# Simulations

## I) Simulations are multiscales

Time

Years — Medicine

Second — $\nabla^2\phi = -\rho$

$\mu s$ — Biochemistry, Chemistry

ps — $F = ma$ — Molecular Mechanics

Femtosecond — $H\psi = E\psi$ — Quantum Mechanics

Length

Yards, Meters — Planes, animals

Centimeters — Materials

$\mu m$ — Material Science

nm — molecules

Atoms

Angstroms — electrons

## II) Two types of simulations

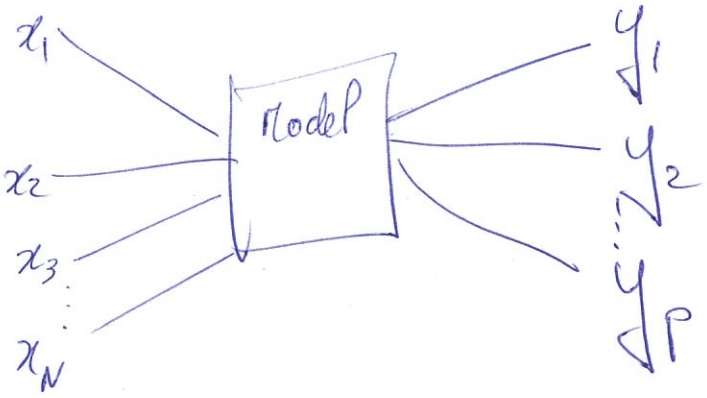
Simulation is the imitation of the operation of a real world process over time.

The act of simulating requires that a model be developped.

The model represent the system, whereas the simulation represents the operation of the system over time.

## Deterministic simulations

They contain no random variables and no degree of randomness, and usually consist mostly of equations, for example differential equations. They have known inputs, and they result in a unique set of outputs

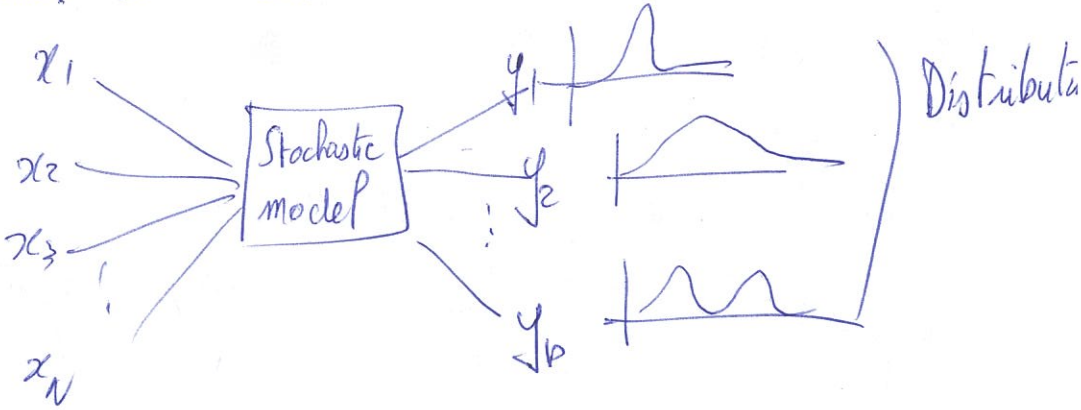



→ Same input → Same output.

