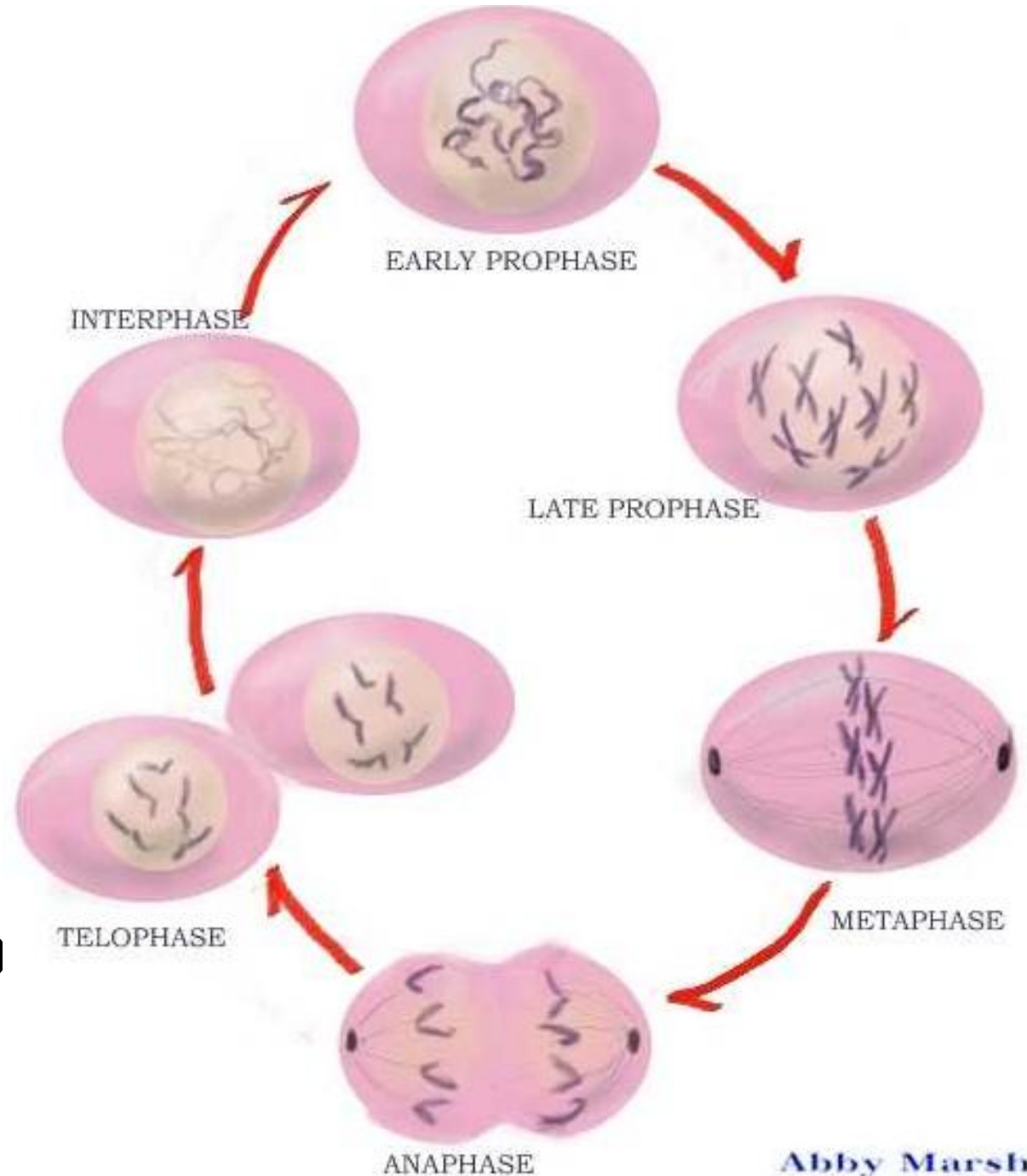# Mitosis and Chromosome Condensation
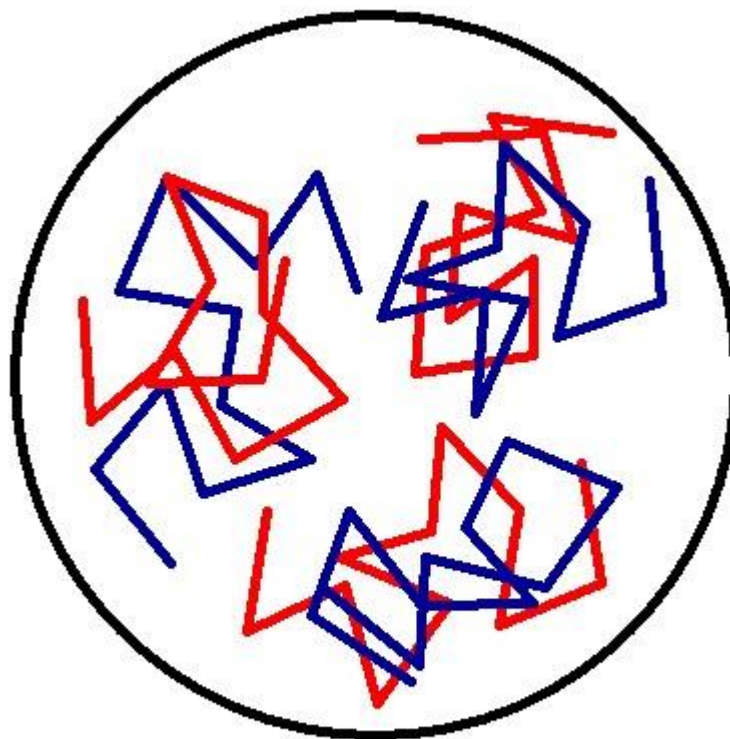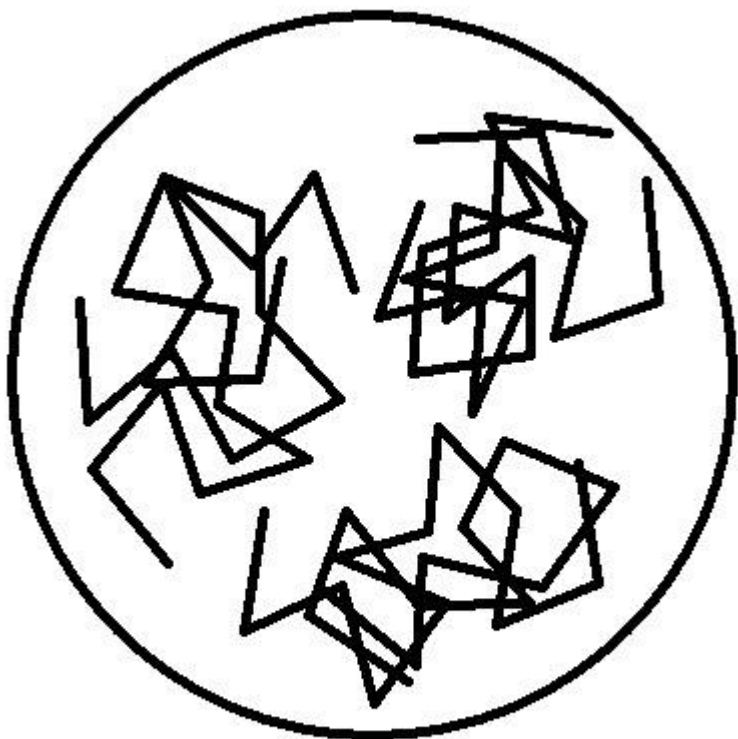
Interphase
Prophase
Metaphase
Anaphase
Telophase

Undergoes some 10,000 – 20,000 fold compaction and separates into sister chromatids
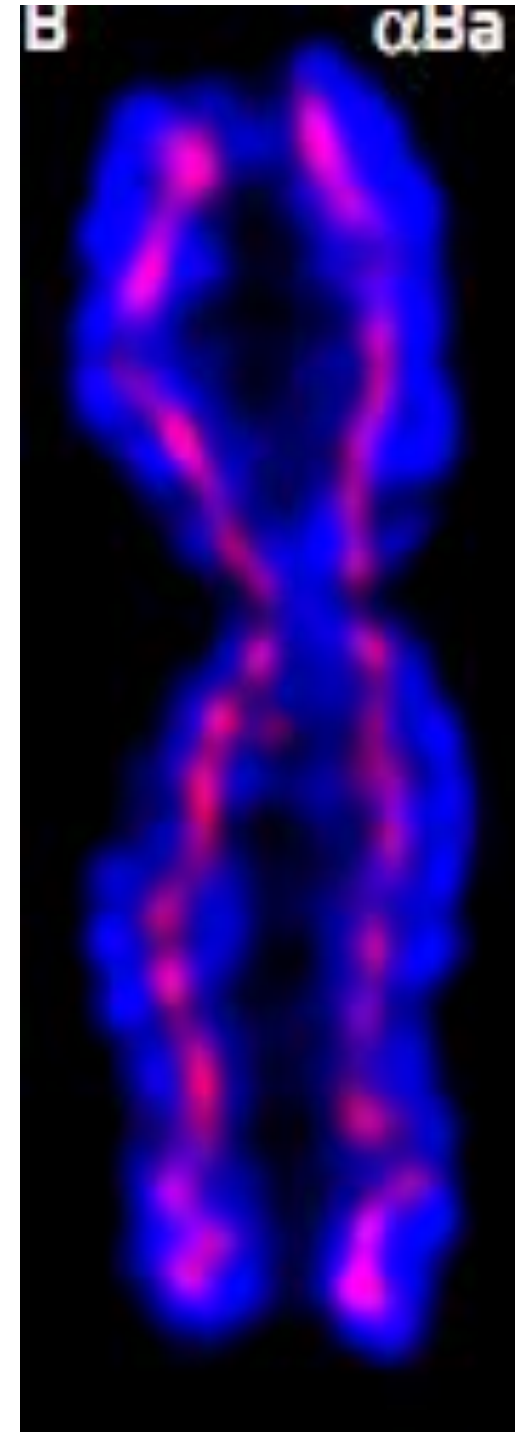
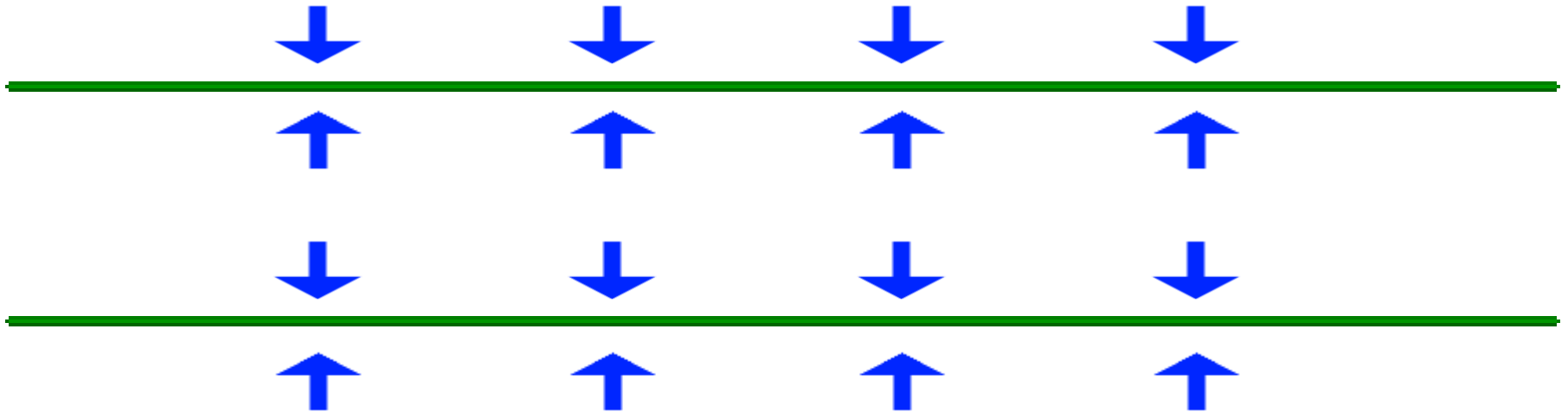# Separating chemically identical chains is a difficult feat

