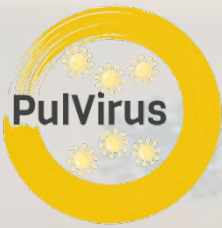


Virus e PM: modellistica molecolare dell'interazione fra la proteina Spike e PM

Caterina Arcangeli
ENEA – Laboratorio Salute e Ambiente



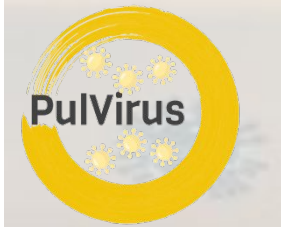
Obiettivo 5 – Attività

Attività 5.1 - Studio *in silico* di modellistica molecolare dell'interazione diretta tra le proteine di superficie del virus SARS-CoV-2 e PM

Attività 5.2 - Studi dell'interazione fra PM e SARS-CoV-2 mediante l'utilizzo di un virus modello e identificazione del microbioma ambientale

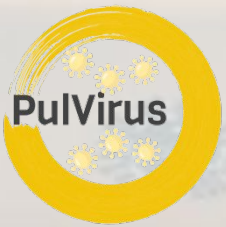
Attività 5.3 - Studi degli eventi molecolari derivanti dall'interazione dei meccanismi di azione del PM e SARS-CoV-2

Attività 5.4 - Studi dell'interazione della distribuzione del bio-aerosol in ambienti confinati (indoor)

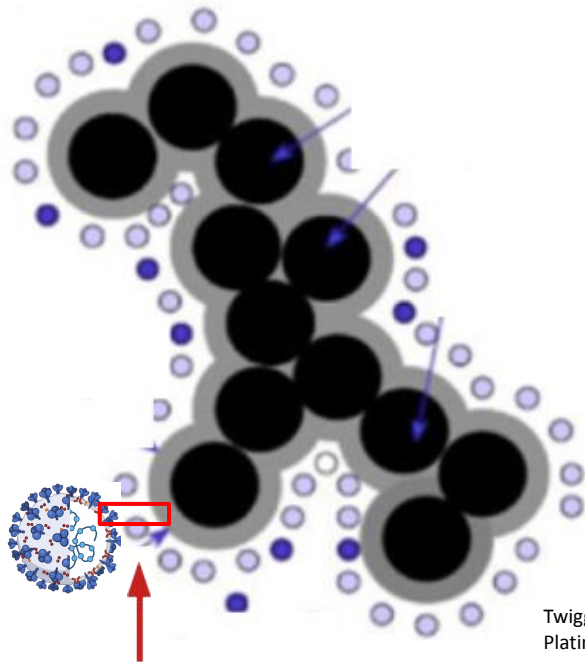


Obiettivo 5.1 – Prodotti

- P5.1.1 Modelli strutturali delle proteine di superficie del Virus SARS-CoV-2
- P5.1.2 Modelli strutturali del PM
- P5.1.3 Interfaccia PM-virus
- P5.1.4 Dinamica e stabilità del complesso PM-virus. Effetto del PM sulle proteine



The PULVIRUS strategy



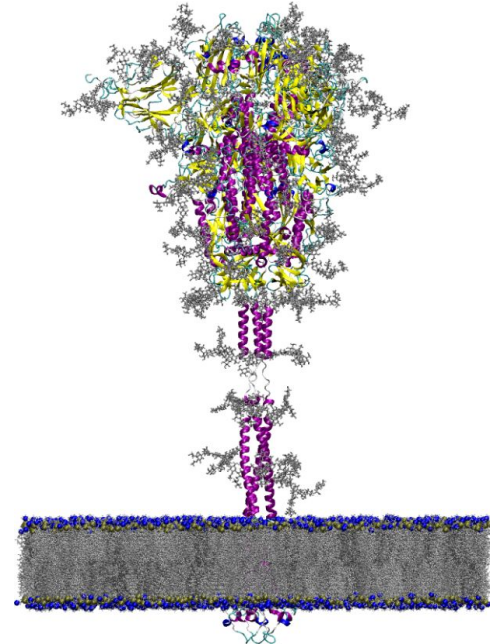
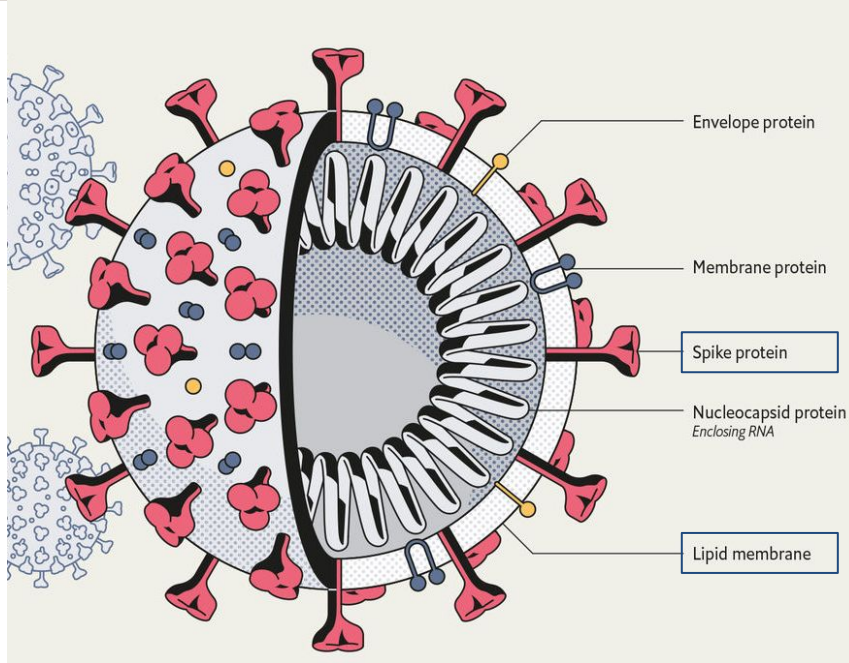
SARS-CoV-2
(\varnothing 150 nm)