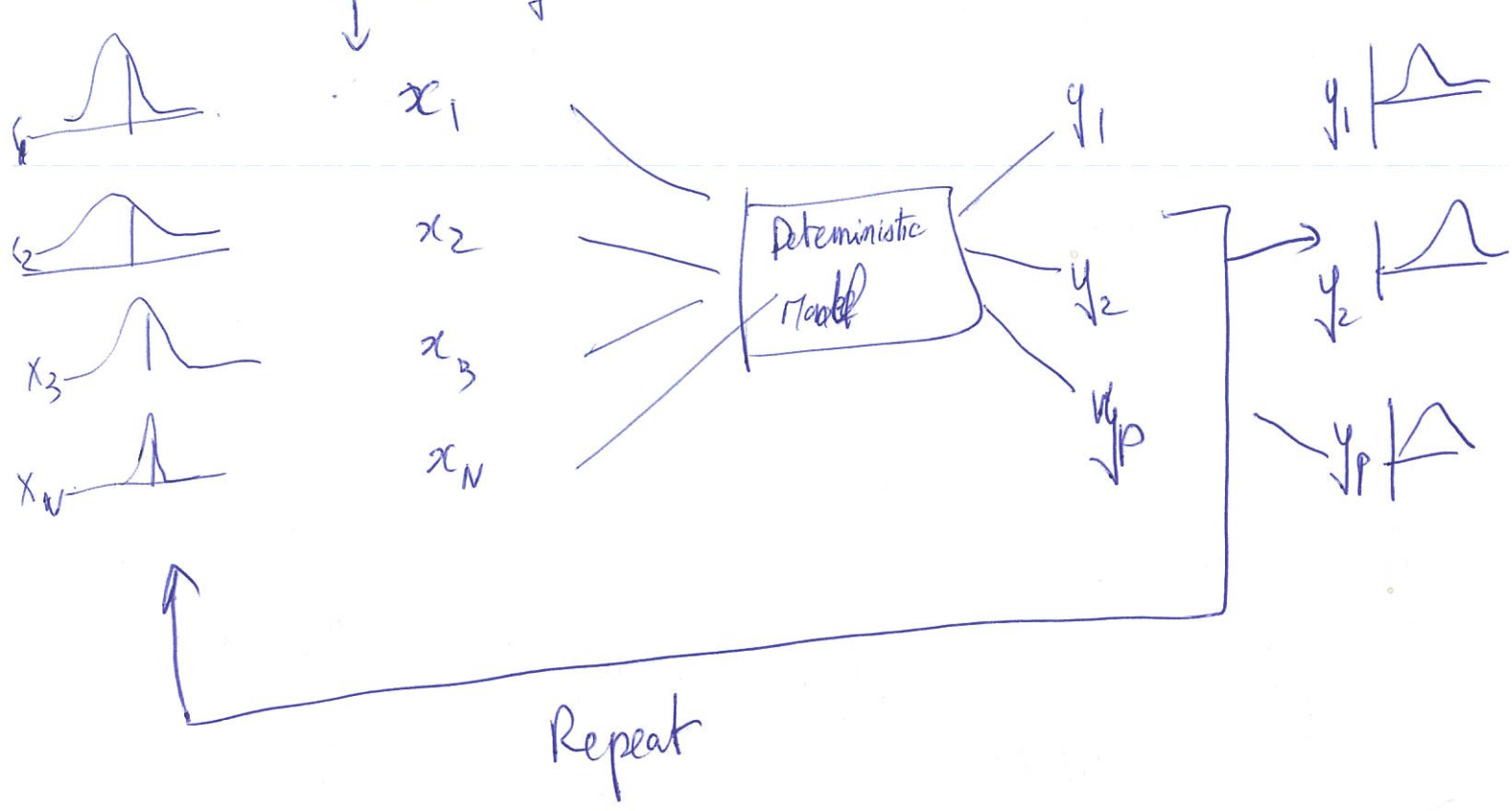
→ often non invertible.

## Stochastic simulations

Stochastic simulations rely on stochastic model, i.e a model with randomness. It is generally not solved analytically. Usually, a random number is drawn to mimic the randomness and execute a trial → Monte Carlo method or Monte Carlo Simulation.



## Combining the two




## III) One example of deterministic simulation: Molecular dynamics (MD)

MD: MD : simulates the behavior of a molecular system as a function of time.

Model : Newton's equation: $\vec{F} = m\vec{a}$

But we need to be more precise:

- Description of the system
- Description of the interaction (how to compute $\vec{F}$)
- Algorithm to solve Newton's equation.

## The system:

what is an atom?

- classical mechanics: a point particle
- parameters: { - position, and mass
  charge (positive or negative)
  usually partial.