Axial Scaffolds

Consists mainly of proteins Topoisomerase IIα and Condensin

Can two identical scaffolds separate two identical sister chromatids?
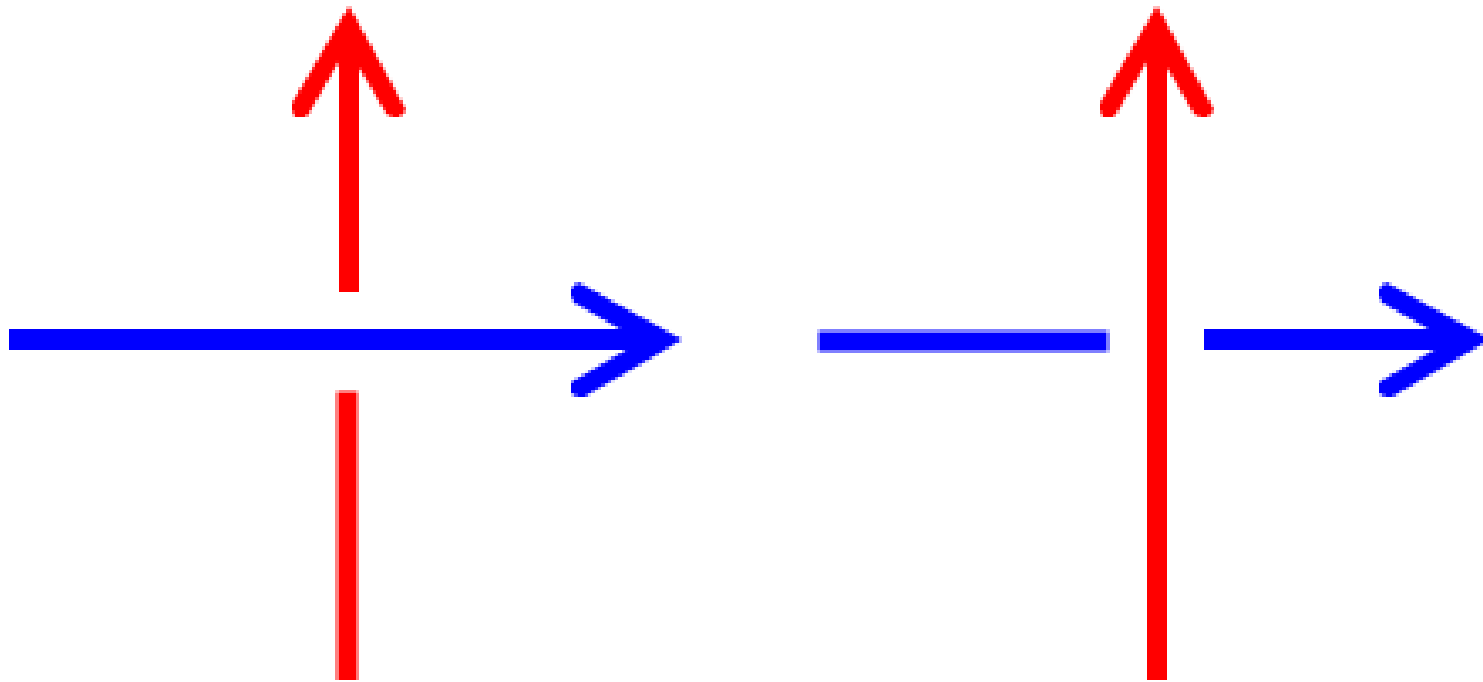
Molecular Dynamics Simulation

Two linear scaffolds in parallel

Short-range attractive potential

Chain length N = 1000

Freely jointed chain

Topoisomerase II introduced via semi-penetrable volume interaction

Topoisomerase passes one strand of DNA through another strand

Parameters Involved

```python
system.addForce(extforce2)

#external force - overall confinement of the system in this case
extforce3 = mm.CustomExternalForce("(step(ab-r)-step(aa-r)) * kb * (sqrt((r-aa)*(r-aa) + t*t)
for i in xrange(N): extforce3.addParticle(i,[])
#assigning parameters of the force
extforce3.addGlobalParameter("kb",0.015*kT/units.angstrom);
extforce3.addGlobalParameter("aa",2*units.angstrom);
extforce3.addGlobalParameter("ab",10*units.angstrom);
extforce3.addGlobalParameter("t", 0.05*units.angstrom);
extforce3.addGlobalParameter("tt",0.03*units.angstrom);
extforce3.addGlobalParameter("sd",50*units.angstrom);
extforce3.addGlobalParameter("kc",0.15*kT/units.angstrom);
extforce3.addGlobalParameter("ac",400*units.angstrom);
extforce3.addGlobalParameter("q", 37.5*kT*units.angstrom*units.angstrom*units.angstrom);  #kb*
system.addForce(extforce3)

#external force - overall confinement of the system in this case
extforce4 = mm.CustomExternalForce("step(p-ac) * kc * (sqrt((p-ac)*(p-ac) + t*t) - t); r = sqr
for i in xrange(N): extforce4.addParticle(i,[])
#assigning parameters of the force
extforce4.addGlobalParameter("kb",0.015*kT/units.angstrom);
extforce4.addGlobalParameter("aa",2*units.angstrom);
extforce4.addGlobalParameter("ab",10*units.angstrom);
extforce4.addGlobalParameter("t", 0.05*units.angstrom);
extforce4.addGlobalParameter("tt",0.03*units.angstrom);
extforce4.addGlobalParameter("sd",50*units.angstrom);
extforce4.addGlobalParameter("kc",0.15*kT/units.angstrom);
extforce4.addGlobalParameter("ac",400*units.angstrom);
```
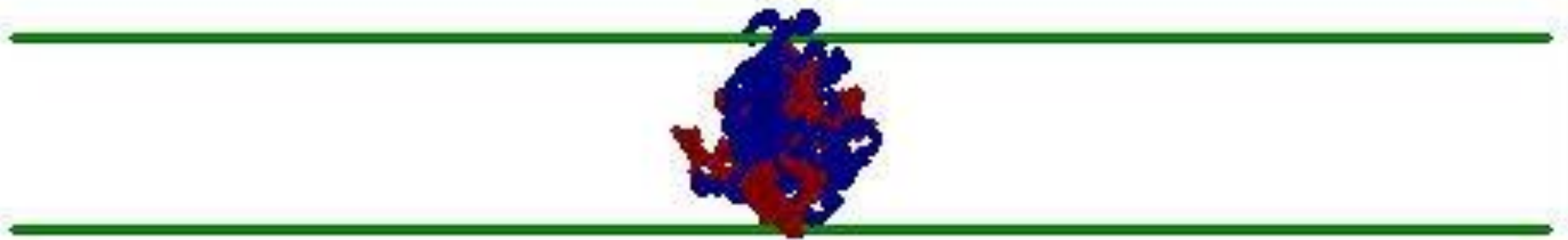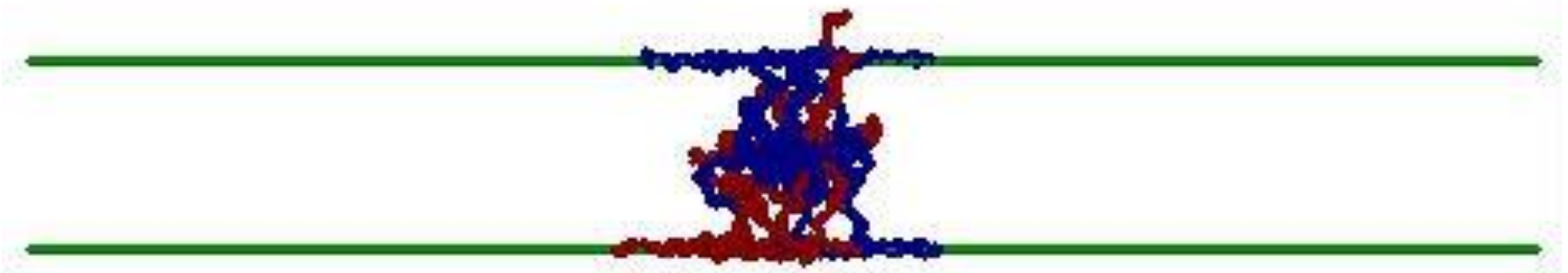
- Strength of attractive potential energy

