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

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PulVirus

Caterina Arcangeli

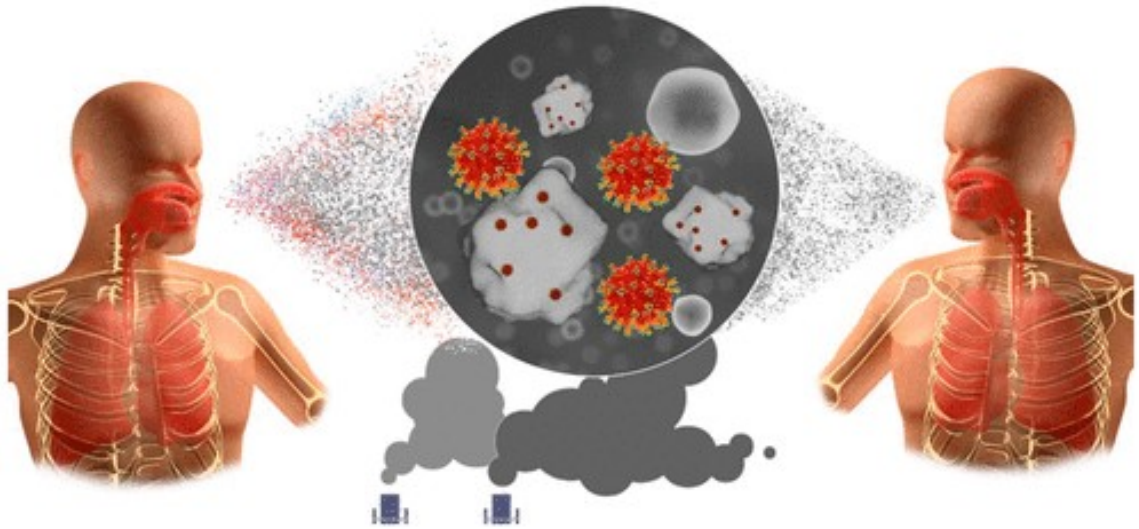
ENEA

PM2022 - Bologna, 18 – 20 maggio

PM 2022

PULVIRUS Project

Airborne Trasmission



Zuo et al., 2020. Airborne transmission of COVID-19: Aerosol Dispersion, Lung Deposition, and Virus-Receptor Interactions. ACS Nano

- Airborne transmission of Covid-19 has not been confirmed by WHO
- Virus particles may bind to aerosol, travel over long distance a float in air for long period
- Pollution is an associated risk factor of Covid-19
- PM as carrier

PM as a carrier of SARS-CoV-2 (controversial)

The number of studies or position papers concerning particle pollution (or atmospheric PM (PM10 or PM2.5)) as a carrier of SARS-CoV-2:

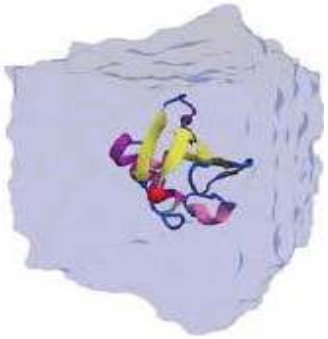
- Setti et al., 2020 (5 papers);
- Società Italiana di Aerosol, 2020;
- Coccia, 2020 (2 papers);
- Anand et al., 2021;
- Al Huraimel et al., 2021;
- Barakat et al., 2020;
- Belosi et al., 2021;
- Bontempi, 2020 (3 papers);
- Borak, 2020;
- Comunian et al., 2020;
- Domingo and Rovira, 2020;
- Kayalar et al., 2021;
- Milton, 2020;
- Sanita` di Toppi et al., 2020;
- Tang et al., 2020;
- The Guardian, 2020;
- Wang et al., 2020;
- Chirumbolo, 2021;
- Kumar et al., 2021;
- Maleki et al., 2021;
- Martelletti and Martelletti, 2020;
- Mehmood et al., 2021;
- Mukherjee et al., 2021;
- Nor et al., 2021;
- Pivato et al., 2021;
- Shao et al., 2021;
- Tung et al., 2021;
- Ishmatov A, 2022

PULVIRUS approach

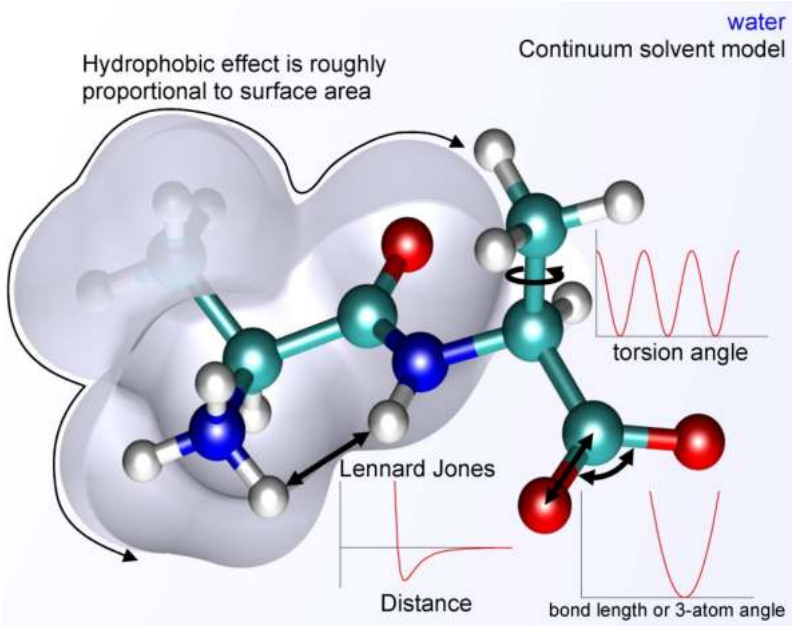
Attività 5.1 - Studio *in silico* di modellistica molecolare dell'interazione diretta tra le proteine di superficie del virus SARS-CoV-2 e PM

- IPOTESI: PM come carrier del virus.
- SCOPO: identificare le potenziali interazioni molecolari tra il PM e le proteine strutturali di superficie.
- APPROCCIO Modellista molecolare e Dinamica Molecolare Simulata

