# Use of modern risk-appraisal and modeling tools in nanotechnology applications (EU Project MUST)

Use of modern modeling techniques in MUST

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# The starting point …

Can Nanomaterials be Toxic? … YES!

- Wide range of materials can be made “nano”
- Nanometer range is where life processes happen – e.g. inhaled ultrafine particles are toxic to lung and cardiovascular system
- Transported easily, go unexpected places
- Accumulate in cellular organelles
- Some components are toxic as chemicals, i.e. they can be toxic both as chemical and nano!
- Many (most?) of possible effects belong to the category of “low-doses-long-term-exposure” which is an unsolved problem in itself, also for “non-nano” materials!
- … Huge knowledge gap: **Currently we have “a nano part” of knowledge needed to assess the toxicity of nanomaterials!** … probably just about $10^{-9}$ of knowledge we have about the toxicity of chemicals! … think about REACH!

**TECHNOLOGY**

↓

**RELEASE**

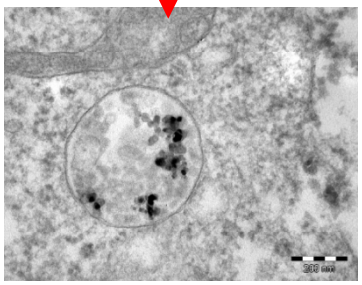
↓

**ENVIRONMENT**

↓

**(HUMAN) TISSUE**

↓



**Aluminum nanoparticles inside an endosome of an A549 cell from an in vitro toxicity experiment (cf. ToxSci 2006)**

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**Short-term and long-term adverse effects: disorders / diseases**

# The starting point …

- What do we have (“good news”)?
  - public and scientific interest
  - Overall methodology/approach (e.g. the IRGC)
  - Running research (US, EU, …)
  - Some methods and tools
- What we still miss (for sure!)
  - clinical research
  - targeted epidemiological research/surveys
  - integration of research: analytical, in silico, in vitro, in vivo …
  - integration of nano-issues into the routine practice of public health … regulatory framework missing!

**TECHNOLOGY**

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**RELEASE**

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**ENVIRONMENT**

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**(HUMAN) TISSUE**

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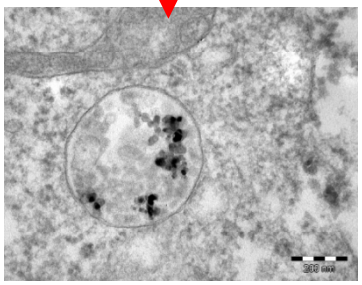