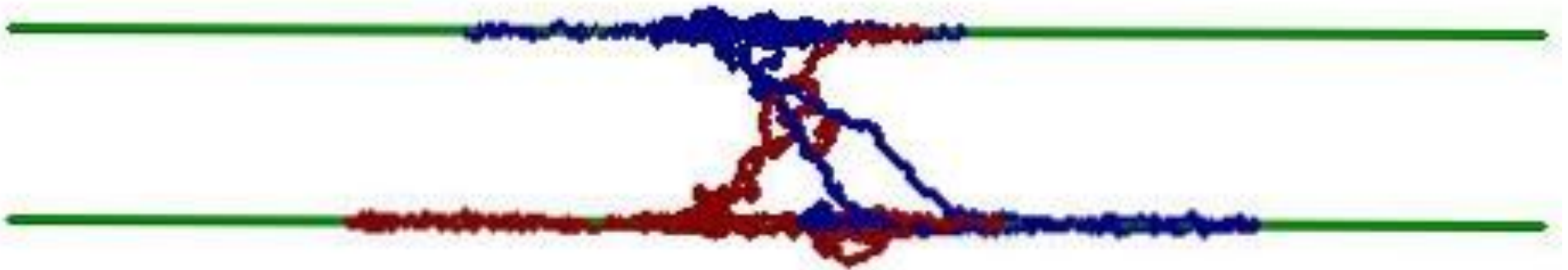- Length of scaffold

- Distance between scaffolds

If attractive force is too strong

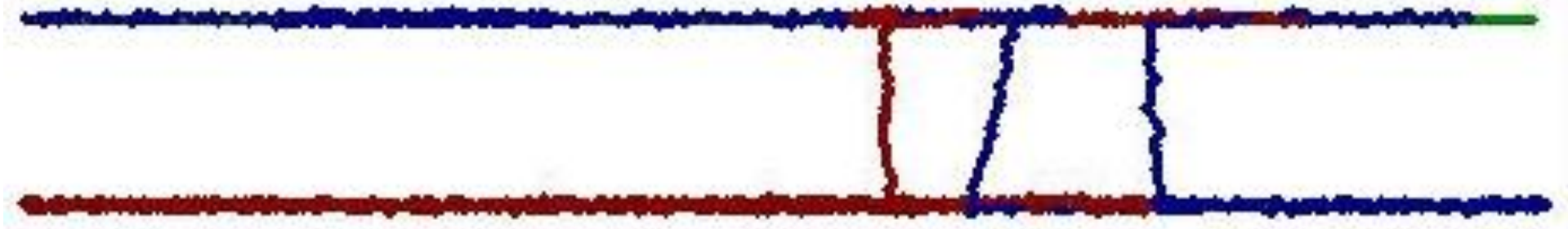# If attractive force is too strong
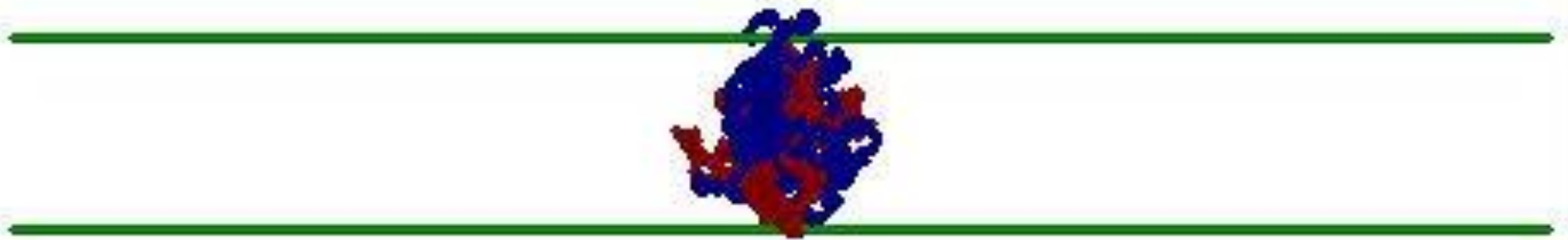
If attractive force is too strong