Molecular Dynamics Simulations



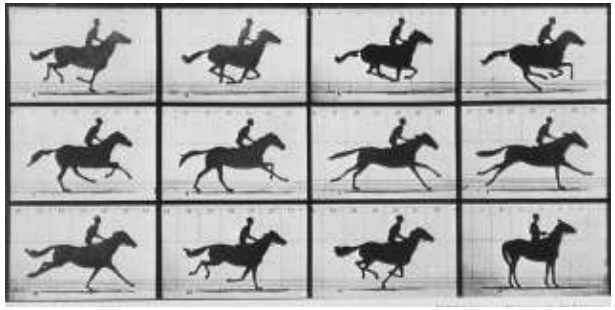
Molecular Model

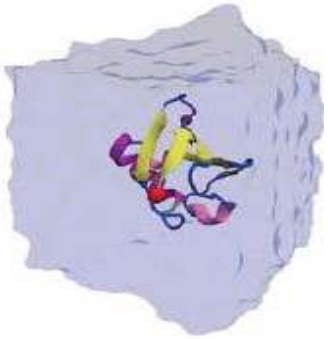


$$U = \sum_{i<j} \sum 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]$$
$$+ \sum_{i<j} \sum \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}$$
$$+ \sum_{bonds} \frac{1}{2} k_b (r - r_0)^2$$
$$+ \sum_{angles} \frac{1}{2} k_a (\theta - \theta_0)^2$$
$$+ \sum_{torsions} k_\phi [1 + \cos(n\phi - \delta)]$$

https://commons.wikimedia.org/wiki/File:MM_PEF.png#/media/File:MM_PEF.png

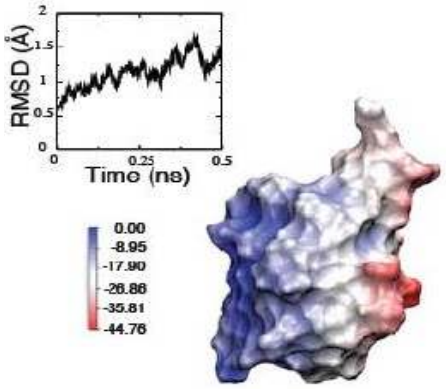
Molecular Dynamics Simulations





Molecular Model

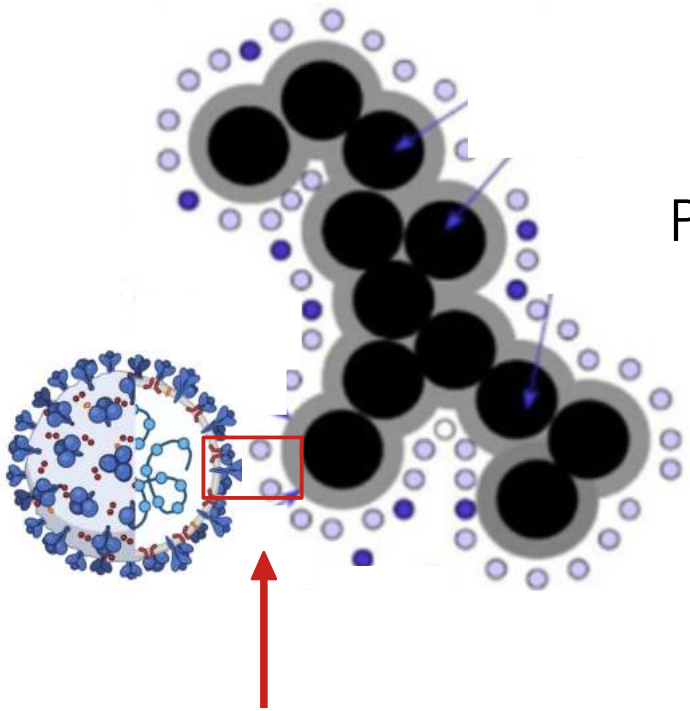
HPC MD Simulations @
ENEA - CRESCO



Trajectory's analysis

- molecular recognition (electrostatic, van der Waals interactions, H-bonds)
- binding thermodynamics
- conformational changes
- stability of the complex