## The force:

$$U = \sum_{\text{all bonds}} \frac{1}{2} K_b (b - b_0)^2$$

$$+ \sum_{\text{all angles}} \frac{1}{2} K_\theta (\theta - \theta_0)^2$$

$$+ \sum_{\text{all torsions}} K_\phi [1 - \cos(n\phi)]$$

$$+ \sum_{i,j \text{ non bonded}} \varepsilon_{ij} \left[ \left( \frac{r_{ij}}{r_{ij}} \right)^{12} - 2 \left( \frac{r_{ij}}{r_{ij}} \right)^{6} \right]$$ Vdw

$$+ \sum_{i,j \text{ non bonded}} \frac{q_i q_j}{4\pi \varepsilon_0 \varepsilon r_{ij}}$$ Lennard Jones.

$$\vec{F}_x = - \frac{\partial U}{\partial \vec{x}}$$

## What is MD?

- shows how the atoms in the system move as a function of time
- typically on the nanosecond timescale
- Atoms are treated like hard balls, and their motions are described by Newton's law

## How do we run an MD

### (a) Get the initial configuration

Experimental structure (in PDB) from X-ray crystallography or NMR spectroscopy.

### (b) Assign initial velocity.

At thermal equilibrium,

$$\langle E_{Kin} \rangle = \frac{1}{2} \sum_{i=1}^{3N} m_i v_i^2 = \frac{1}{2}(3N) k_B T$$

$\rightarrow$ Assign $\frac{1}{2} m_i \langle v_i^2 \rangle \simeq \frac{1}{2} k_B T$

$\rightarrow$ $\langle v_i^2 \rangle \simeq \frac{k_B T}{m_i}$

$\rightarrow$ pick $v_i$ from a Gaussian distribution with mean 0 and variance $\frac{k_B T}{m_i}$

(c) For each time step.

Compute force on each atom.

$$F(x) = -\nabla U = -\frac{\partial U}{\partial x}$$

Solve one step for:

$$m\ddot{x} = F(x) \rightarrow \begin{cases} m\frac{dV}{dt} = F(x) \\ \frac{dx}{dt} = V \end{cases}$$

(d) Repeat over N time steps

$$\begin{cases} V(t+\Delta t) = V(t) + \Delta t \frac{F(x)}{m} \\ x(t+\Delta t) = x(t) + \Delta t\, V(t) \end{cases}$$

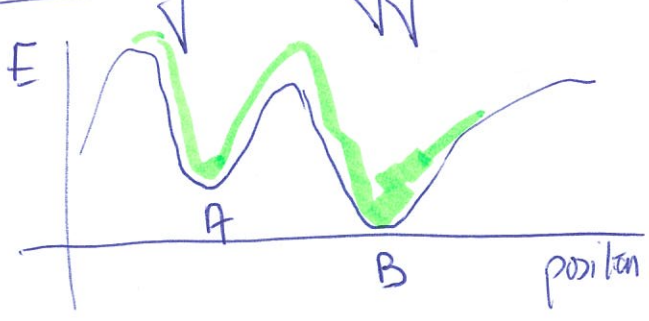
$\Delta t$ needs to be small enough.

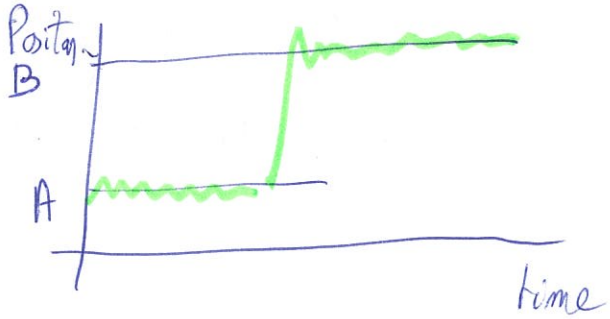
usually, $\Delta t \simeq 10^{-15}$

* MD can be a tool for minimization

MD uses thermal energy to explore the energy surface.


* Crossing energy barriers.



The actual transition time from A to B is very quick (a few pico seconds).
What takes time is waiting. The average waiting time:

$$\tau_{A \to B} = C e^{\frac{\Delta G}{RT}}$$

## IV Stochastic simulations: Monte Carlo

### A simple example: evaluate integrals.

let us consider: $I = \int_a^b f(x)\,dx$

Let $\bar{f}$ be the mean value of $f$ over $[a\ b]$

Then: $I = (b-a)\,\bar{f}$

For continuous function, this does not help, as $\bar{f}$ is usually evaluated with $I$!