If attractive force is too strong

If attractive force is too strong
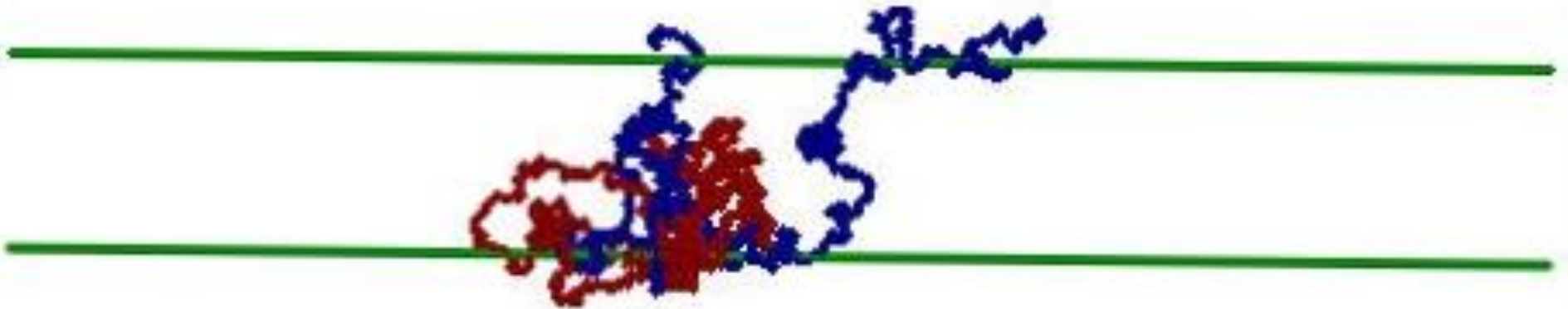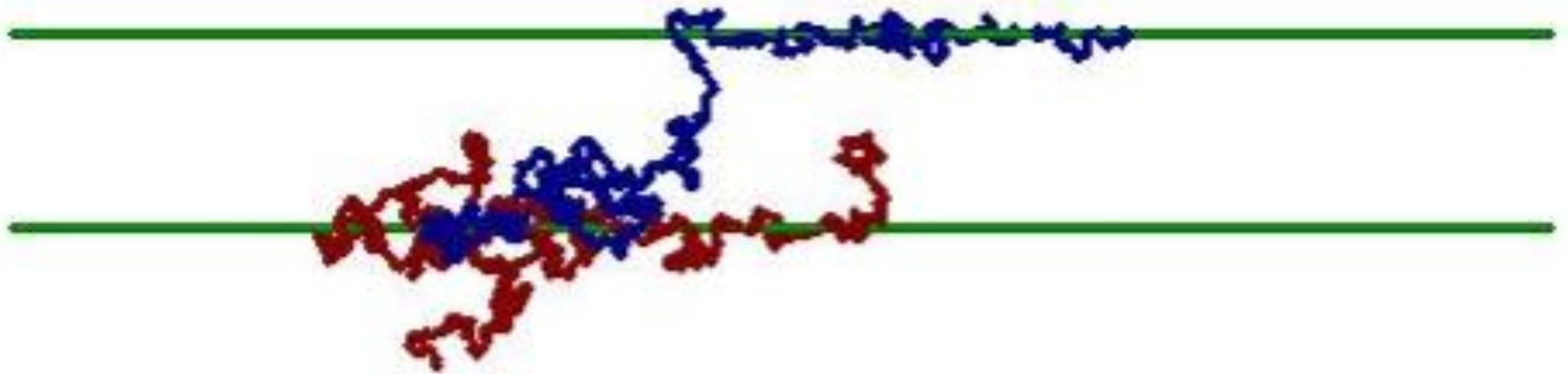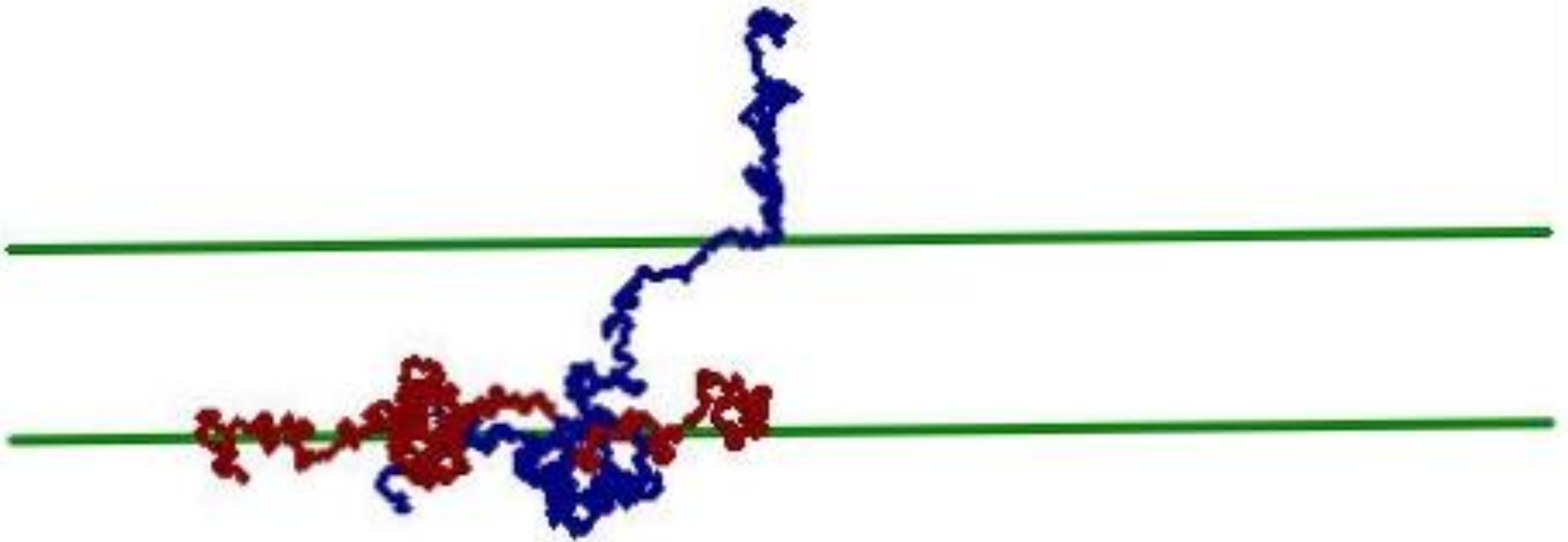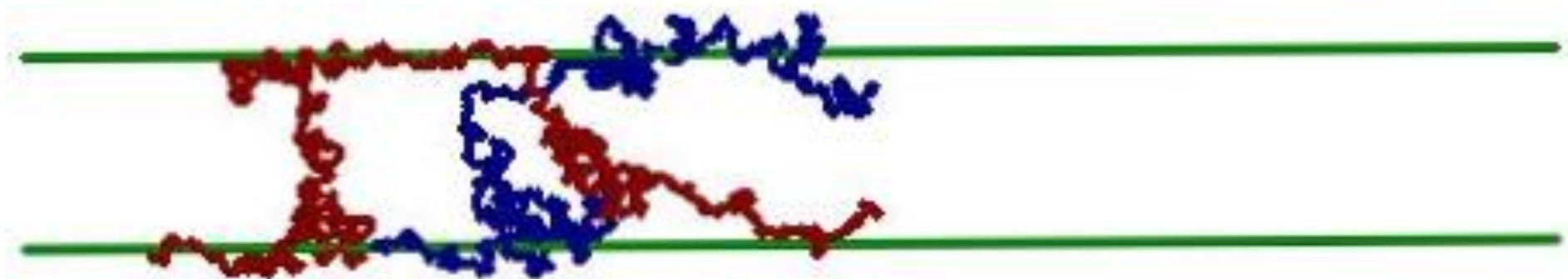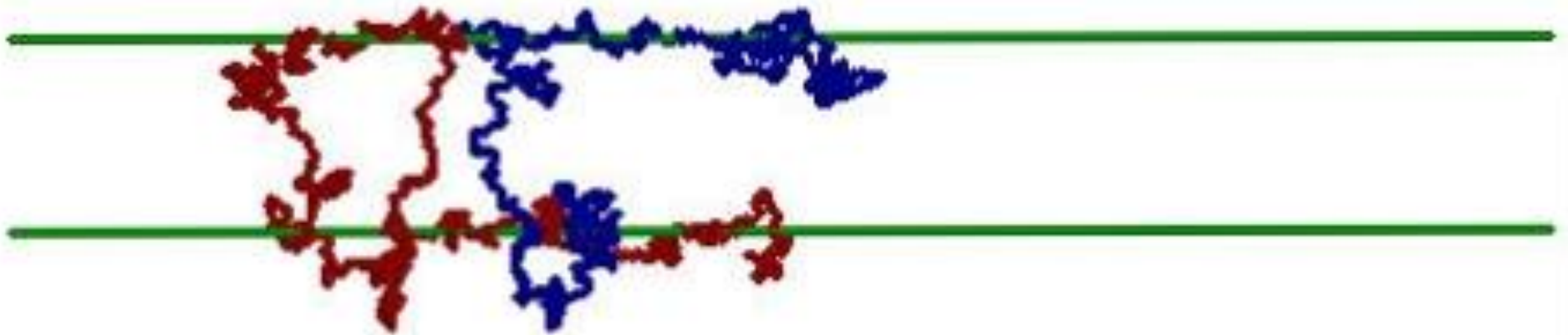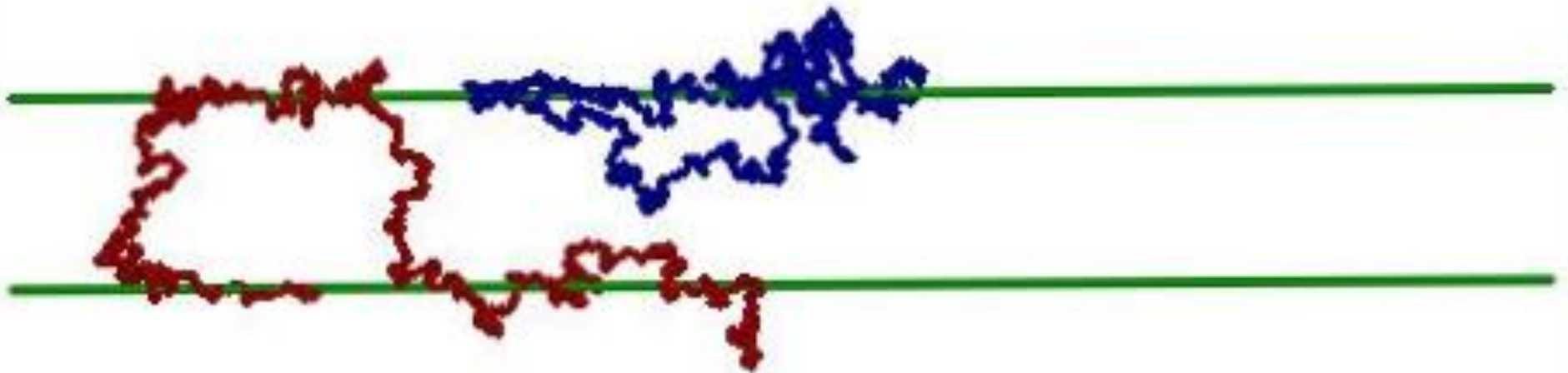
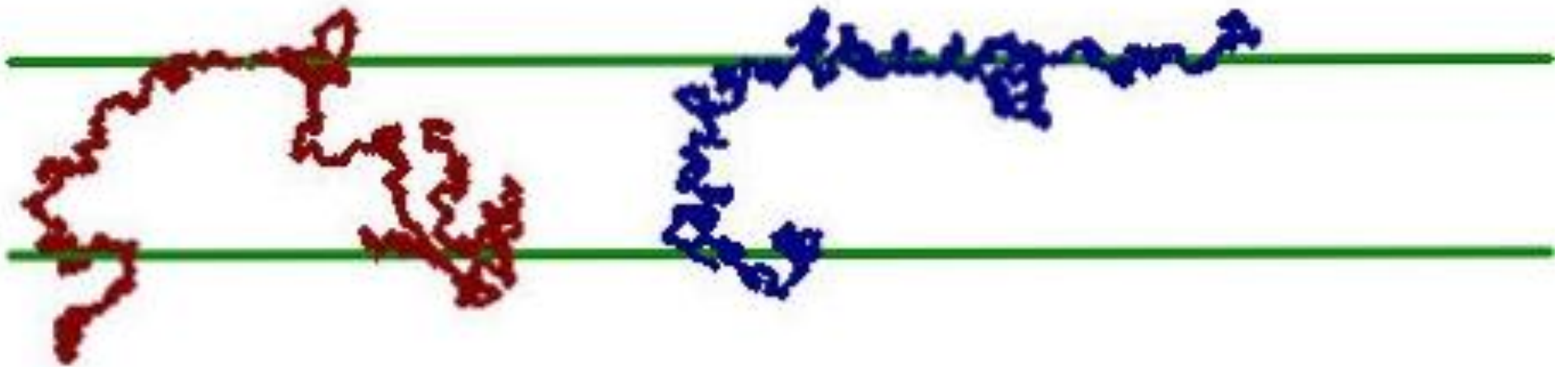# If too weak

If too weak

If too weak

If too weak

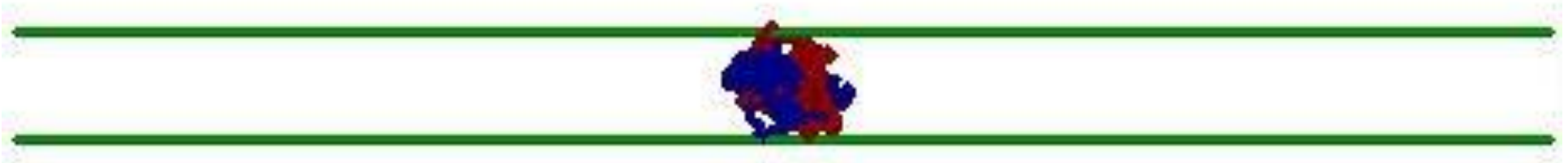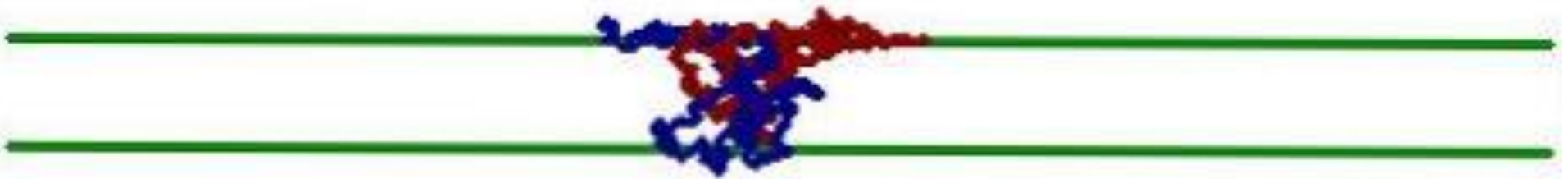# If too weak