The strategy adopted in Pulvirus



PM

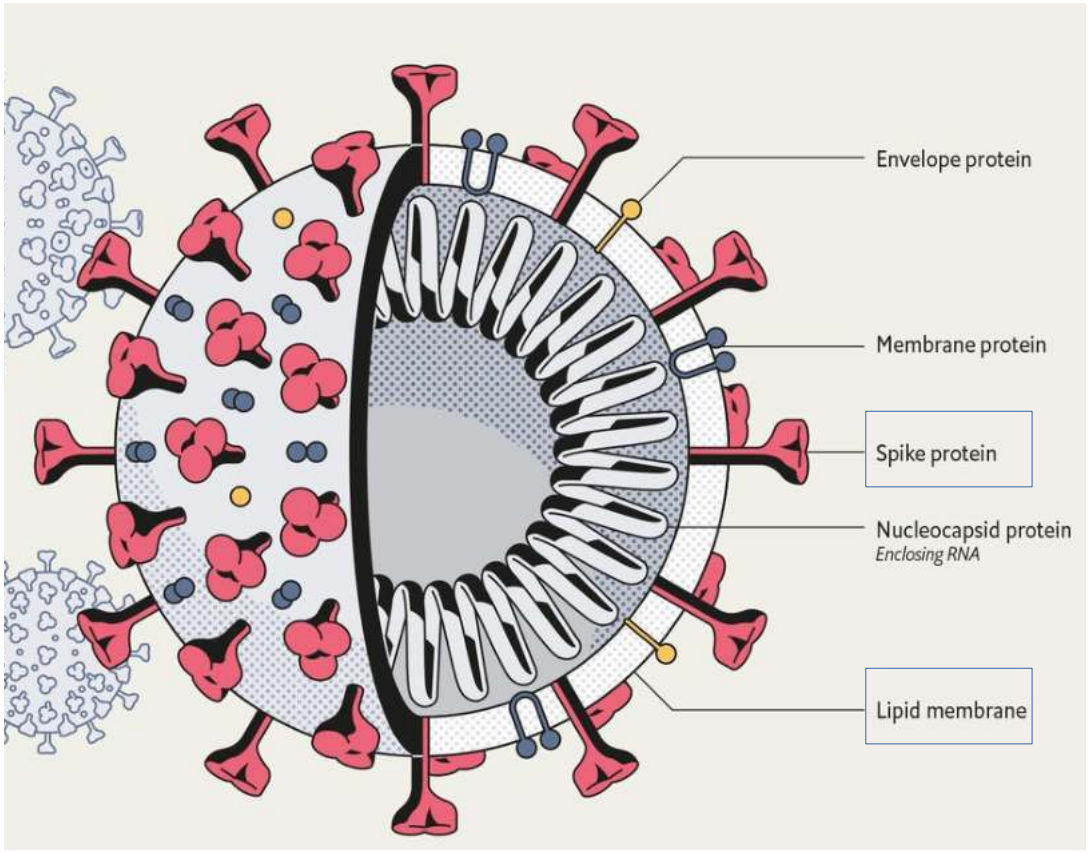
SARS-CoV-2

PM-virus interface

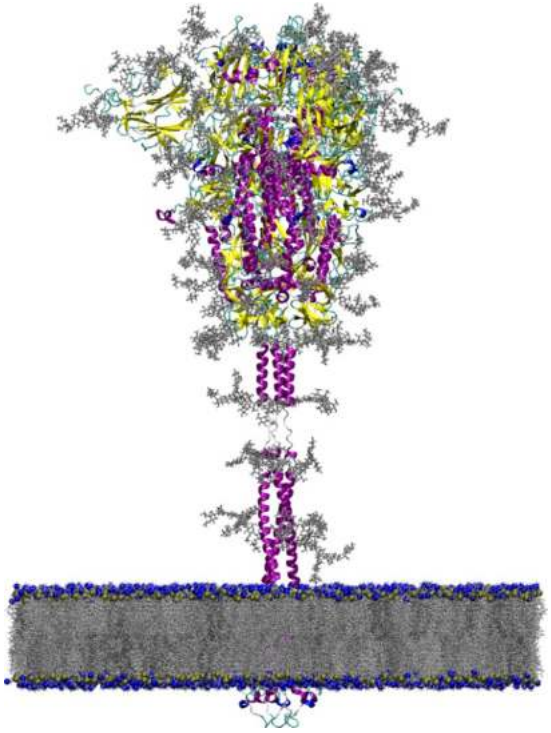
Twigg, M.V., & Phillips, P.R. (2009). Platinum Metals Review, 53, 27-34.

Modeling of the virus

SARS-CoV-2 Architecture



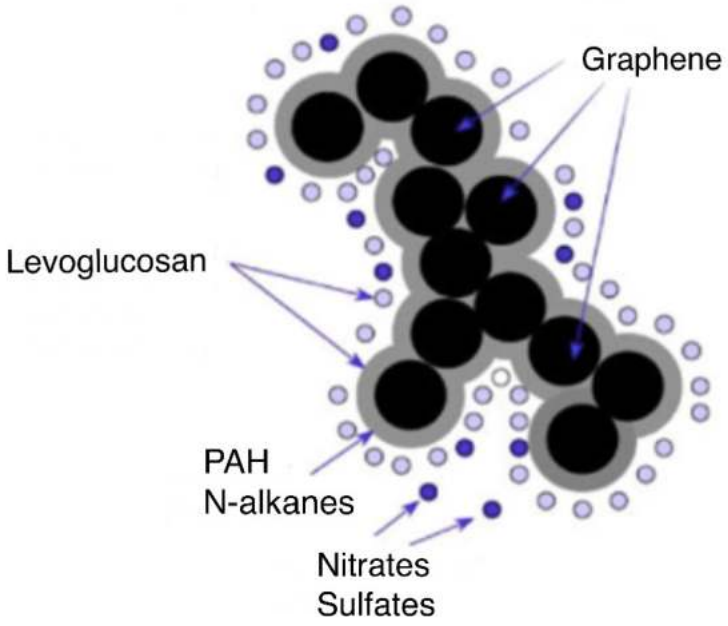
approx. 150 nm



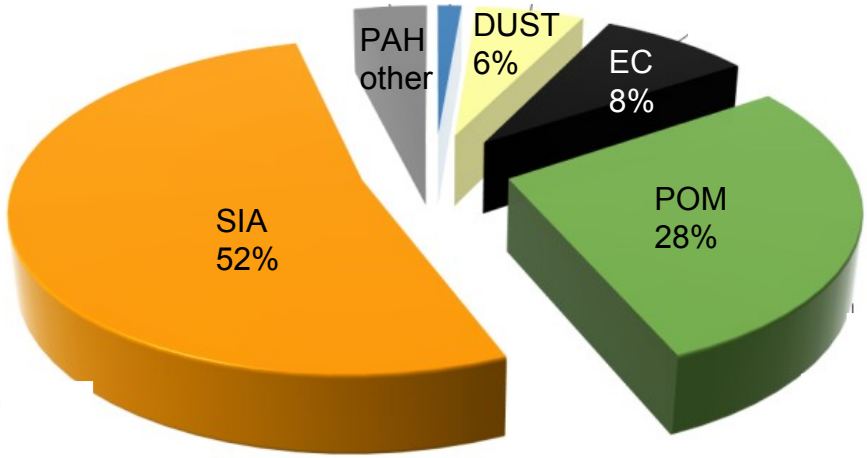
Woo,H. et al (2020) J. Phys. Chem. B. 124:7128–7137

Modeling of the $PM_{2.5}$

- **SIA**
  - Ammonium Nitrate (NH_4NO_3)
- **SOA**
  - Anidro Sugars (POM)
  - n-alkaloid Acid
  - Aromatic Polycarboxylic Acids
  - Aliphatic Dicarboxylic Acids
  - PAH
- **Carbonaceous component**
  - Organic Carbon – Graphene (Soot)
- **Metals**
  - Sodium (Na^+), Cloride (Cl^-)