**Aluminum nanoparticles inside an endosome of an A549 cell from an in vitro toxicity experiment (cf. ToxSci 2006)**

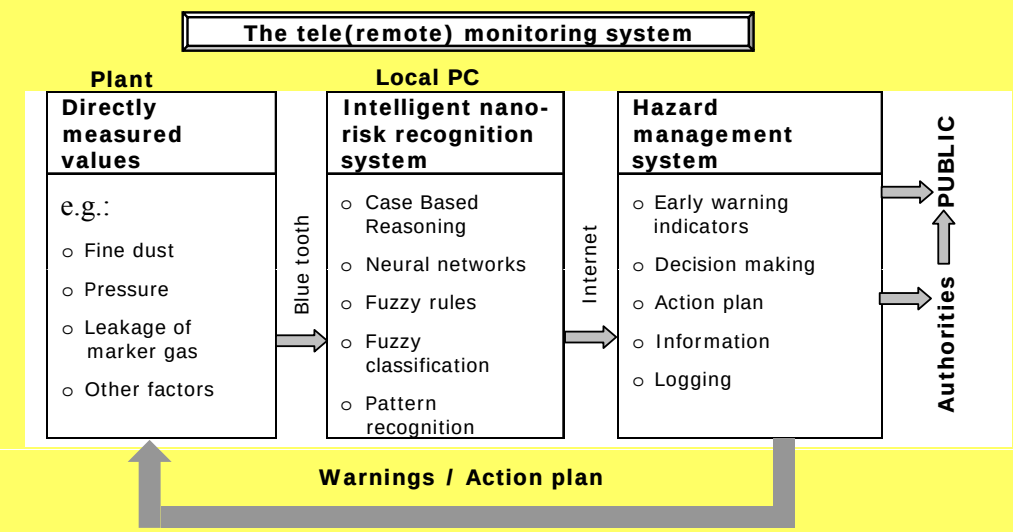
↓

**Short-term and long-term adverse effects: disorders / diseases**

# Public health and medical issues related to nanomaterials

- Few or no information about the specific risks of a technology and substances already used in consumer products.
- Risks due to toxicity, fire, explosion, etc. to the workers handling nano-materials and nano technology
- Risk to the environment and public due to exposure of airborne particles from nano technology and nano materials
- Lack of specific regulations or legislations for NT. This raises the general problems of liability for the industry
- Societal acceptance not sure (at least on the long run)