If too weak

If too weak

If too weak

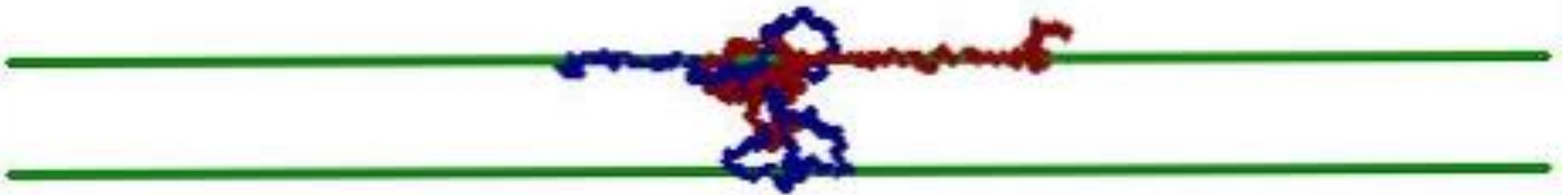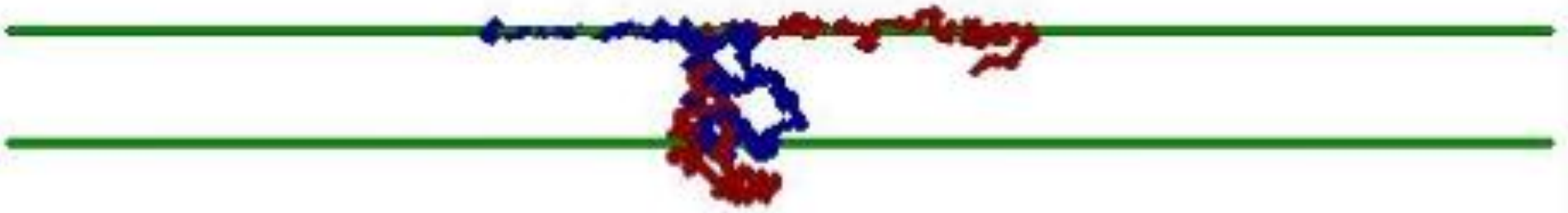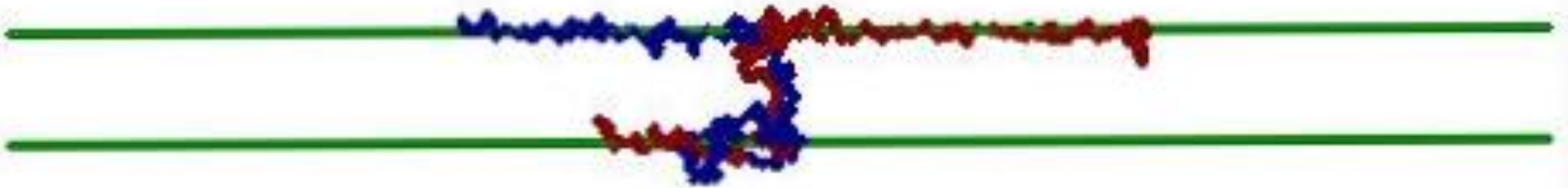# If scaffolds are too long

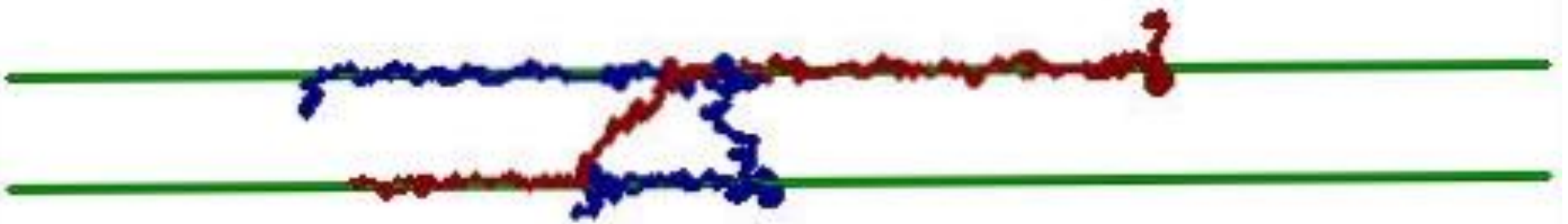# If scaffolds are too long
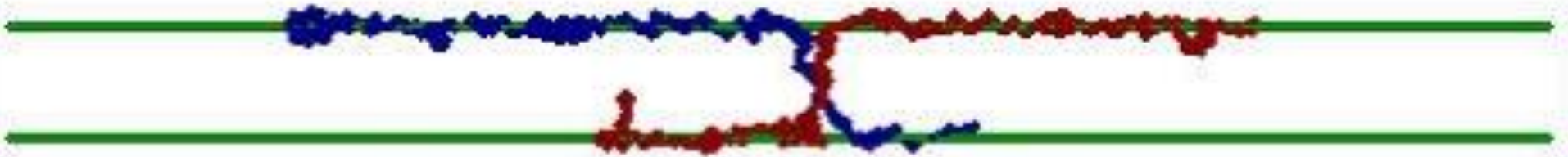
If scaffolds are too long

If scaffolds are too long

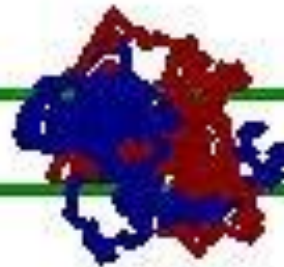# If scaffolds are too long

If scaffolds are too long
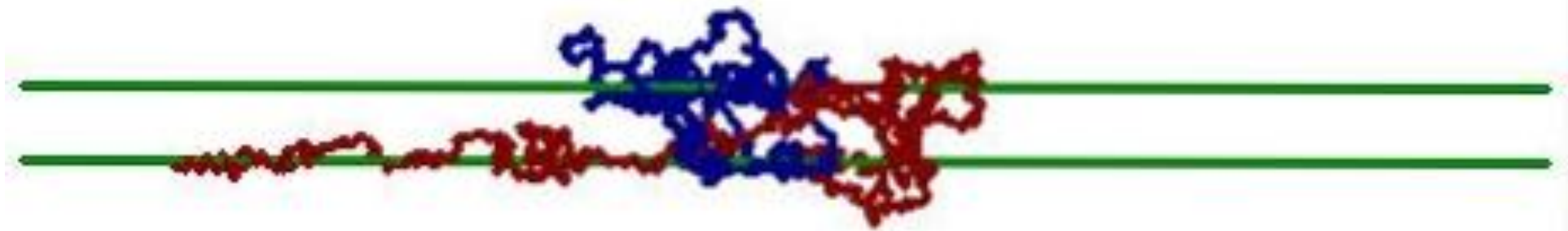
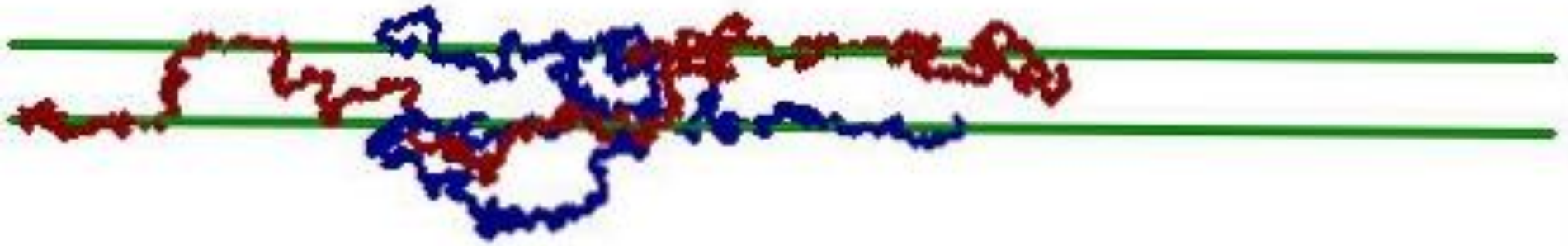# If scaffolds are too long

If scaffolds are too long

If the distance between the scaffolds is too small

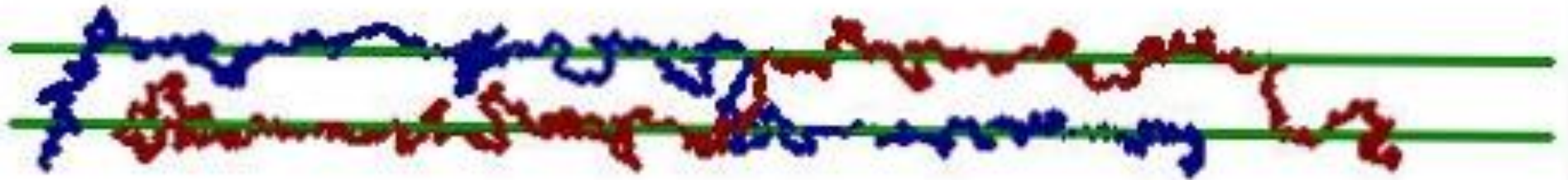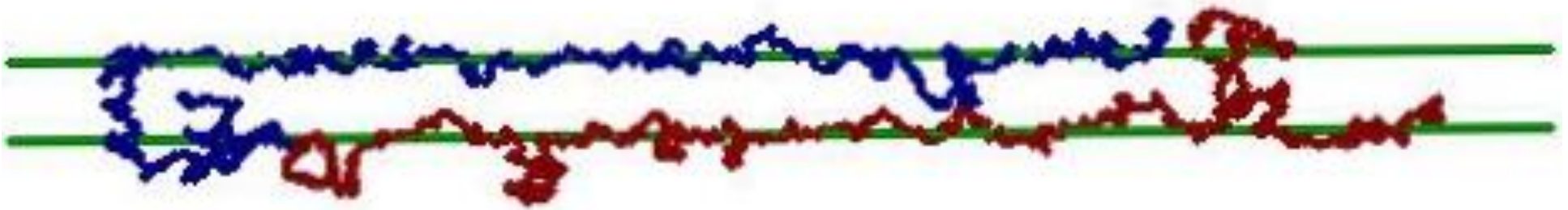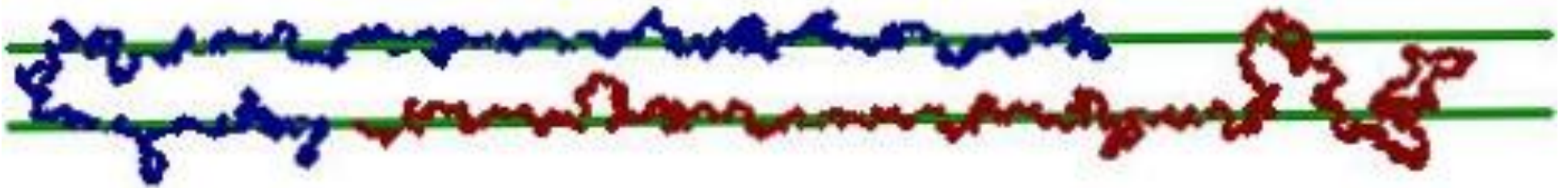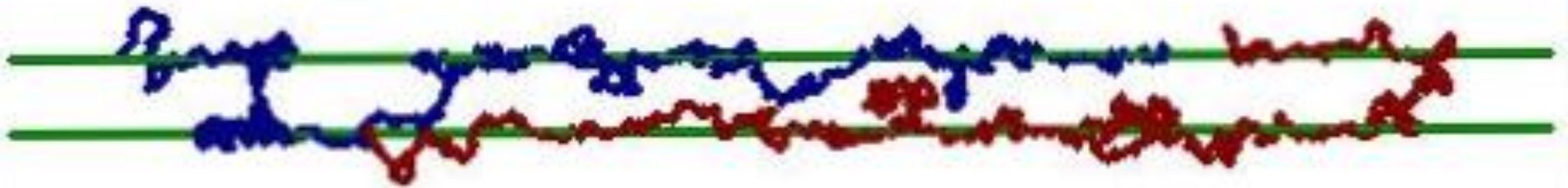# If the distance between the scaffolds is too small