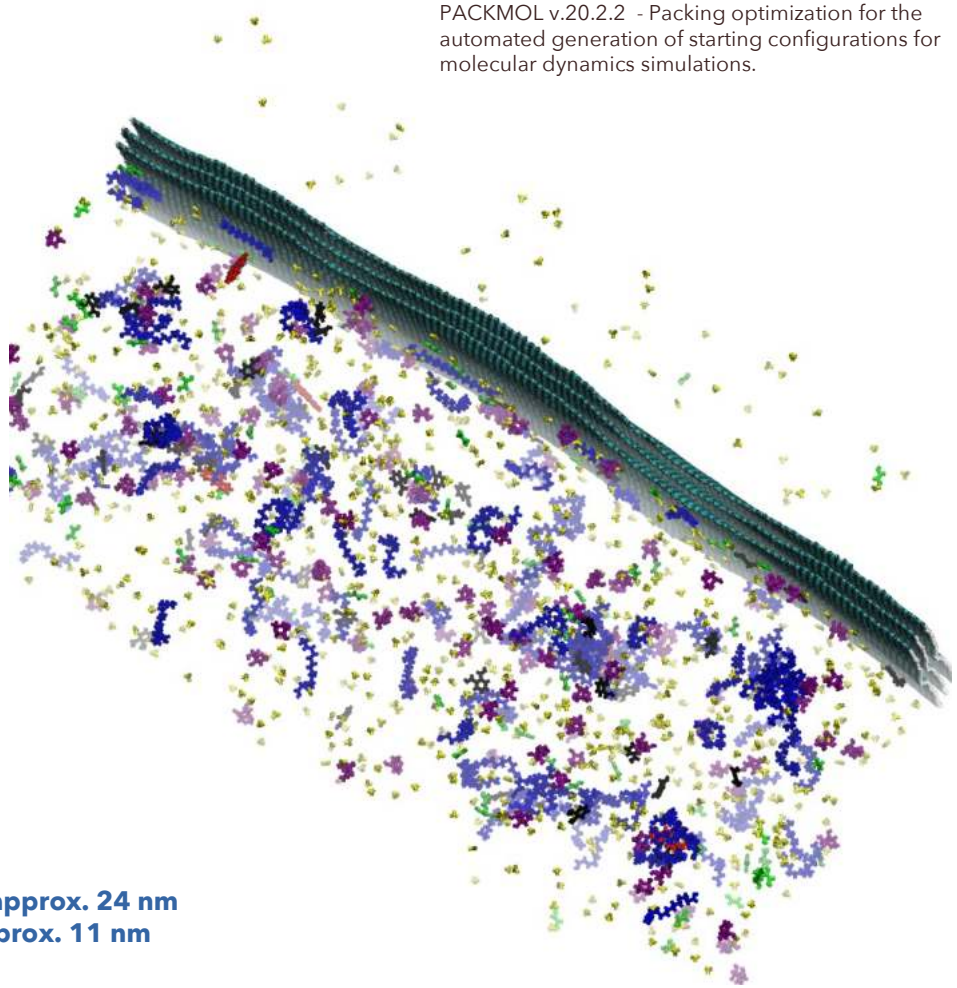


PM 2,5 Bologna 2018

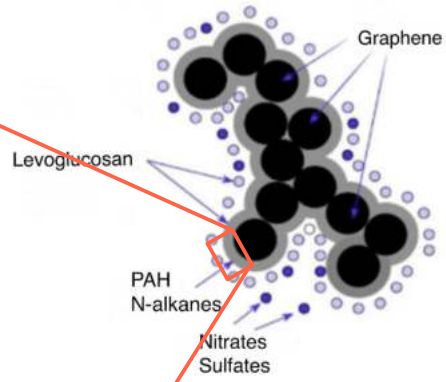


PM model

PACKMOL v.20.2.2 - Packing optimization for the automated generation of starting configurations for molecular dynamics simulations.