**SOLUTION:**

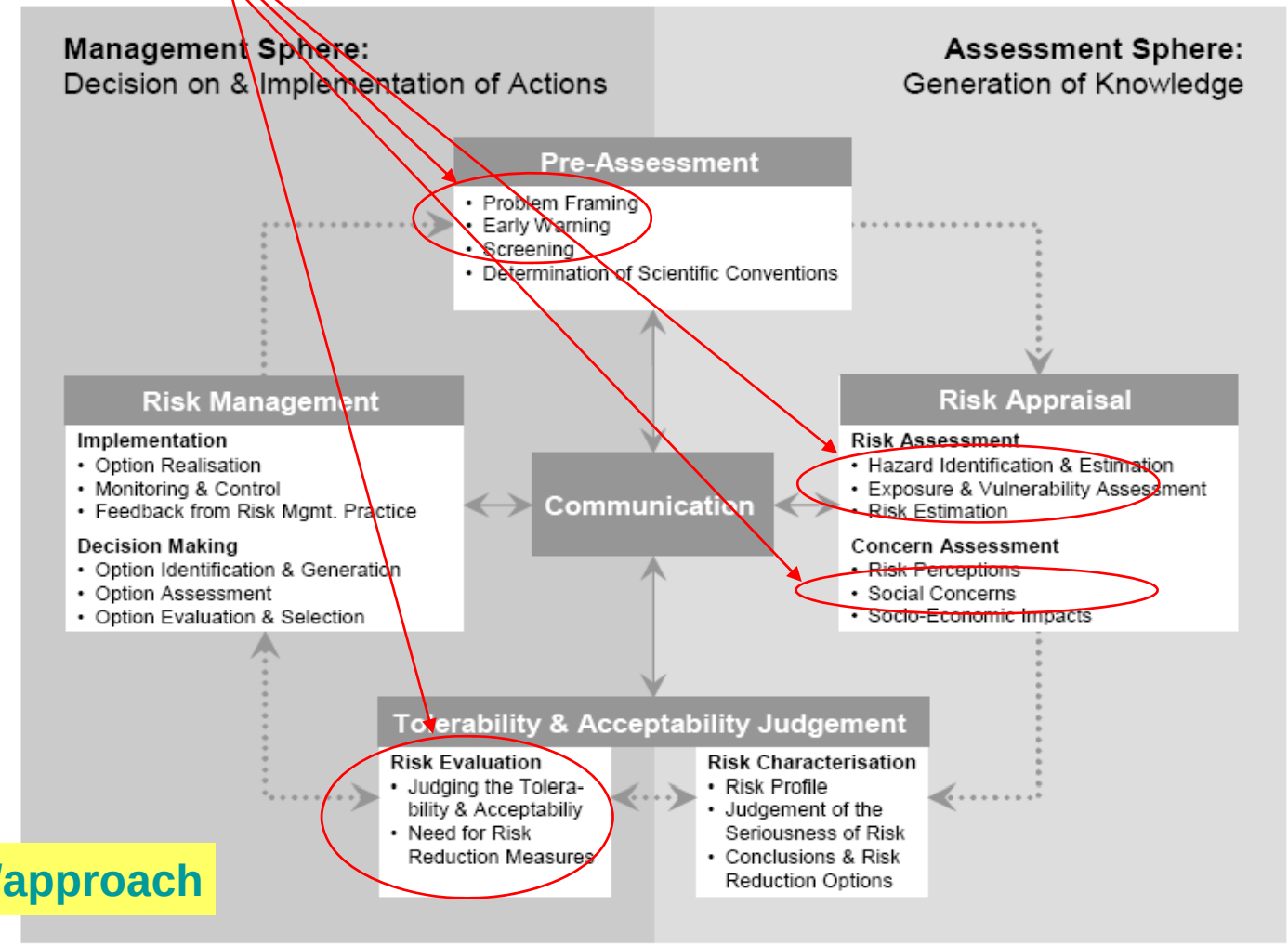



iNTeg-Risk

# IRGC RISK GOVERNANCE FRAMEWORK (II/III): CORE PROCESS

**What is so specific about nano-technologies with respect to public health?**

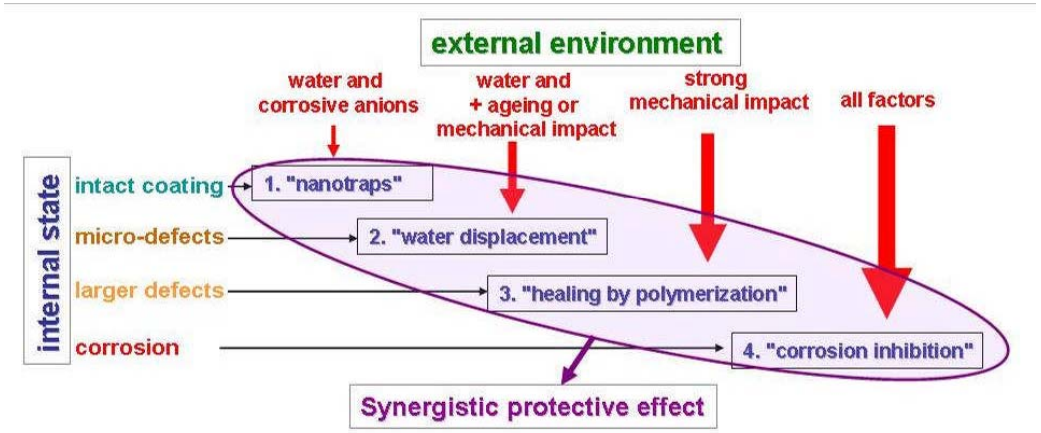
Public Health (primary concerns)

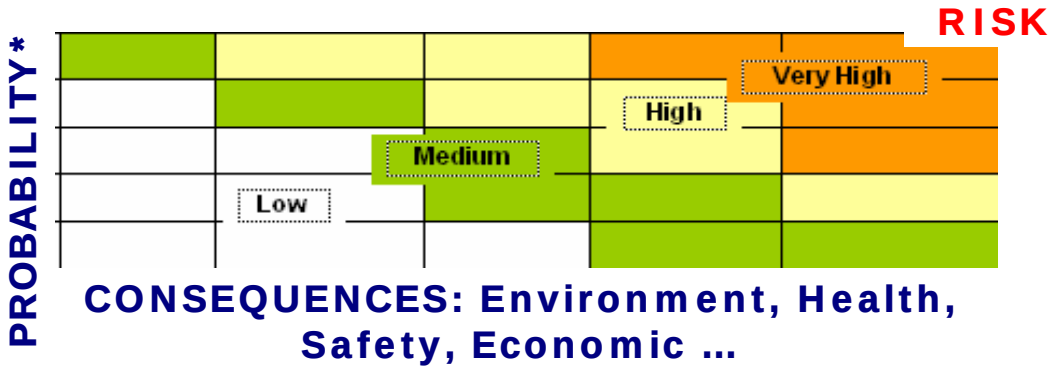



**methodology/approach**

# Nanocontainers – what can go wrong? Non-performance….

- Impacts – occupational health & safety (in production)
- Impacts – heath & safety of the intermediate/end user
- Impacts – environment – normal use
- Impacts – environment – abnormal use
- Impact - "low-dose-long-exposure" scenarios
- Impact - security