Fine particulate matter
PM2.5
(\varnothing 2500 nm)

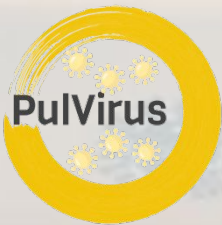
virus-PM interface

Twiggs, M.V., & Phillips, P.R. (2009).
Platinum Metals Review, 53, 27-34.

VIRUS model

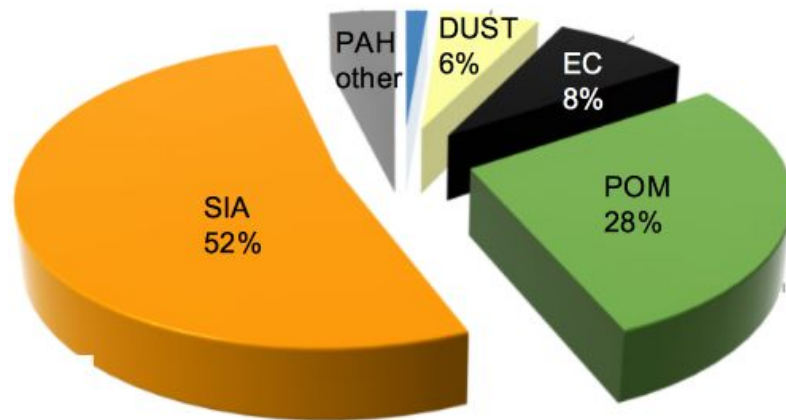


Woo,H. et al (2020) J. Phys. Chem. B.
124:7128–7137

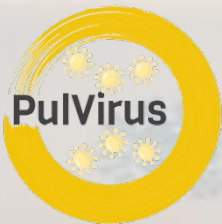


PM model

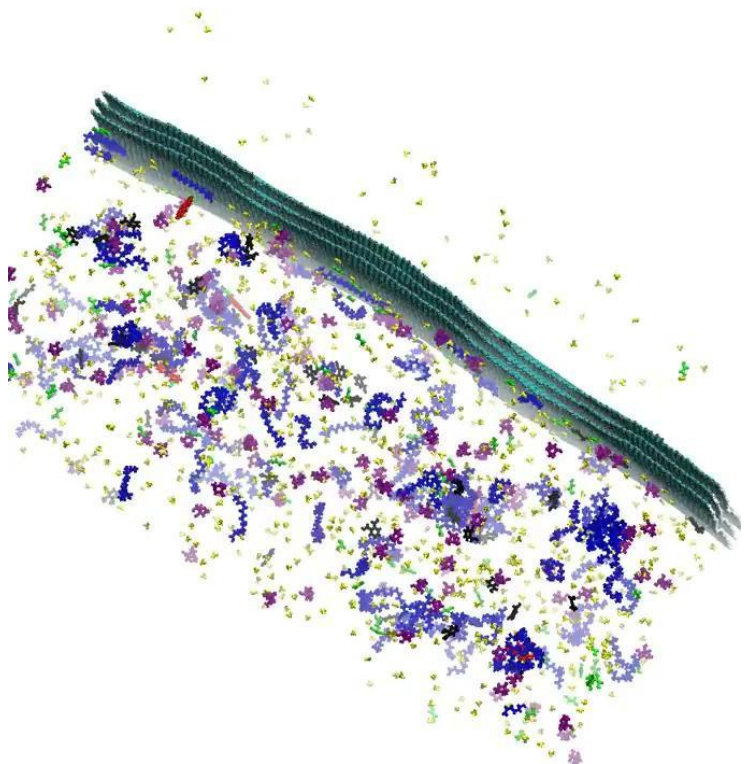
- **Secondary Inorganic Aerosol (SIA)**
 - Ammonium Nitrate ($\text{NH}_4 \cdot \text{NO}_3$)
- **Secondary Organic Aerosol (SOA)**
 - PAH – benzo[a]pyrene
 - Aromatic Acids – phtalic acid
 - Aliphatic Acids – oxalic acid
 - Alkaloid Acids – palmitic acid
 - Carbohydrates (POM) – levoglucosan