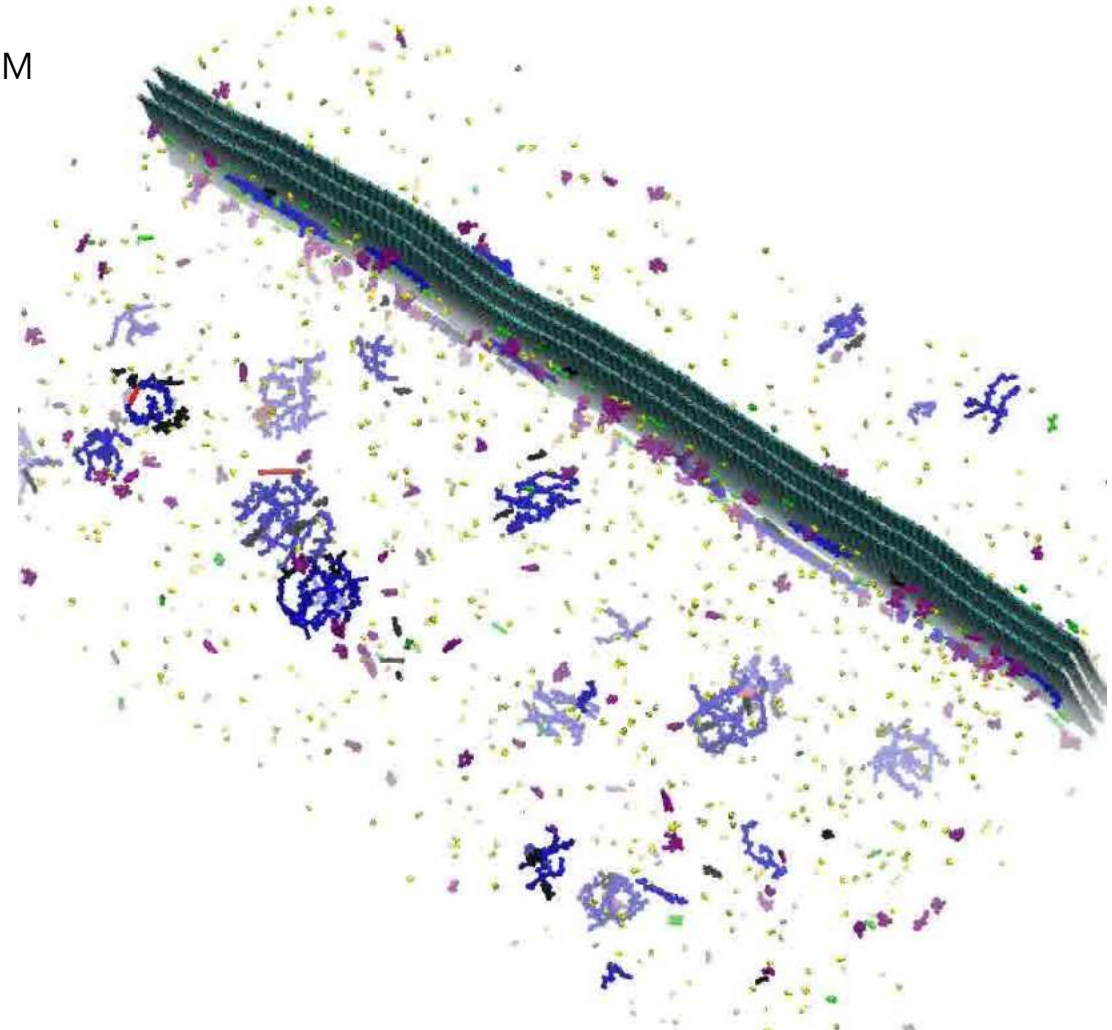
X,Y approx. 24 nm
Z approx. 11 nm



MD simulation of the PM model

NAMD
Scalable Molecular Dynamics

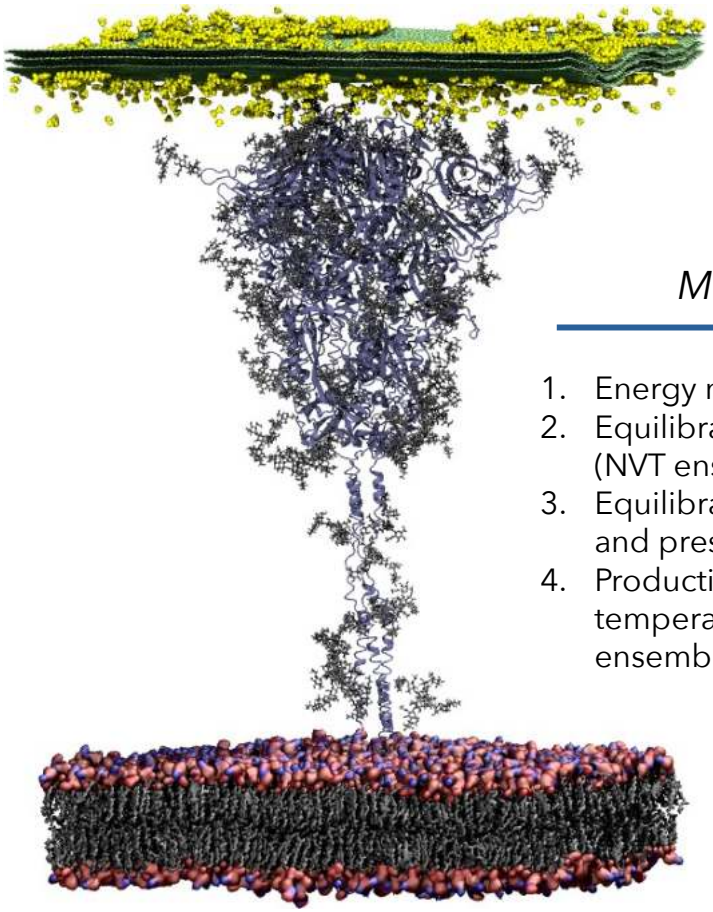
Force field: CGenFF + CHARMM
TIP3P solvent model
921786 atoms
200 ns



Simulation of the Spike – PM complex

NAMD Scalable Molecular Dynamics

Force field: CHARMM36

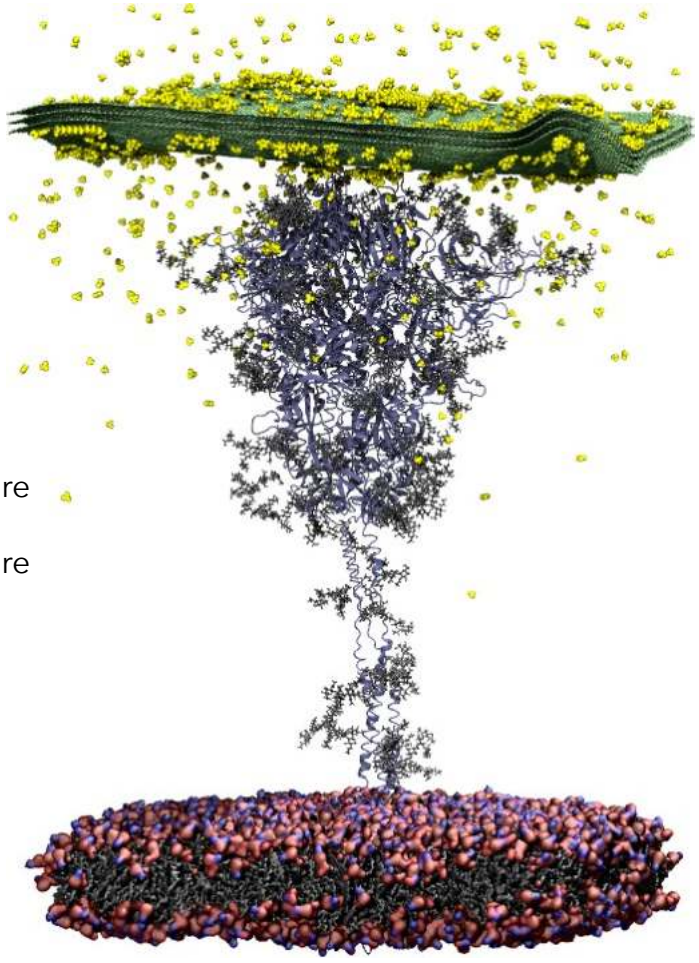


t = 0

MD simulation

1. Energy minimization
2. Equilibration at constant temperature (NVT ensemble)
3. Equilibration at constant temperature and pressure (NPT ensemble)
4. Production MD at constant temperature and pressure (NPT ensemble)