If the distance between the scaffolds is too small

If the distance between the scaffolds is too small

If the distance between the scaffolds is too small

If the distance between the scaffolds is too small

If the distance between the scaffolds is too small

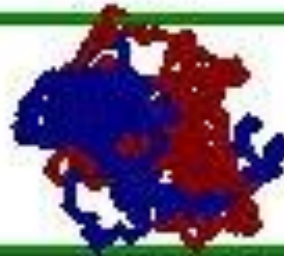If the distance between the scaffolds is too small

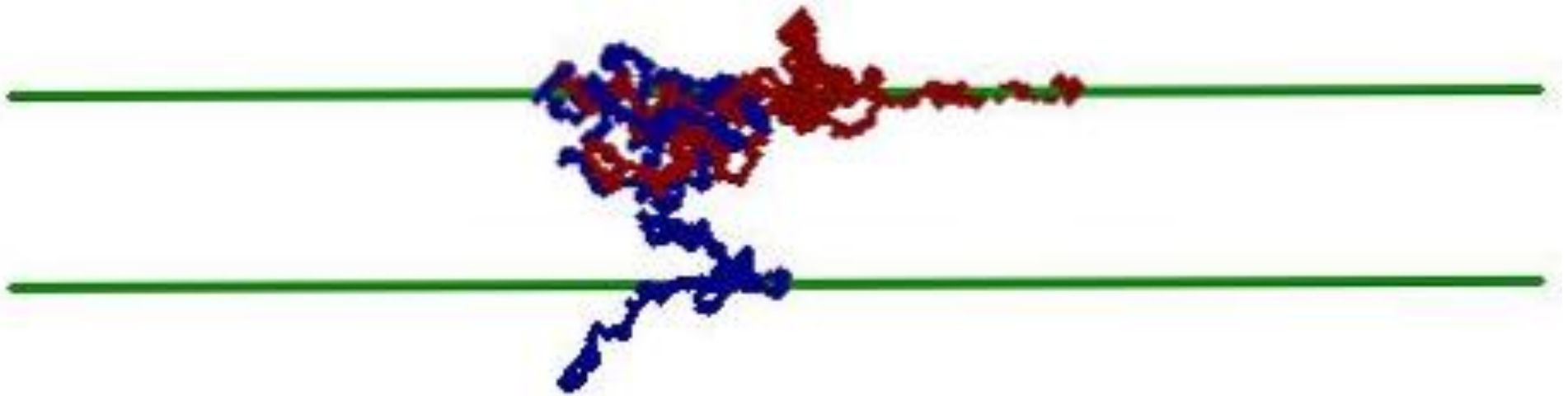# If the distance between the scaffolds is too small

If the distance between the scaffolds is too small

However, when the parameters fall within certain ideal ranges

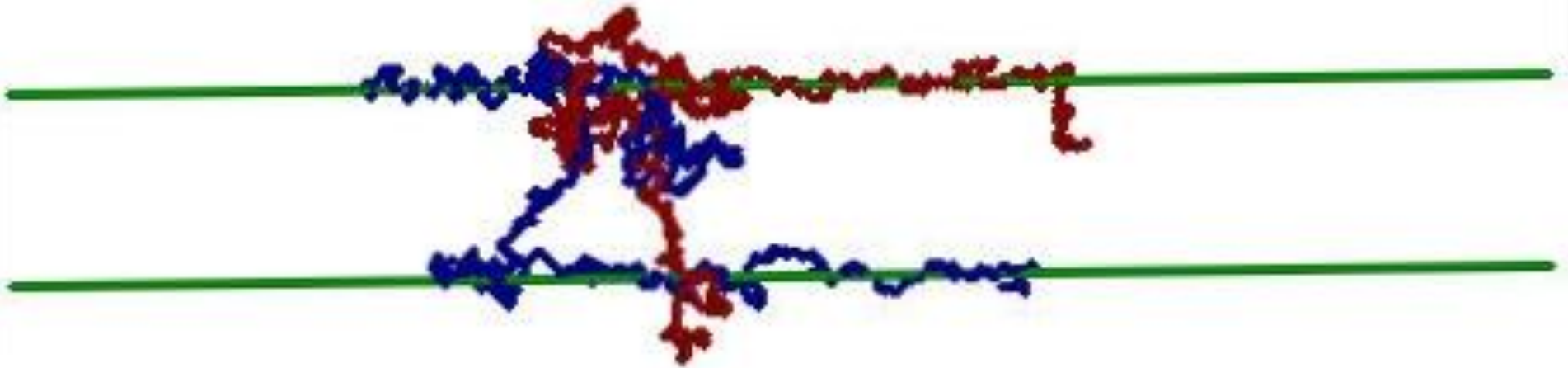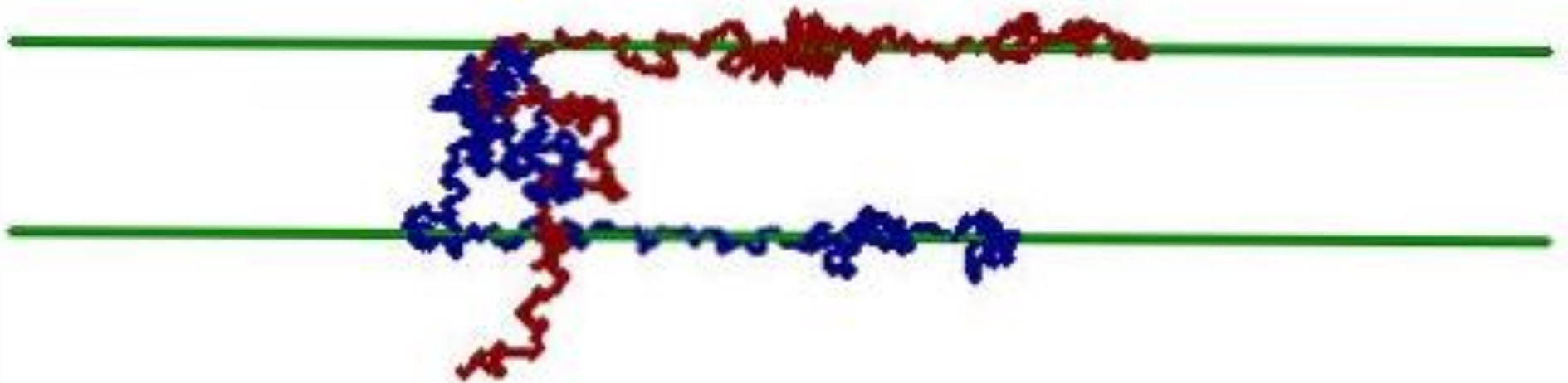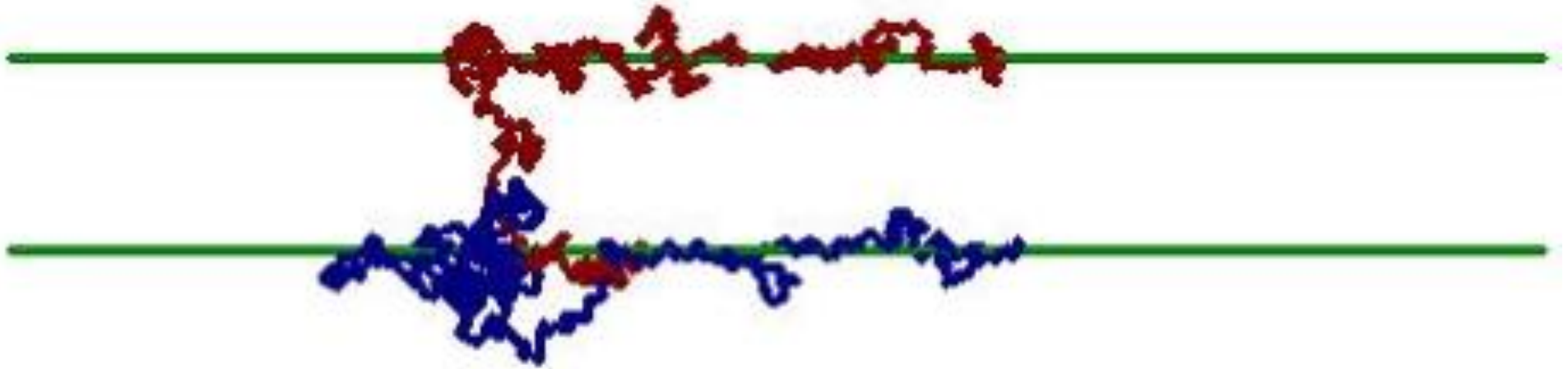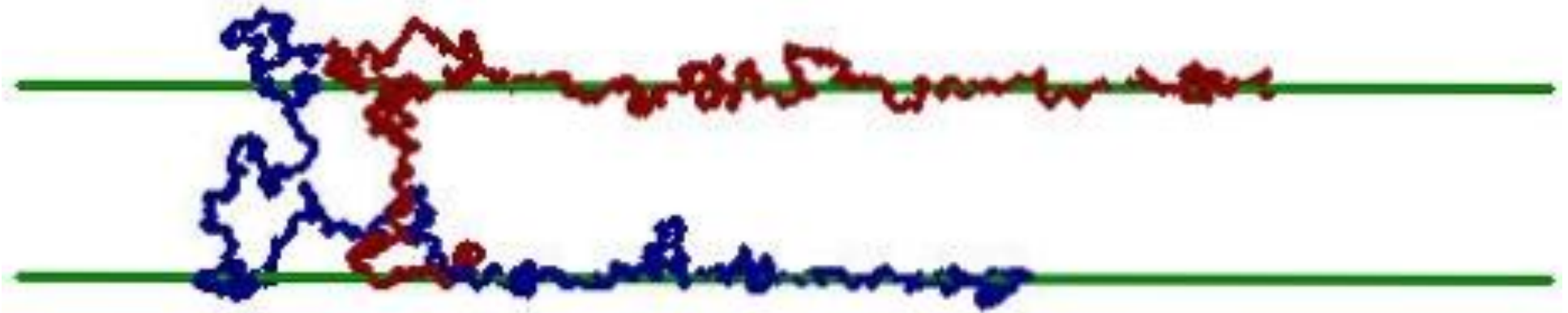However, when the parameters fall within certain ideal ranges