However, if we can build an approximation of $\bar{f}$: $\hat{\bar{f}} \simeq \frac{1}{N} \sum_{i=N}^{N} f(x_i)$, with $x_i \in [a, b]$

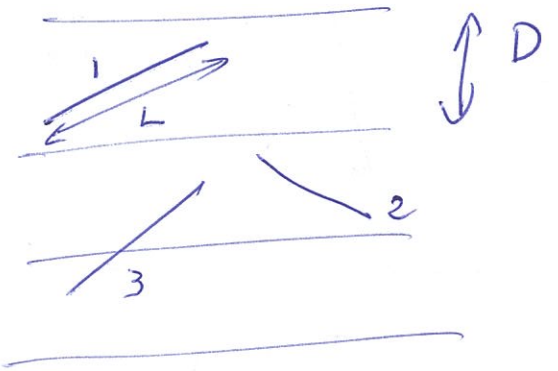
then $I \simeq (b-a)\,\hat{\bar{f}}$

This is the concept of Monte Carlo integration!

# A famous example: Buffon's needle problem.

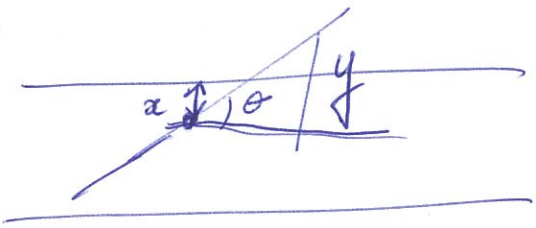
Let us consider:

Suppose we have a floor made of parallel strip of woods, of width D, and we drop a needle of length L (with $L < D$) onto the floor. What is the probability that the needle will lie across a line between 2 strips?




1 and 2 do not cross while 3 crosses.

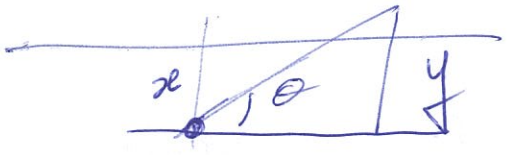
Analytical answer:



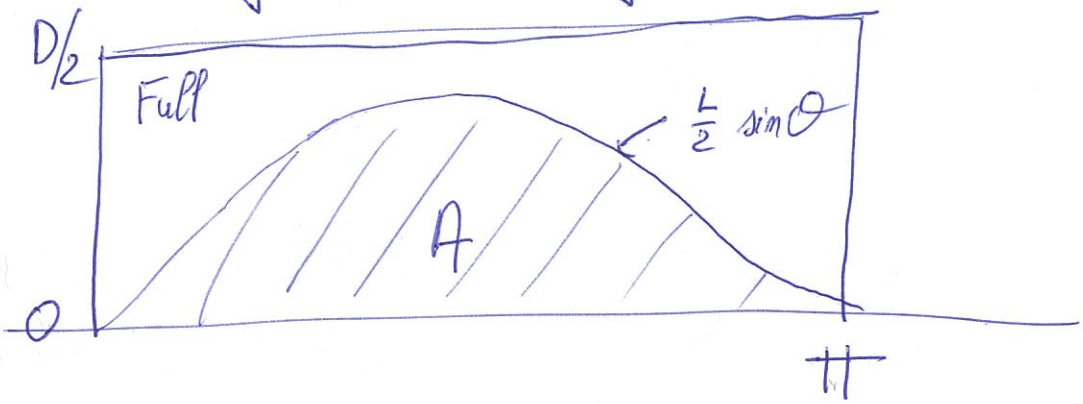

The position of the needle is defined by two variables:

$x$: distance between the middle of the needle and the closest line: $x$ can take any values between 0 and $\frac{D}{2}$

$\theta$: angle between needle and the lines: $\theta$ can take any values between 0 and $\pi$