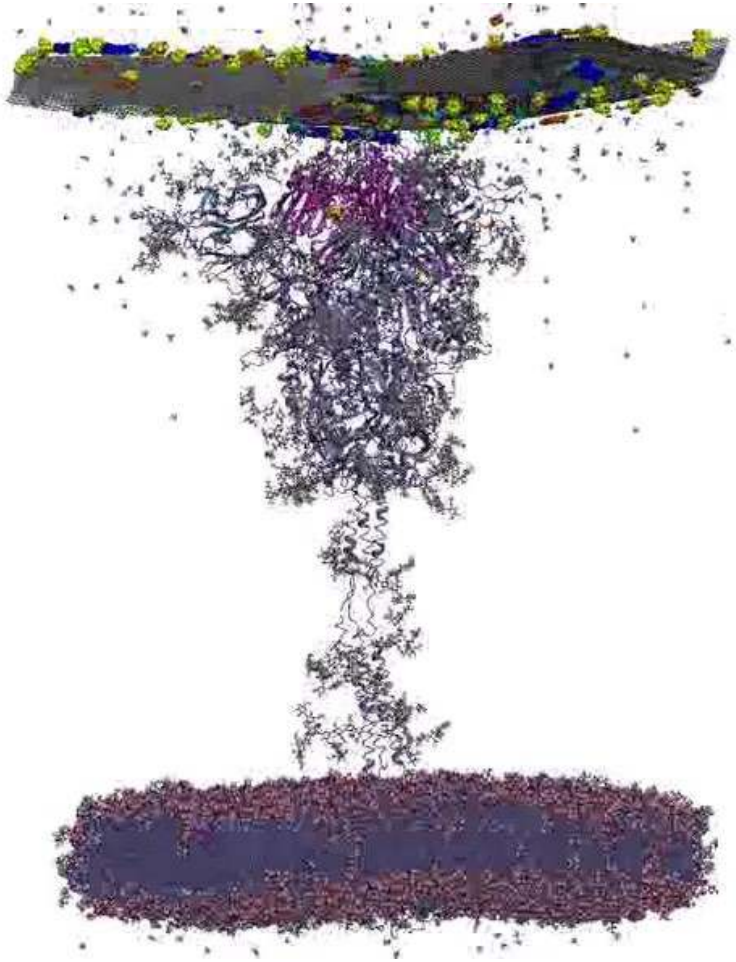
2,48 milions of atoms

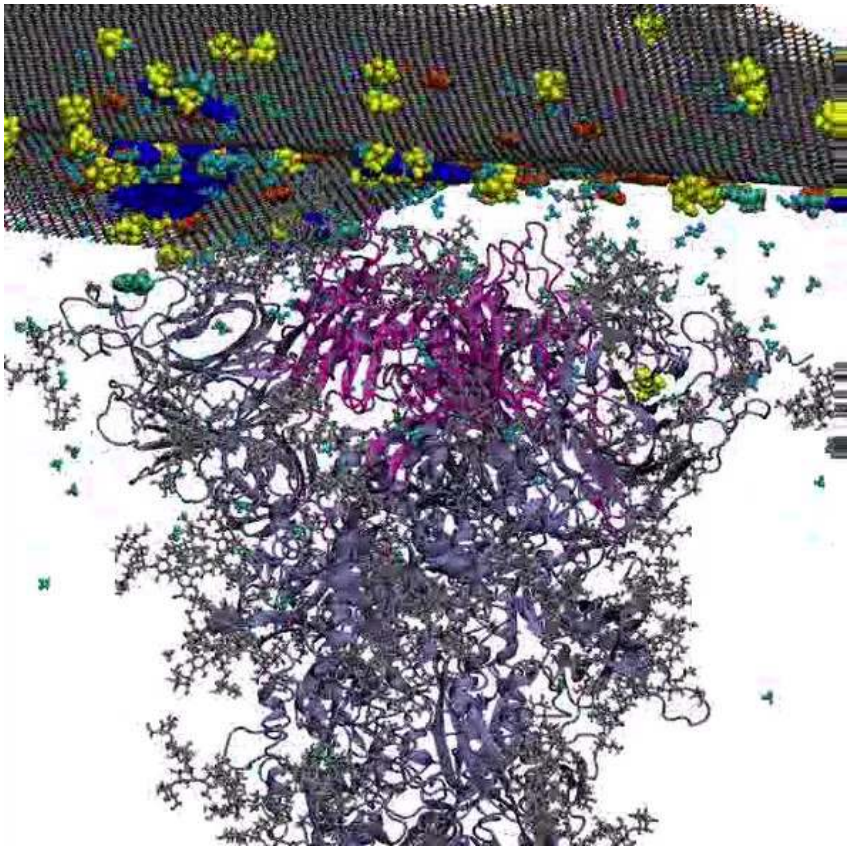


t = 40 ns

Performace: about 2 ns/day
(on 14 nodes of the CRESCO6 HPC cluster)

