LIÈGE université
Gembloux
Agro-Bio Tech

AgricultureIsLife.be

Use of molecular dynamics simulations to study the interactions between barley allelochemicals and plant plasma membrane

S. Lebecque[1,2], JM Crowet[2], P. du Jardin[3], ML Fauconnier[4], B. M. Delory[5], M. Deleu[2], L. Lins[2]

[1]TERRA – AgricultureIsLife, [2]Laboratory of Molecular Biophysics at Interfaces, [3] Laboratory of Plant Biology, [4]General and Organic Chemistry Laboratory, **Gembloux Agro-Bio Tech, University of Liège, Belgium**
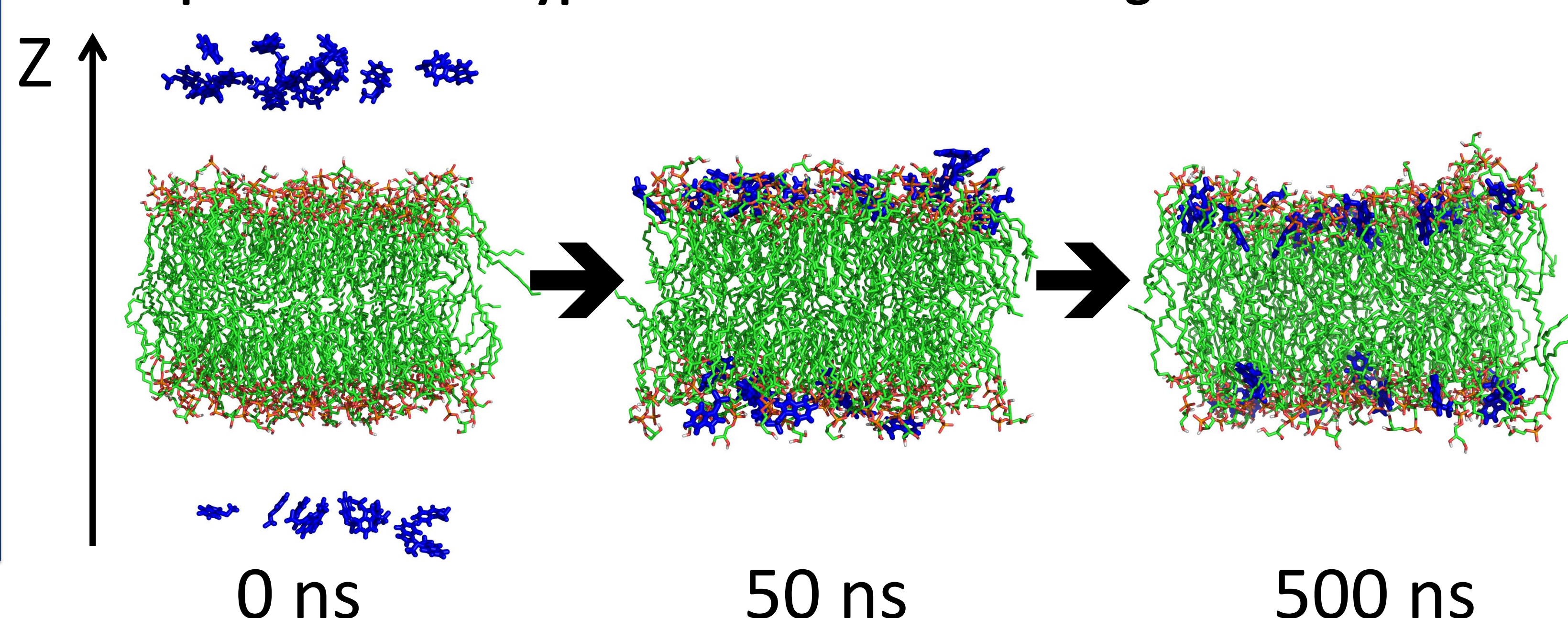[5]Institute of Ecology, **Leuphana University, Lüneburg, Germany**

Background

Gramine and hordenine, two alkaloids produced by barley, were shown to inhibit the growth of a common weed (*Matricaria recutita* L.). This feature could be useful in order to reach a more sustainable weeds management. *In vitro* experiments have proven that both molecules do interact with lipid bilayers (made of a phosphatidylglycerol (PG) lipid) mimicking plant plasma membranes and are able to modify some of their properties.