PM 2,5 Bologna 2018



MD simulation of PM_{2.5}

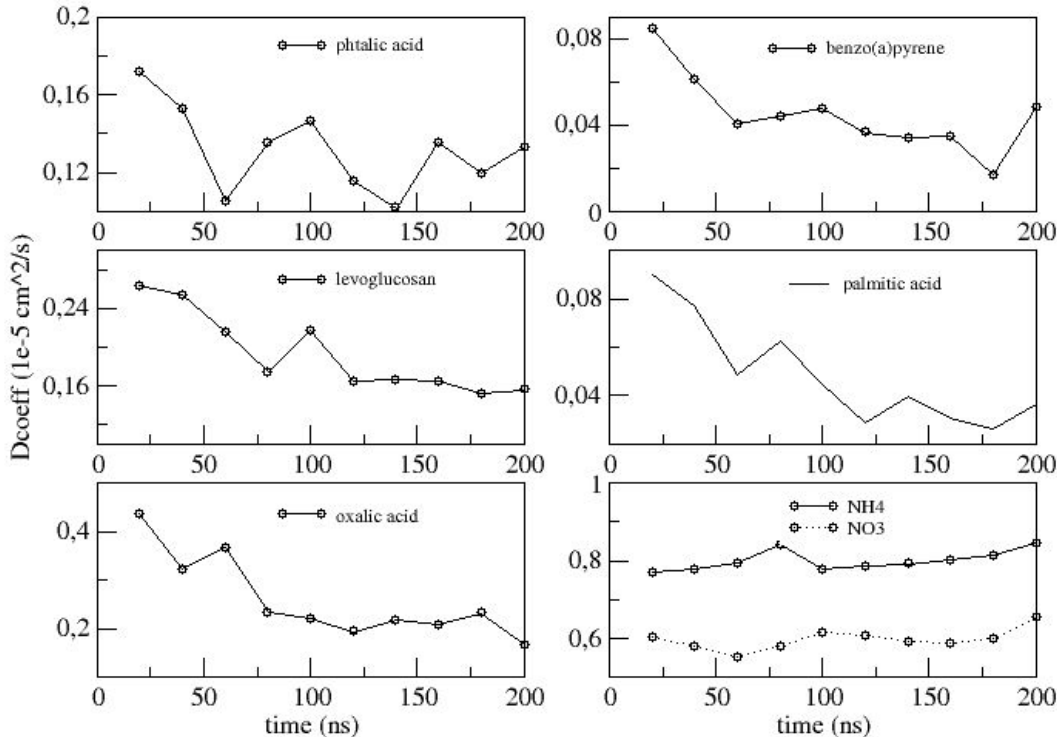


NAMD
Scalable Molecular Dynamics



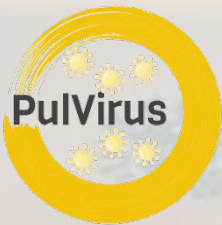
- ❑ Force field: CGenFF + CHARMM
- ❑ TIP3P solvent model (not shown)
- ❑ ca. 922.000 atoms
- ❑ 200 ns
- ❑ performance 3.5 ns/day (12 nodes CRESCO 6 HPC cluster)

Diffusion Coefficient

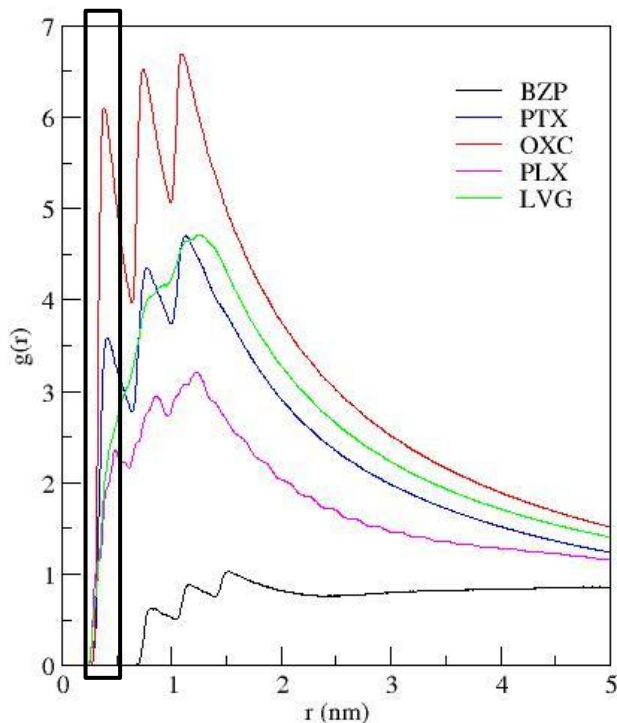


Are the molecules able to diffuse freely in the solvent or their movements are limited by some constraints?