However, when the parameters fall within certain ideal ranges

However, when the parameters fall within certain ideal ranges

However, when the parameters fall within certain ideal ranges
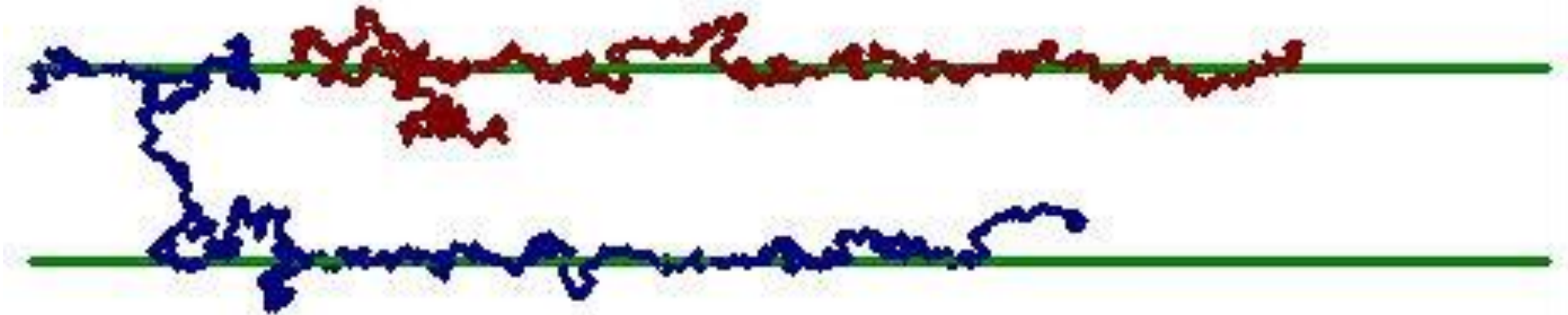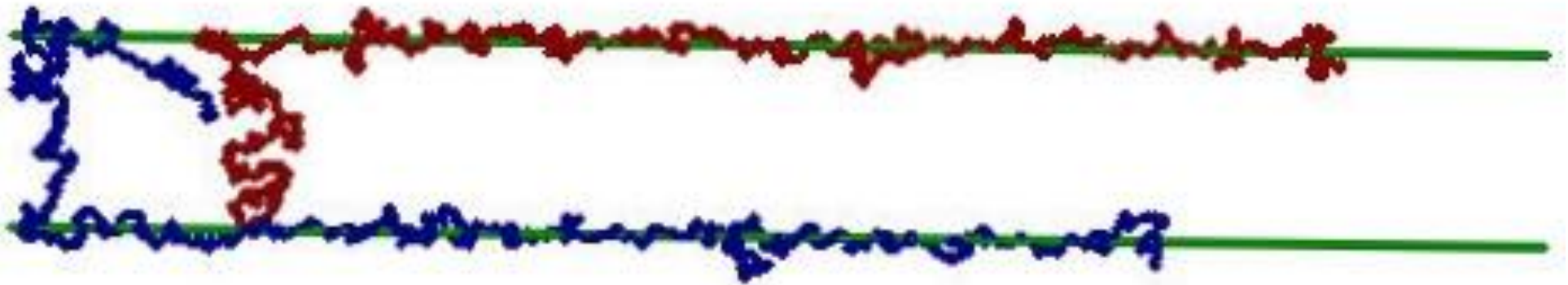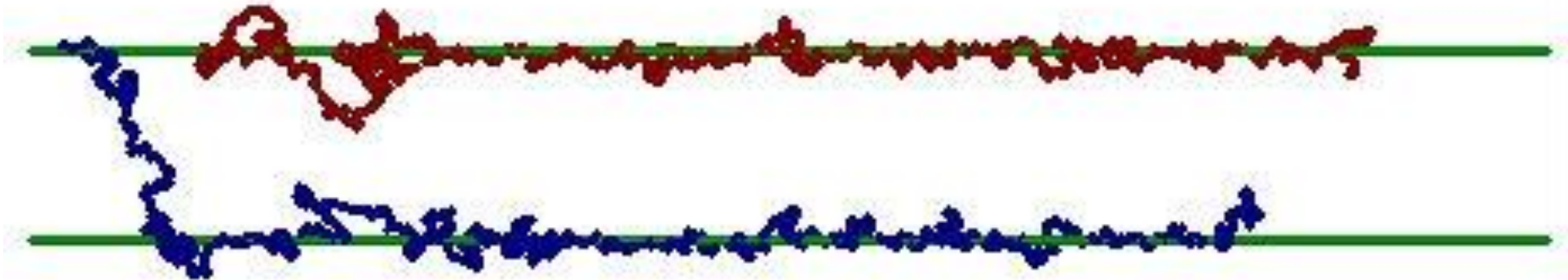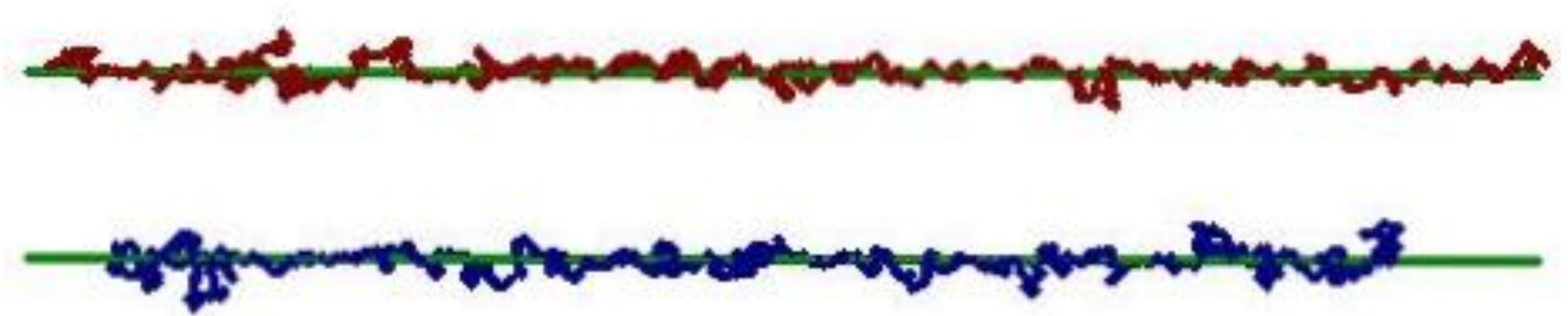
However, when the parameters fall within certain ideal ranges

However, when the parameters fall within certain ideal ranges

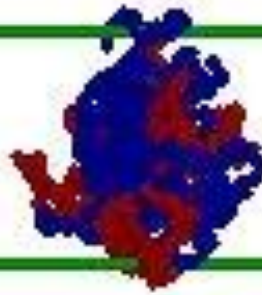However, when the parameters fall within certain ideal ranges

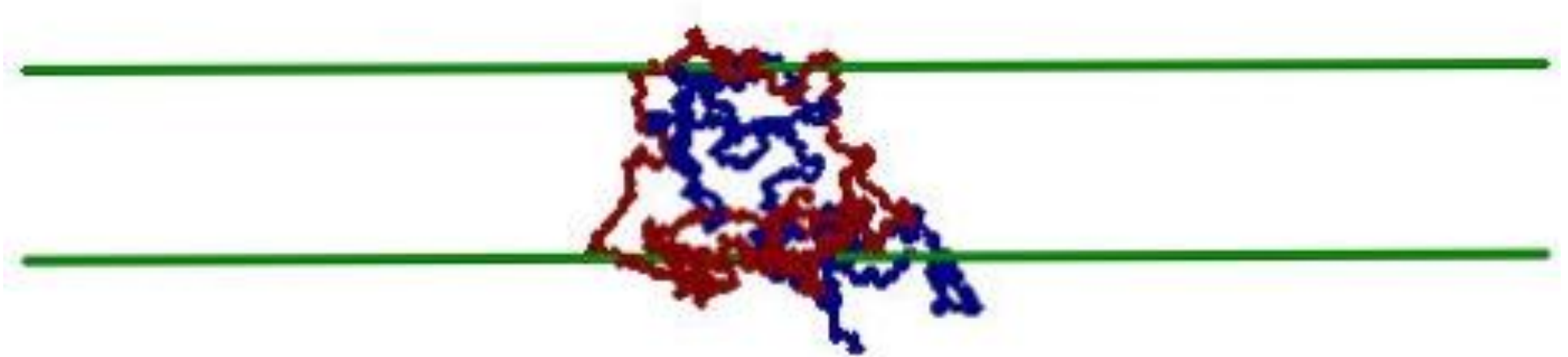However, when the parameters fall within certain ideal ranges