Moreover, gramine was shown to be more effective than hordenine in both inhibiting weeds growth and altering lipid bilayers properties, suggesting that interactions with membranes could be linked to their mode of action. Molecular dynamics (MD) simulations are carried out in order to get an insight into the molecular mechanisms that underlie these interactions with model membranes and to discriminate between gramine behavior and hordenine behavior.
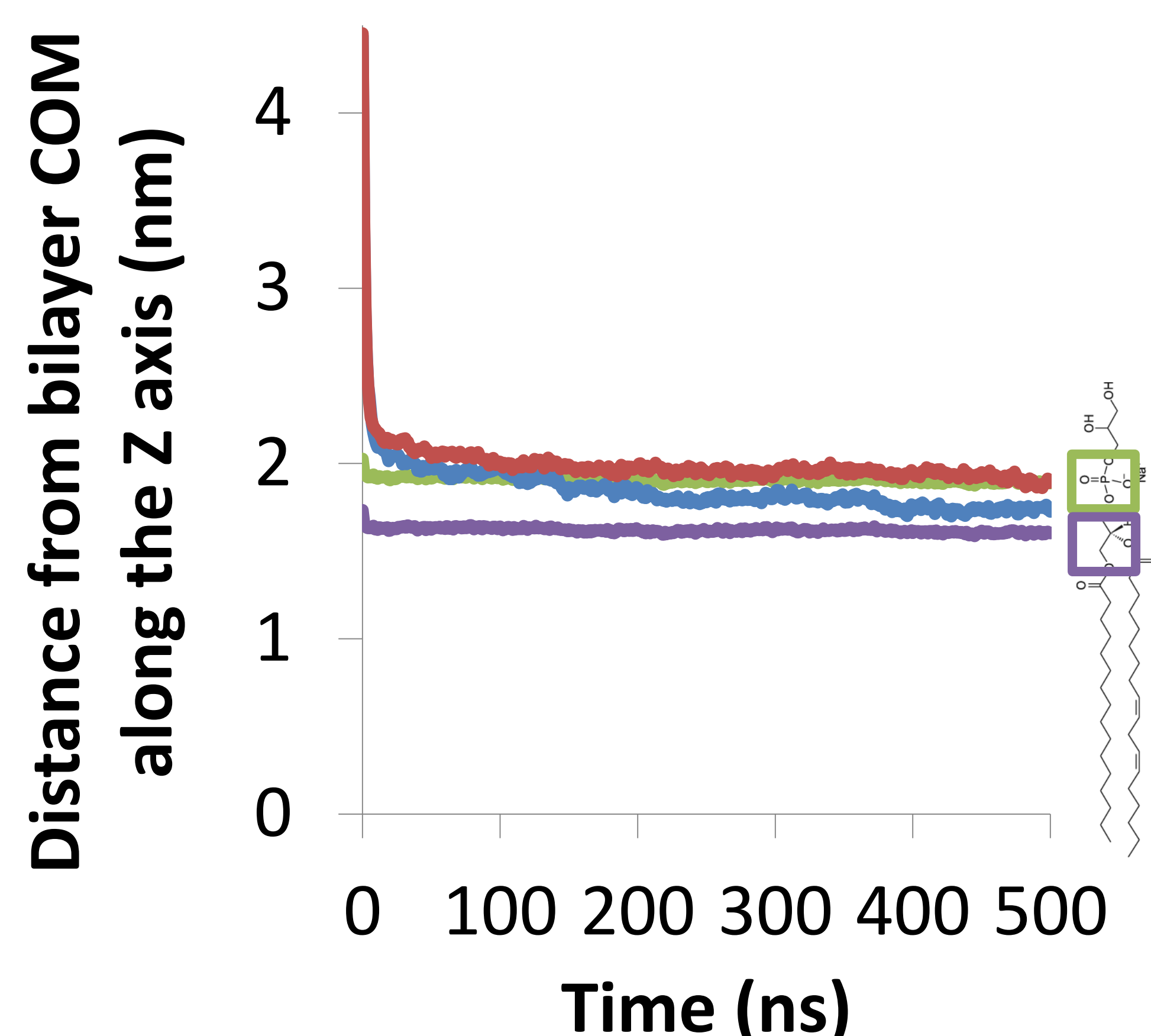
Simulations details