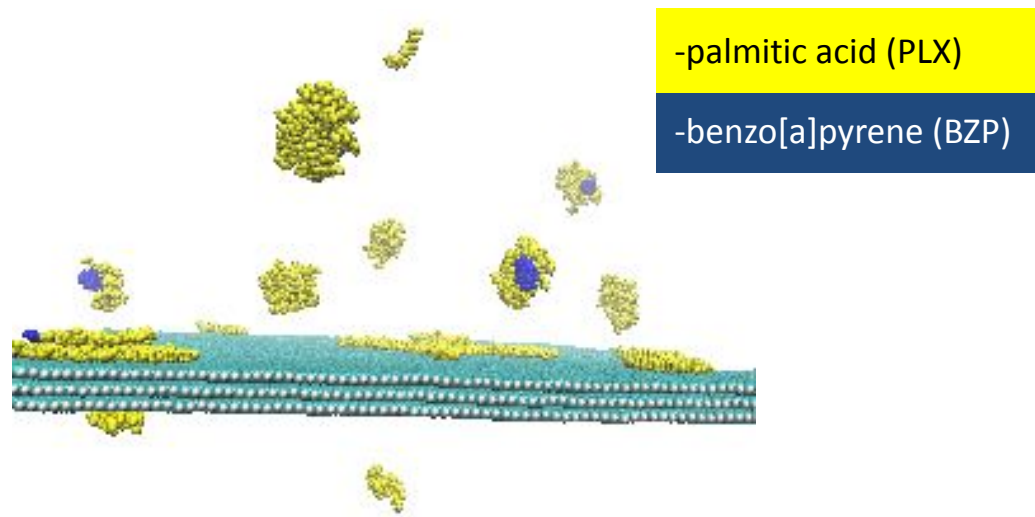
In this simulation the constraint is represented by the interaction of the molecules with graphene or by the formation of aggregates.

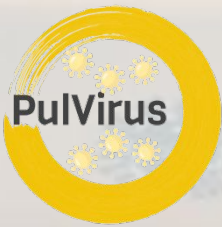


Radial Distribution Function

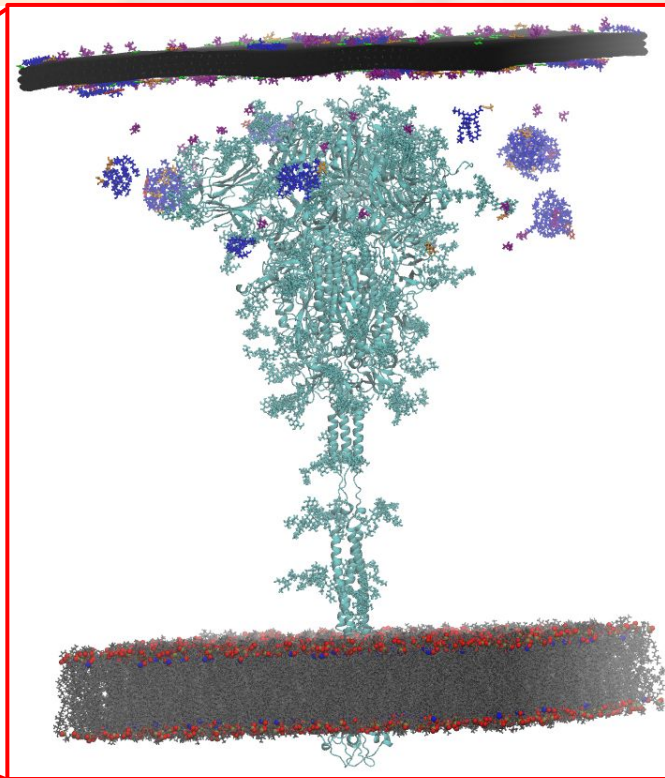
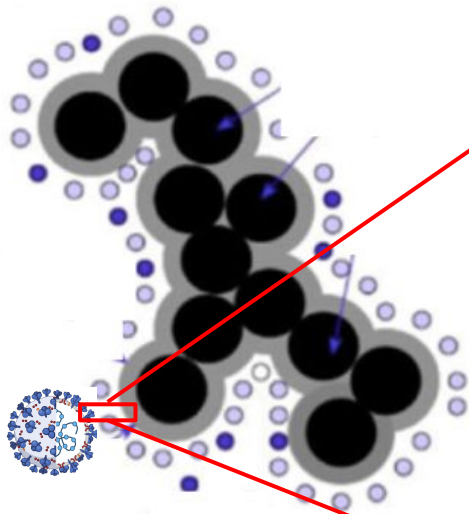


The function $g(r)$ measures the probability of finding the PM's molecules within a distance " r " from the graphene.