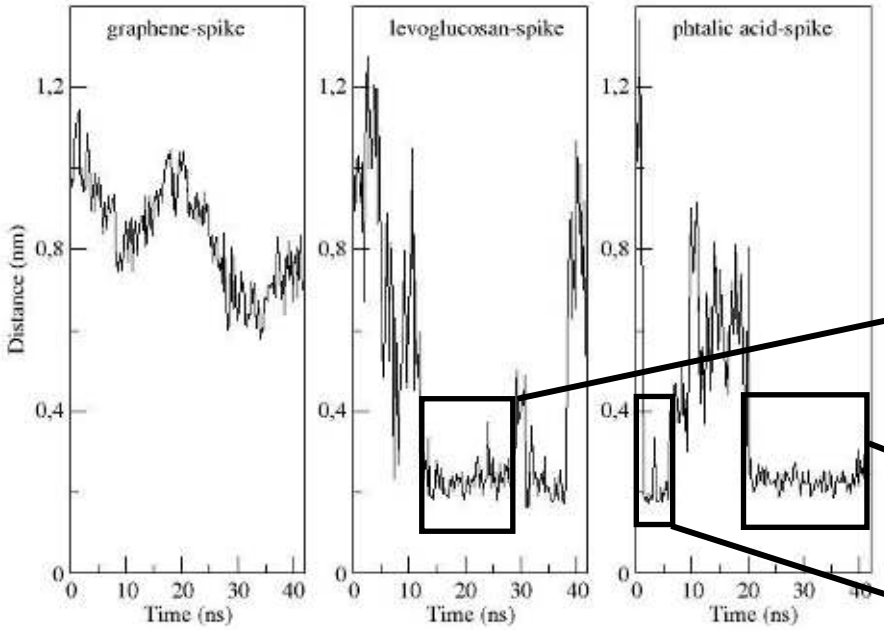
Simulation of the Spike – PM complex



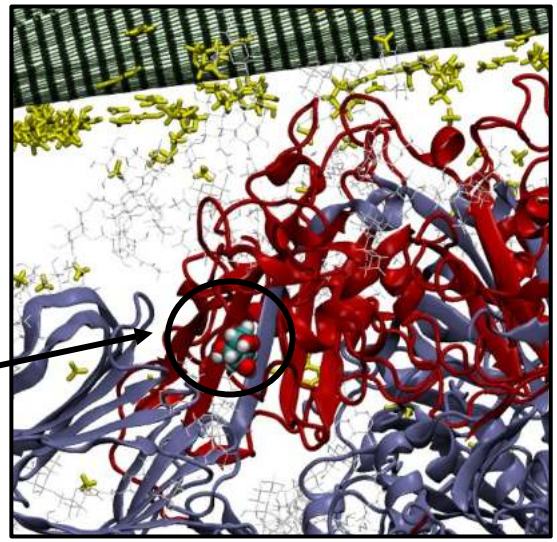


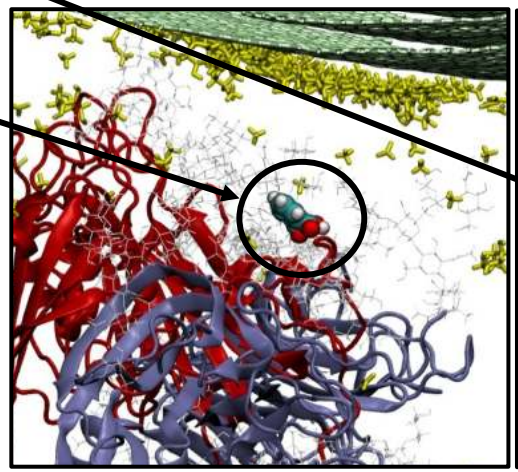
Virus – PM interactions

Distance analyses

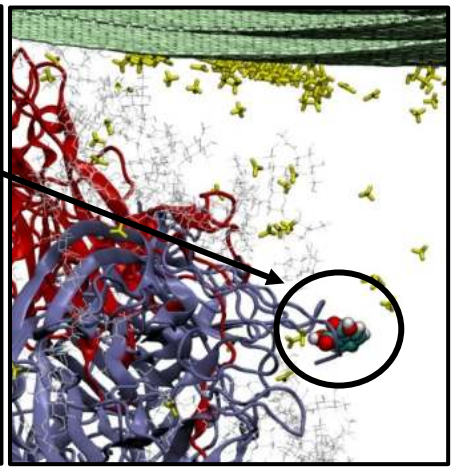


Levoglucosan - RBD





Phtalic acid - RBD

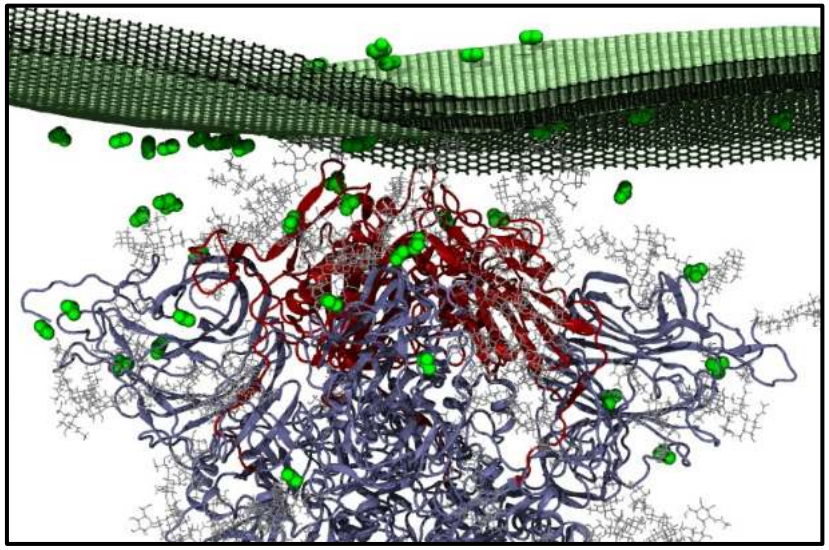


Phtalic acid - NTD

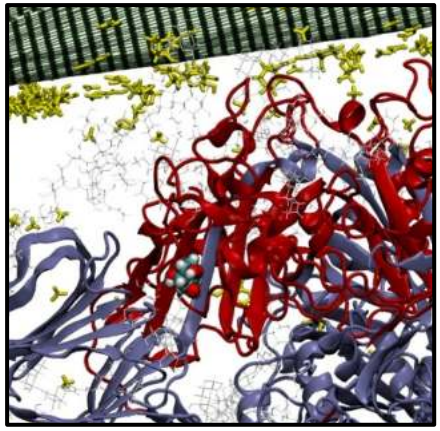
Virus – PM interactions

Hydrogen Bonds (HB)		
PM compounds	***Spike RBD residues***	
NH_4NO_3	ARG 357, THR 478, GLU 484	RBD Chain A
Phtalic acid	ASN 481, GLY 482	RBD Chain B
NH_4NO_3	ARG 335	RBD Chain B
NH_4NO_3	ASN 440, LEU 441, ASN 448, ASP 467	RBD Chain C
Levoglucosan	LYS 458, SER 459, GLU 471, ALA 475, GLY 476, THR 478	RBD Chain C