For a given value of $\theta$, the needle crosses the line if $x \leq y$, with $y = \frac{L}{2}\sin\theta$




$$P = \frac{\text{Area (A)}}{\text{Area (Full)}}$$

$$\text{Area (Full)} = \frac{\pi D}{2}$$

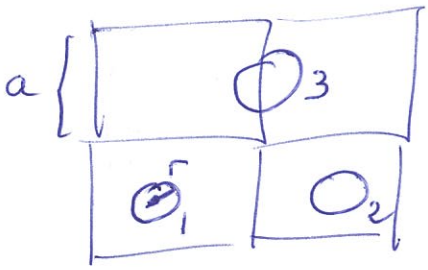
$$\text{Area (A)} = \int_0^{\pi} \frac{L}{2}\sin\theta\, d\theta = \frac{L}{2}\left[-\cos\theta\right]_0^{\pi} = \frac{L}{2}(1+1) = L$$

Therefore $$\boxed{P = \frac{2L}{\pi D}}$$

Buffon then wrote: $\pi = \frac{2L}{PD}$, estimated P by actually doing the experiment (!) and found a reasonable estimate of $\pi$!

Small esercice:

Consider a floor made of regular square of woods, with side $a$. We drop a coin of radius $r$ (with $r < a$) onto the floor. What is the probability that the coin will be across a line between 2 squares?




1 and 2 do not cross, while 3 crosses.

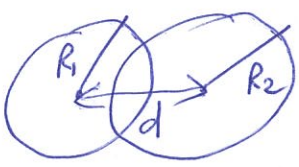
Answer: $$P = \frac{4ar - 4r^2}{a^2}$$

Example of application: Measure the surface area of a union of overlapping disks.

- If I have one disk:


$$S = 4\pi R^2$$

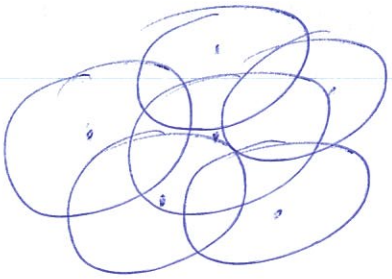
- If I have two disks:




already complicated! Answer with google..

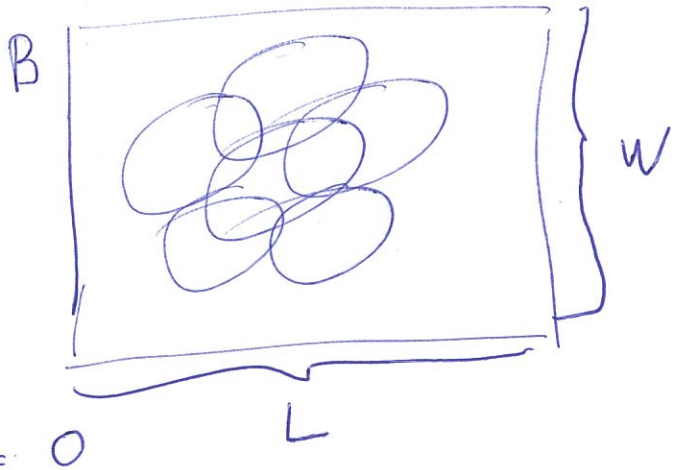
More than 2 disks... you won't find the answer!

Let us use a Monte Carlo Method:



Let us consider N disks, with disk i described by center $C_i$ and radius $R_i$.

(i) Find box B (squared) that contains all the disks:




(ii) Initiate $\bar{F} = 0$

(iii) For M random points:

~~Initiate F.~~

(a) position point m randomly in the box:

$P_M$

(b) Check if $P_M$ inside a disk a not:

For each disk i, compute $d(P_M, C_i)$ and compare with $R_i$

if $P_M$ inside (at least) one disk,

$$\bar{F} = \bar{F} + 1$$

otherwise $\bar{F}$ stays the same.

(iv) Set $\bar{F} = \dfrac{\bar{F}}{M}$

$\bar{F}$ is the probability that a random point $P_M$ falls in the union of disk.

$$\bar{F} = \frac{\text{Area (Union)}}{\text{Area (Box)}}$$

Therefore, $\text{Area (Union)} = \bar{F}\ \text{Area (Box)}$

$$= \bar{F} \times (W \times L)$$

Thank you!