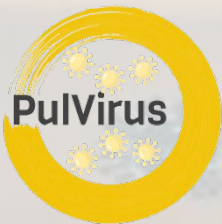
Virus-PM interface model



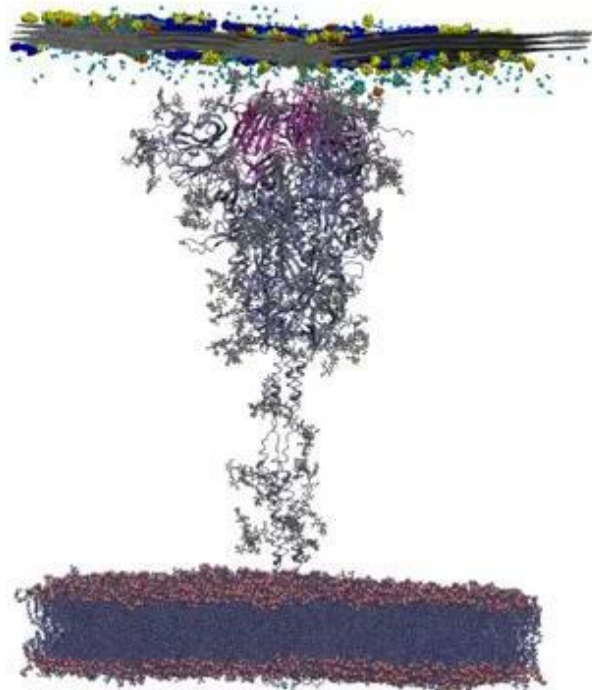
PM

Spike
glycoprotein

Viral
membrane



Virus-PM simulation



NAMD
Scalable Molecular Dynamics



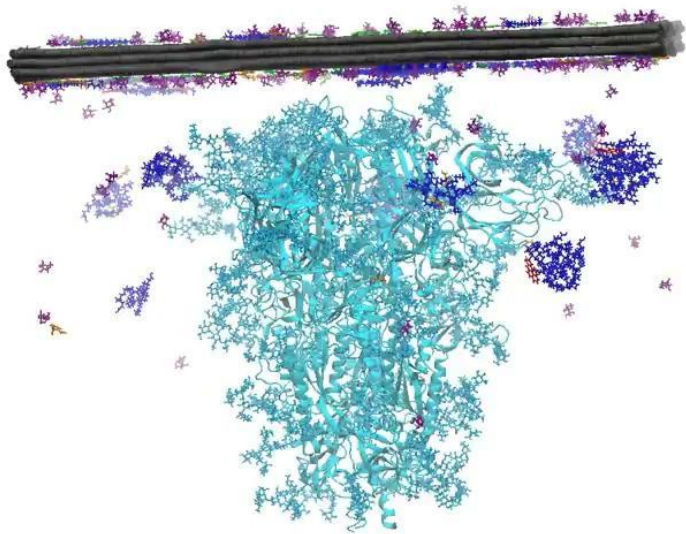
- ❑ ca. 2.48 millions of atoms
- ❑ 40 ns
- ❑ performance 2 ns/day (14 nodes CRESCO 6 HPC cluster)

Spike-PM simulation

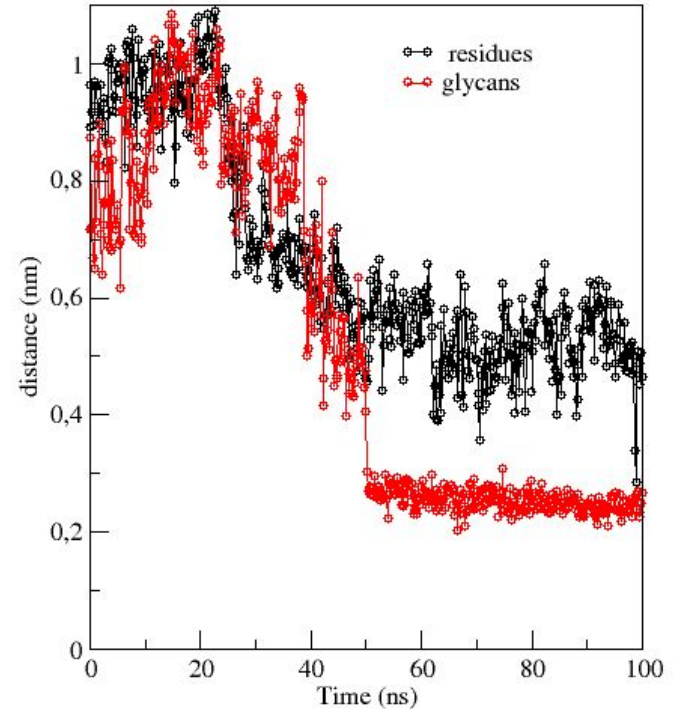
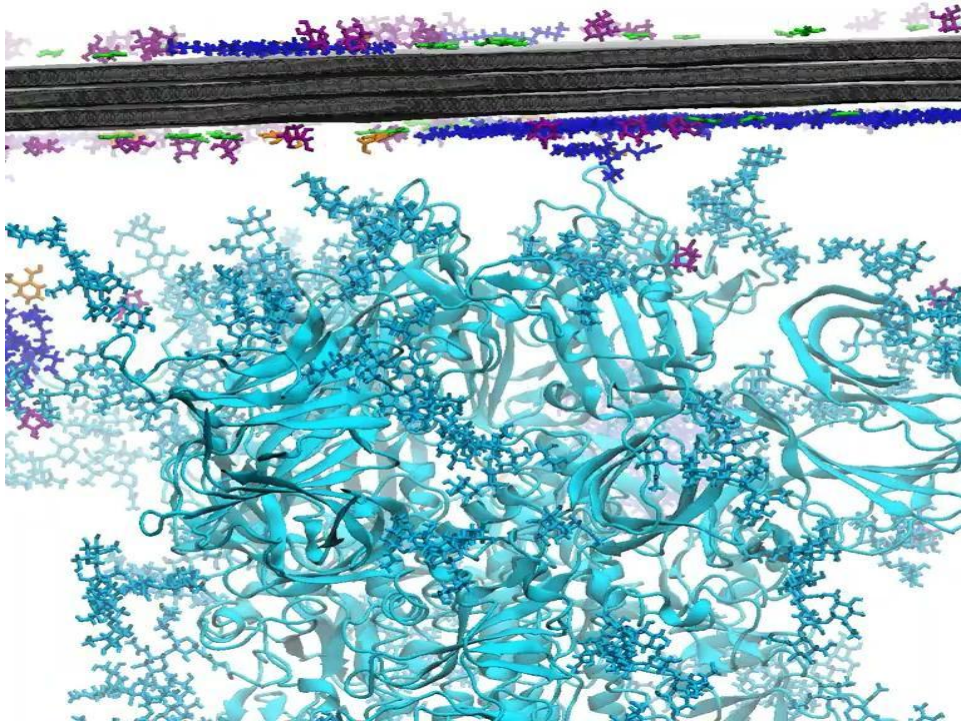
NAMD
Scalable Molecular Dynamics