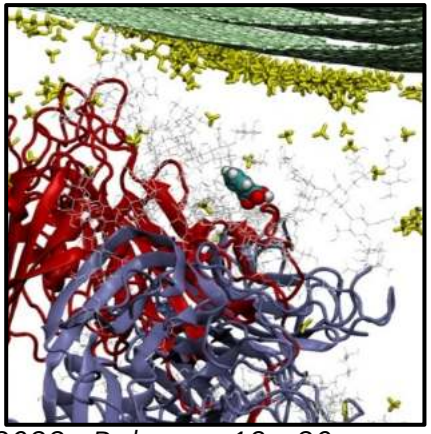
NH_4NO_3



Levoglucosan - RBD



Phtalic acid - RBD



Work in progress…

- Extend the simulation time up to 100 ns
- Analysis of the the Spike protein (stability, hydrogen bonding pattern, salt-bridge, effect of the PM on the structural integrity of the protein….)
- Analysis of the dynamics at the virus-PM interface (molecular interaction and their persistence …)
- Quantifications of the Binding Energy (if any) by MM/PBSA method

Working Group

Modeling and High Performance MD Simulations

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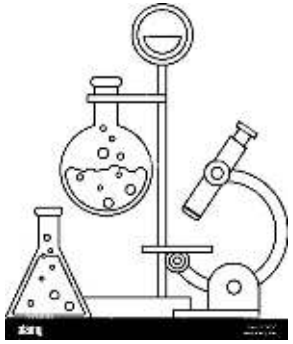
Mattia Falconi – Tor Vergata, Roma
Caterina Arcangeli – ENEA C.R. Roma

Experimental Support



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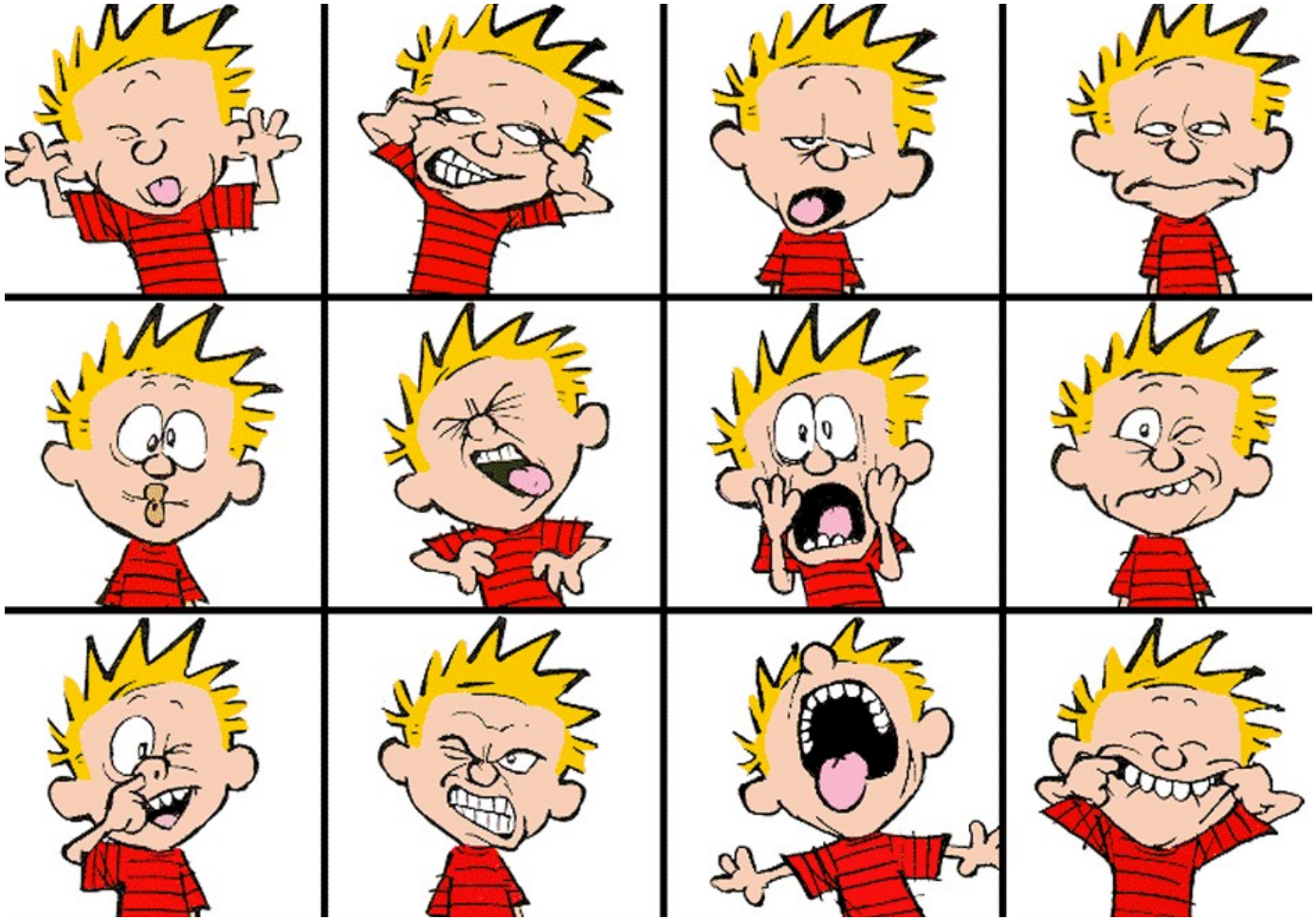
Massimo Santoro – ENEA C.R. Bologna
Barbara Benassi – ENEA C.R. Roma
Carmela Marino – ENEA C.R. Roma
Gabriele Zanini – ENEA C.R.Bologna

Thank you…



…for your attention

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