However, when the parameters fall within certain ideal ranges
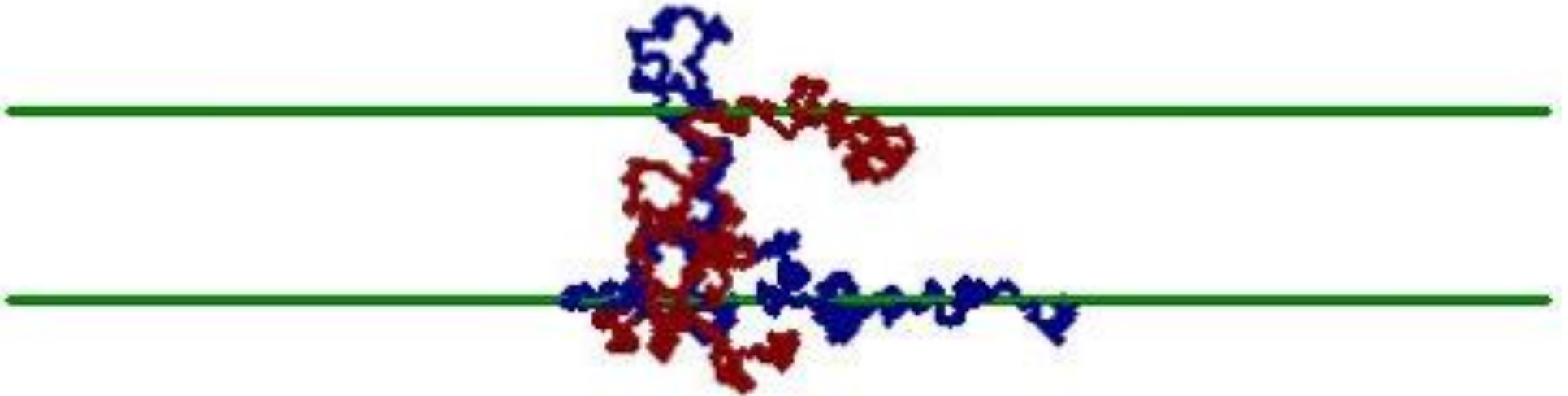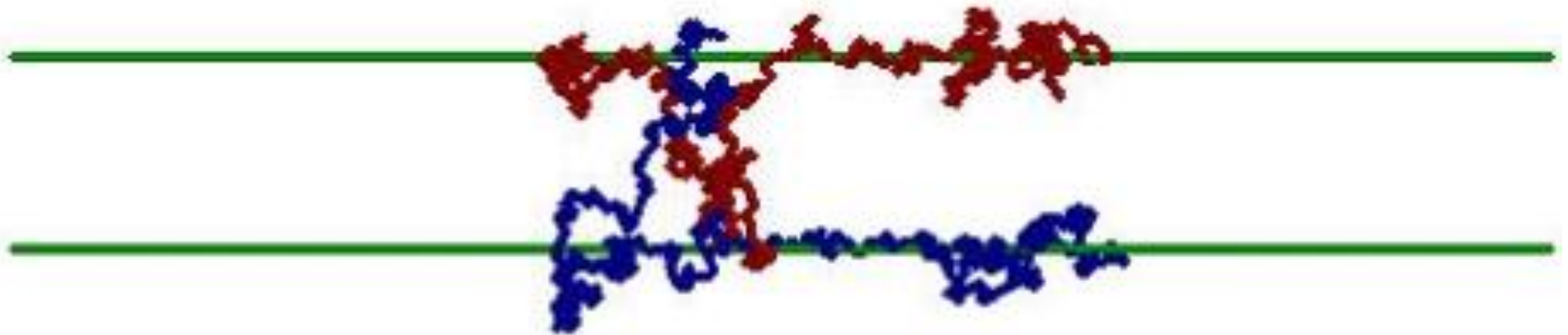

Quick and reliable separation occurs
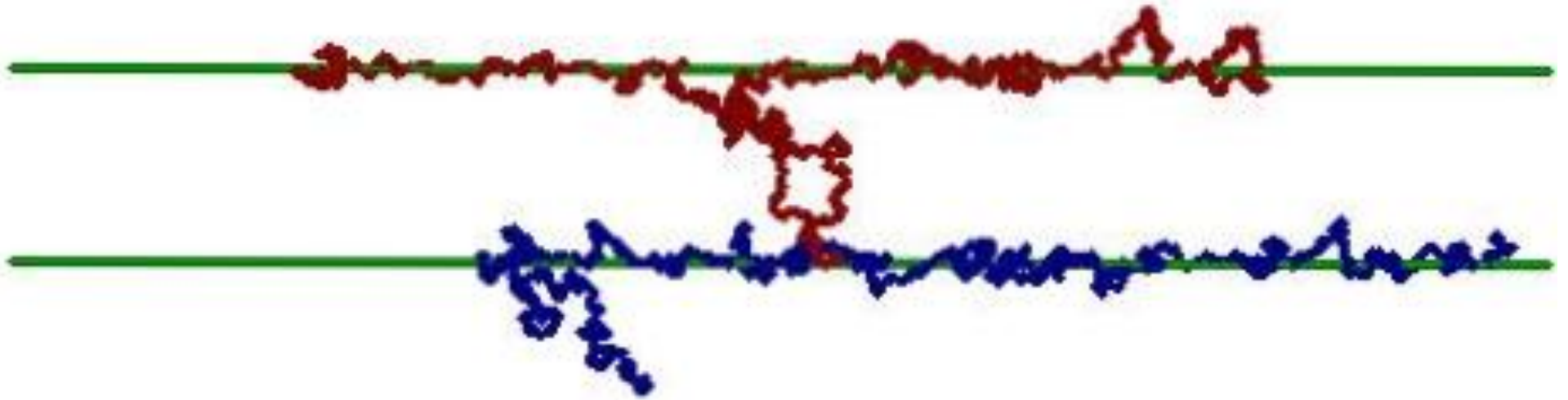
Another Example

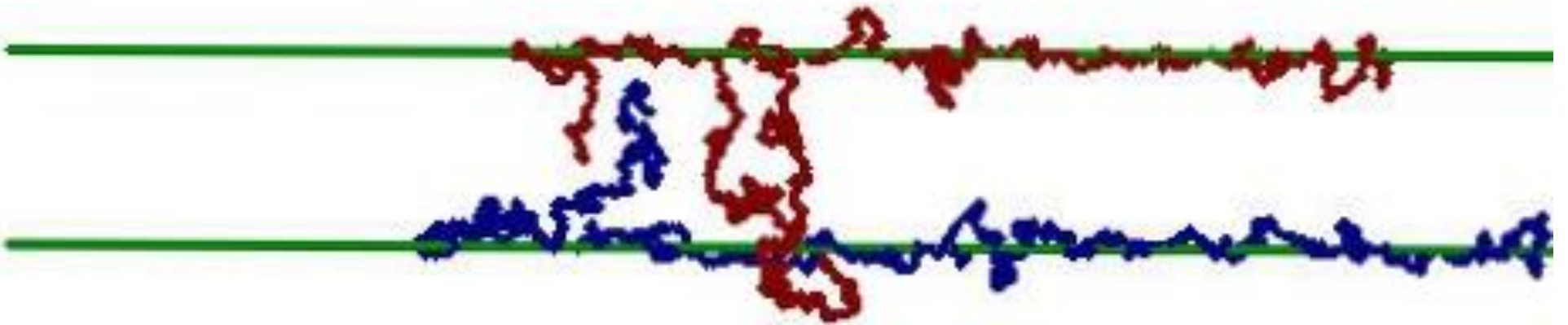# Another Example
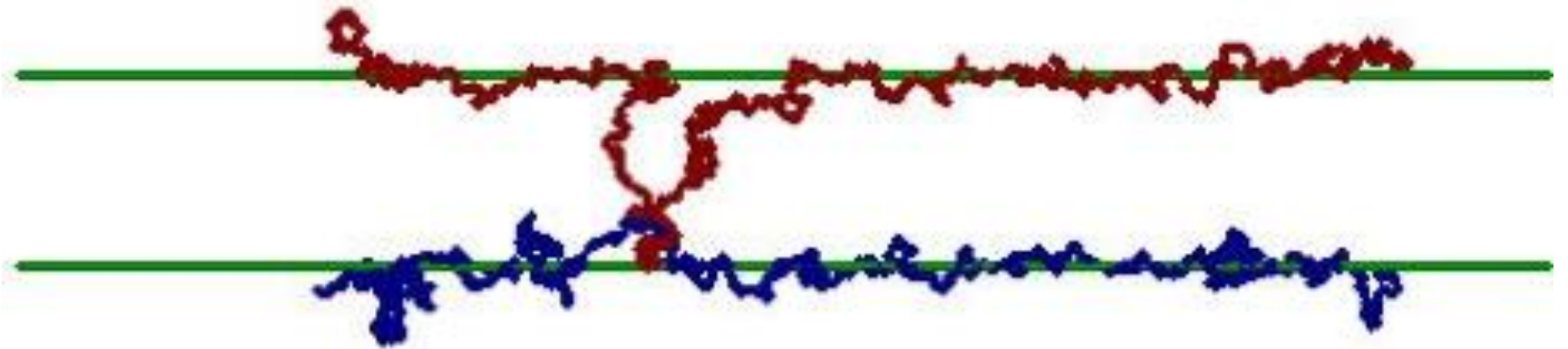
Another Example

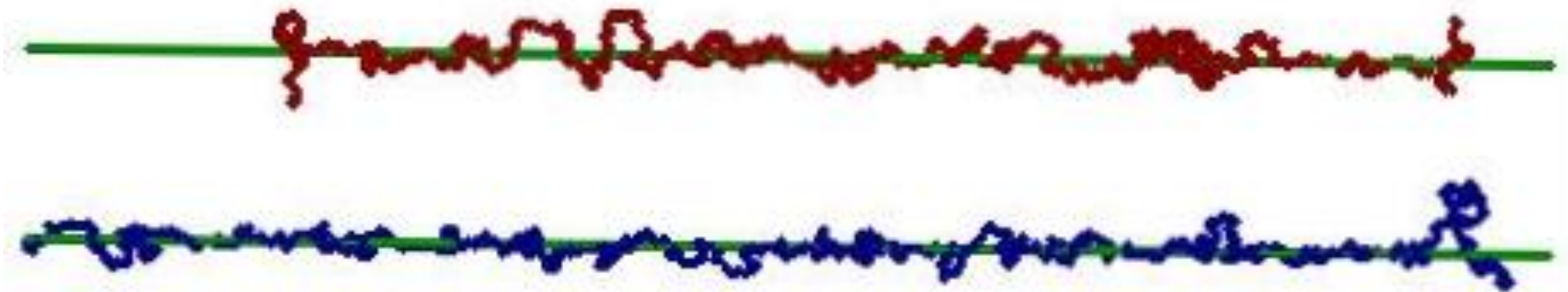# Another Example

Another Example

Another Example

Another Example

Another Example

Successful separation achieved under certain regimes suggests that scaffold assisted condensation may be a feasible mechanism

Future directions

Gather quantifiable data concerning parameters involved and try to characterize ideal parameters numerically

Try more chain lengths and different starting chain positions

Look for other parameters that may be involved

Simulate a model more resembling the X-shape of the chromosome

Great Thanks to:

PRIMES
Prof. Leonid Mirny
Geoffrey Fudenberg and
Maxim Imakaev