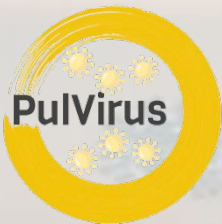


- ❑ ca. 1.60 millions of atoms
- ❑ 100 ns
- ❑ performance 3.5 ns/day (14 nodes CRESCO 6 HPC cluster)

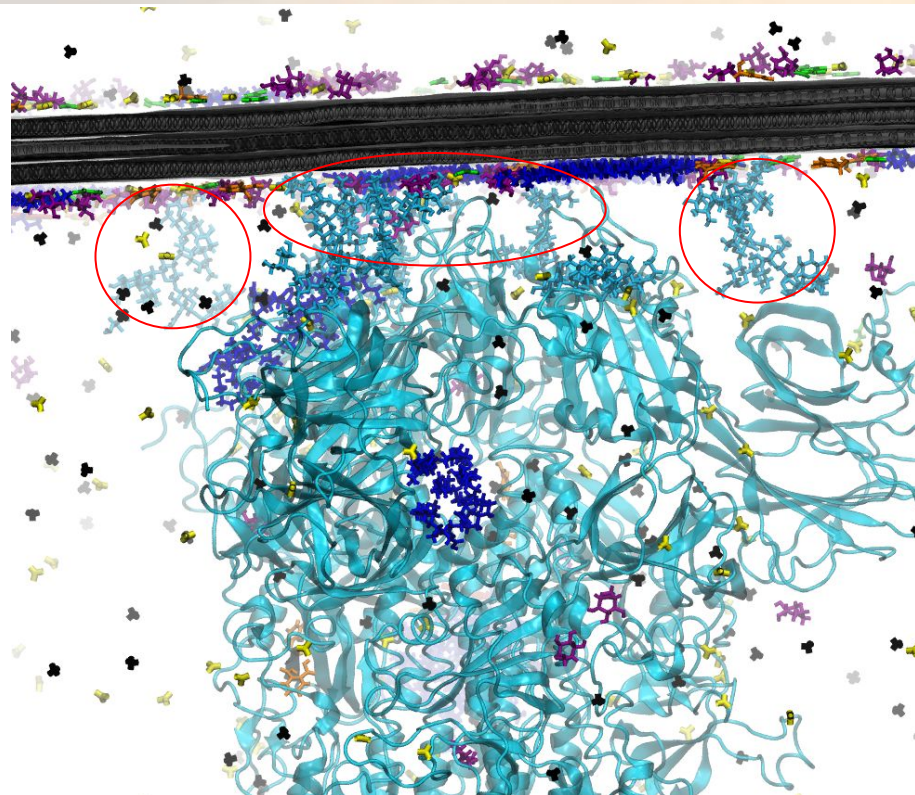


Spike-PM interaction





The glycans interact with graphene

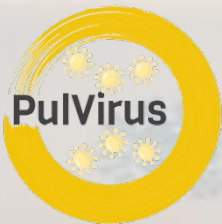


Hydrogen bonds
Glycans – Graphene

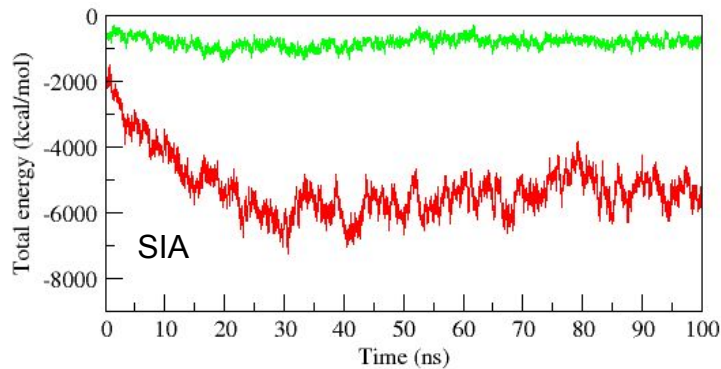
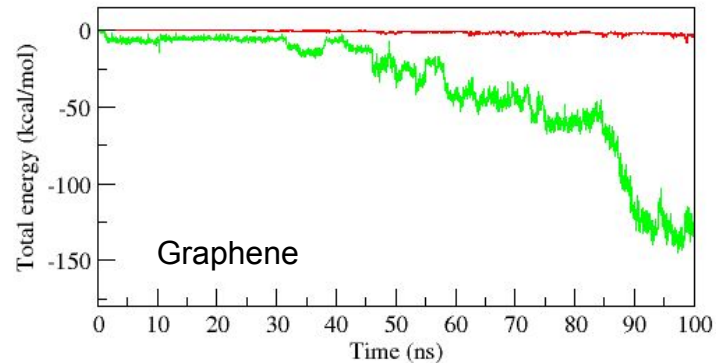
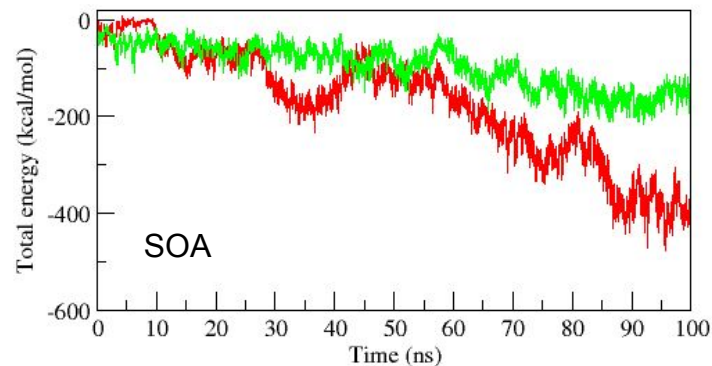
L-Fucose

D-Glucose

D-Galactose

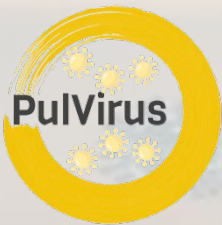


Total interaction energy (Electrostatic + VdW)



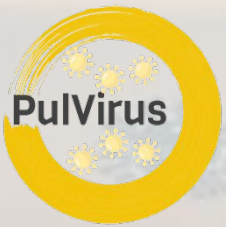
— Protein
— Glycans