- Starting from a box that includes:
  - 128 PG lipid molecules forming a bilayer
  - 32 gramine (blue-colored in snapshots) or hordenine molecules located outside the bilayer
  - water molecules and ions (omitted in snapshots for clarity)
- Software = GROMACS ➔ simulates the evolution of the system
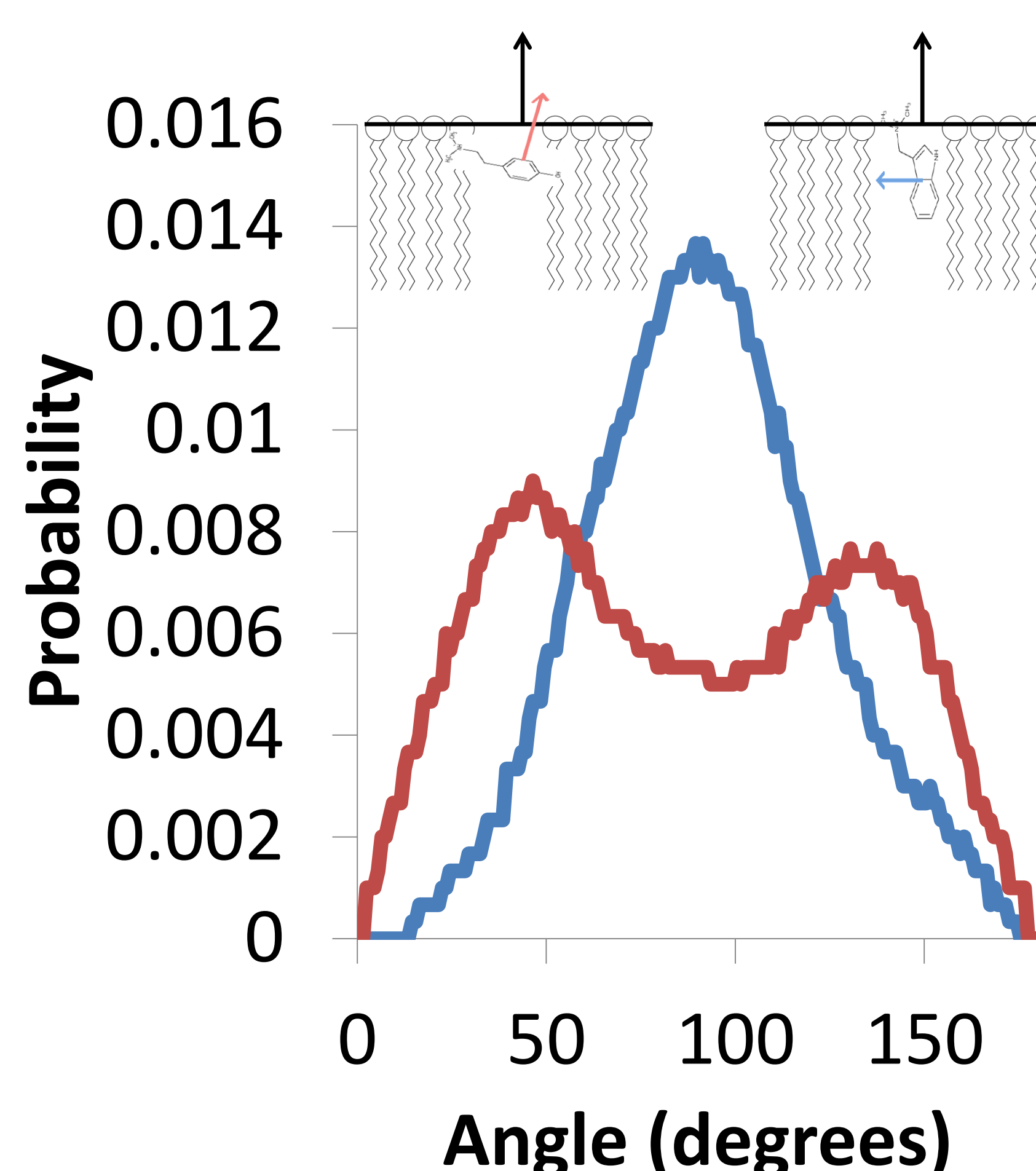- Simulation length = 500 ns