Note: All favorable interaction energies are <0 kJ/mol, and hence have a negative sign



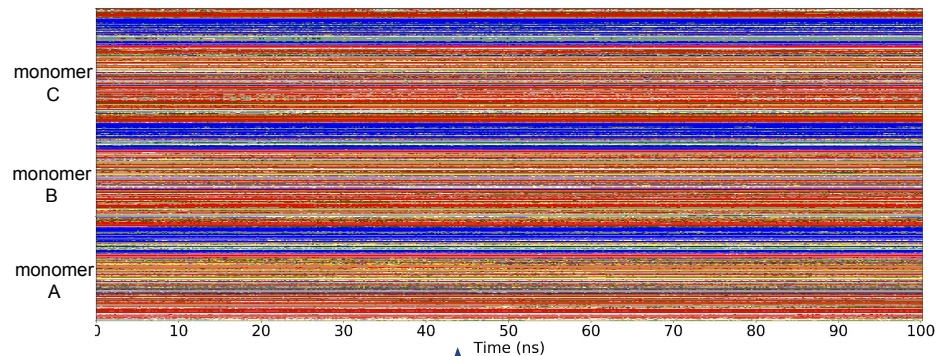
Average interaction energy (last 50 ns)

Interactor 1	Interactor 2	Electrostatic (kcal/mol)	Van der Waals (kcal/mol)
Spike glycoprotein	Graphene layer	/	-67.3 ± 36.1
	SOA	-144.6 ± 60.5	-245.6 ± 71.4
	SIA	-5942.1 ± 490.4	-180.8 ± 29.0
protein	Graphene layer	/	-1.8 ± 0.8
	SOA	-95.3 ± 46.7	-164.5 ± 54.0
	SIA	-5256.9 ± 466.4	-97.2 ± 25.6
glycans	Graphene layer	/	-65.6 ± 35.6
	SOA	-49.3 ± 21.3	-81.1 ± 20.8
	SIA	-685.3 ± 118.0	-83.6 ± 14.8



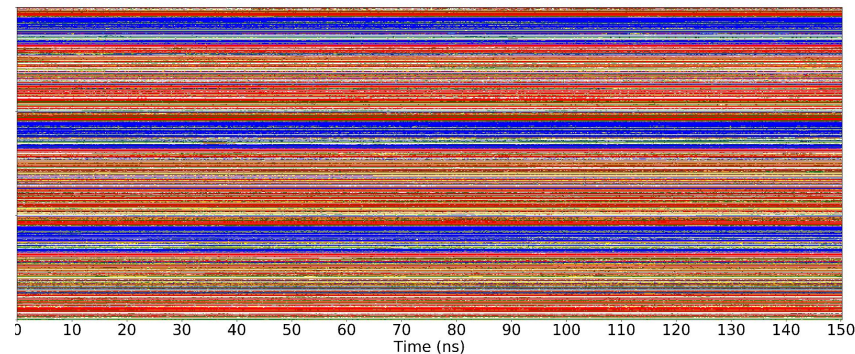
Secondary Structure

Spike-PM
(this simulation)

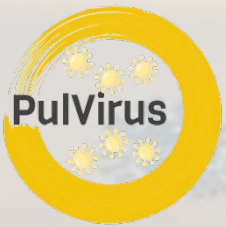


interaction with the PM

Spike free
(simulation from Romeo et al. 2022)



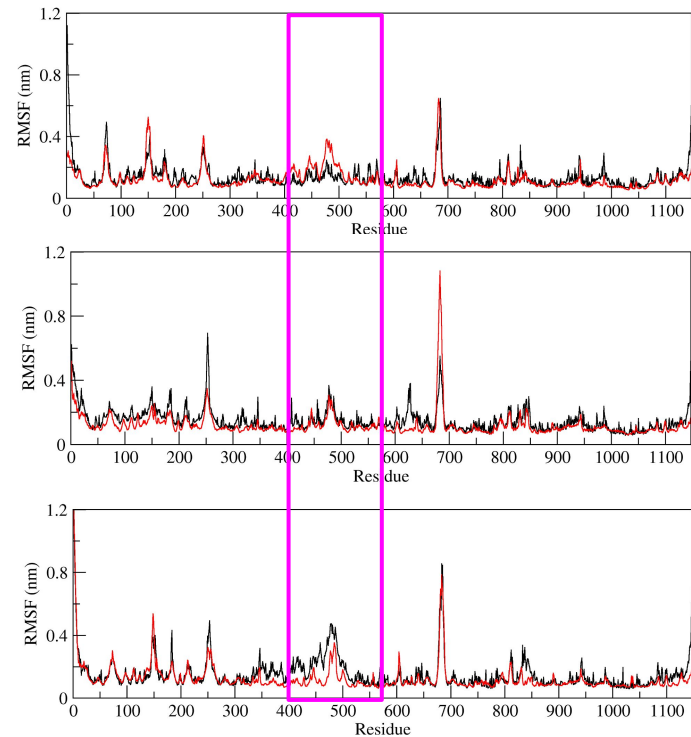
□ Coil ■ B-Sheet ■ B-Bridge ■ Bend ■ Turn ■ A-Helix ■ 3-Helix

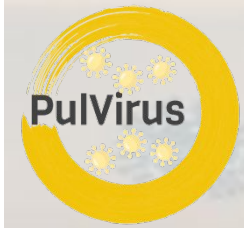


Fluctuations (RMSF)

RMSF measures the structural mobility
important for the functionality of the
glycoprotein Spike

- Spike-PM (this simulation)
- Spike free (simulation from Romeo et al. 2022)





Conclusions (and Perspectives)

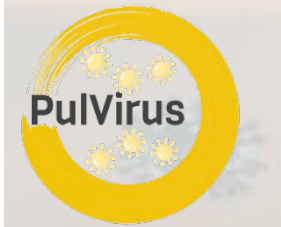
- Our simulation gives the **first structural** model of PM_{2.5}
- Virus and secondary aerosol **tend to interact**;
- The Spike's **glycans bind (weakly) the black carbon** of the PM;
- The **inorganic fraction of PM** plays a role of “glue” **between the virus and the PM**
- The **integrity of the protein is maintained after the interaction with PM**

The transport of the virus by PM cannot be excluded...

....**BUT**...

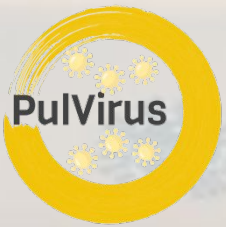
...is the virus-PM complex stable for the entire duration of the PM dispersion and transformation processes in the atmosphere?

...is the the entire virus still alive and active?



Dissemination

- 3 **reports** available at <https://www.pulvirus.it/index.php/documentazione-obiettivo-5/>
- 1 **oral presentation** at “X Convegno sul Particolato Atmosferico (PM2022)- Bologna”
Title: “Simulazioni di Dinamica Molecolare mediante Calcolo ad Alte Prestazioni (HPC) per identificare le interazioni tra PM2.5 e SARS-CoV-2 nell’ambito del progetto Pulvirus”
- 1 **peer-reviewed manuscript** (in preparation): Romeo A. et al 2022



Working group



Agenzia nazionale per le nuove tecnologie,
l'energia e lo sviluppo economico sostenibile

Laboratorio Salute e Ambiente
Laboratorio Inquinamento Atmosferico

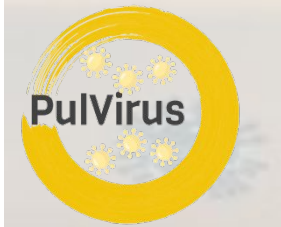
Maurizio Gualtieri
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Mattia Falconi



Thank you!