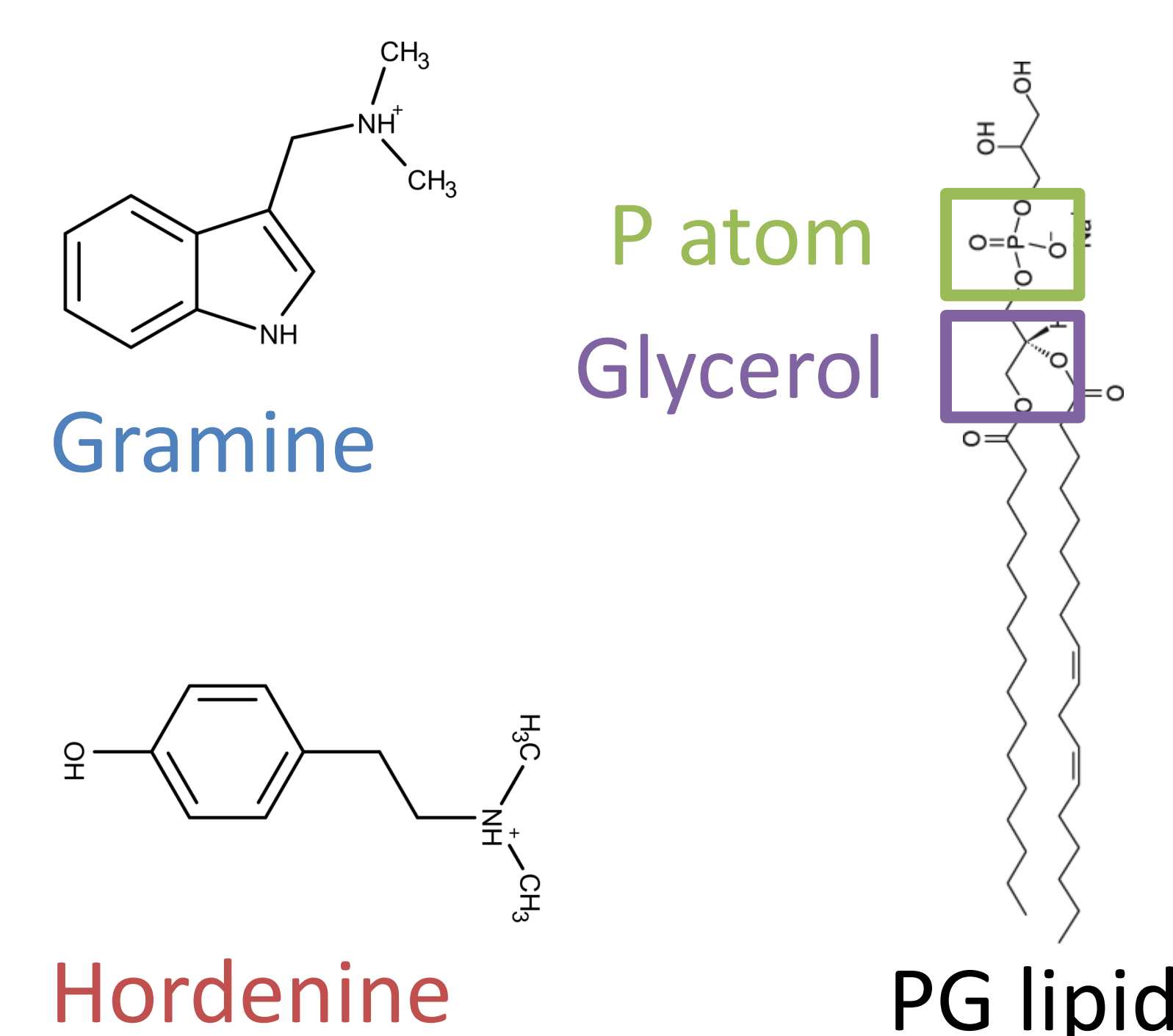### Snapshots from a typical simulation with 32 gramine molecules

0 ns → 50 ns → 500 ns

What is their location?

Time evolution of the average distance between the center of mass of the bilayer and molecules or atom groups (see legend on the right) along the Z axis. As demonstrated by *in vitro* experiments, gramine and hordenine molecules spontaneously insert into lipid bilayer. Hordenine is located around P atoms of lipids, while gramine is located deeper within the bilayer.

What is their orientation?

Distribution of angles between the bilayer normal and vectors orthogonal to the cyclic plane of each alkaloid during the last 100 ns of simulation. The unimodal, 90°-centered distribution observed for gramine indicates that gramine cycle is buried roughly perpendicularly to the bilayer surface. On the contrary, hordenine cycle is preferentially more parallel to the bilayer surface.

Molecular structures and legend

Gramine

Hordenine

P atom
Glycerol

PG lipid

Is that all MD has to offer? No!

It is possible to monitor various parameters, such as bilayer thickness, area per lipid, lipid order parameter, hydrogen bonds between molecules and lipids... In addition, lipid composition can be modified in order to model different types of membranes or to highlight any specific interaction that occurs between a molecule and a given lipid species.

Conclusion

A detailed picture of gramine and hordenine positioning within lipid bilayers is given by molecular dynamics simulations and differences in their respective location and orientation are evidenced. It contributes to a better understanding of how and why gramine is more able to disturb lipid bilayers than hordenine which could, ultimately, be linked to their mode of action.