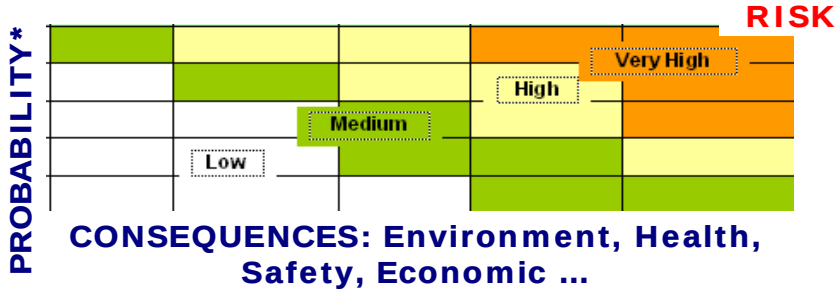




* - *Calculated and/or perceived by the society*

# (integrated) Risk assessment and management should:

- combine quantitative and qualitative assessment
- deal with low-quality, scattered, inconsistent and few data
- match the model-based and behavior-based assessment be seamlessly combined with the preliminary screening analysis
- provide a preliminary assessment of risks and effects of low-doses long exposure effects in the (usually!) short times available in research projects

**methods & tools**



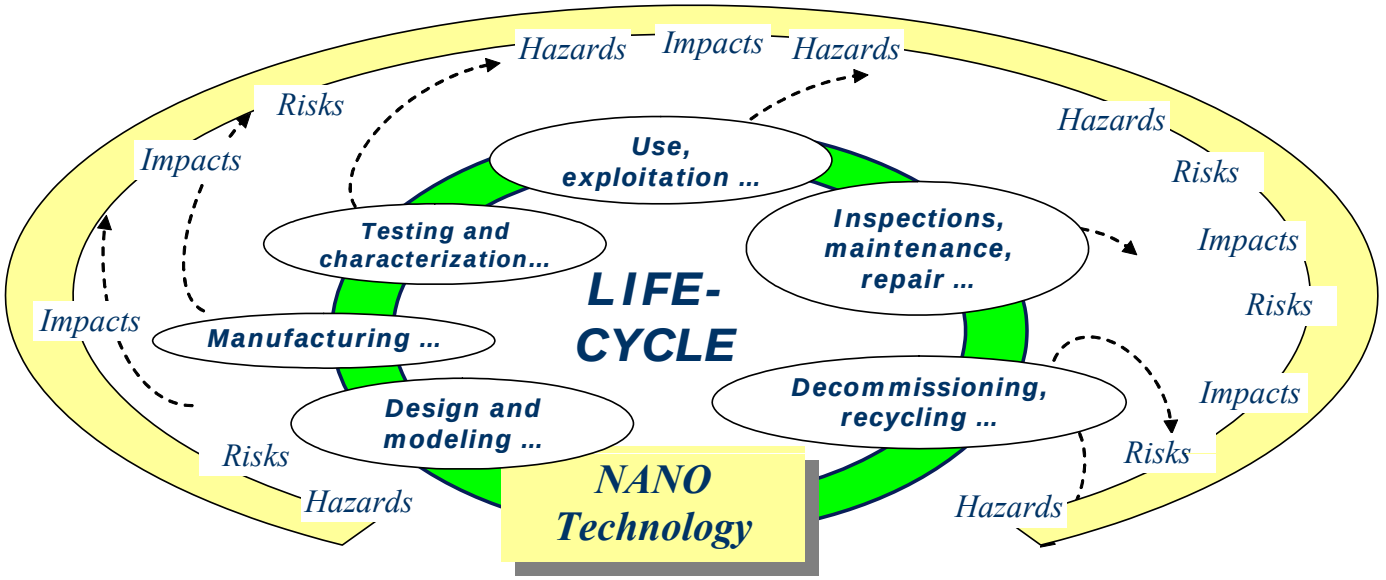

* - *Calculated and/or perceived by the society*

- IT infrastructures (databases, communication possibilities ...)
- simulation
- bio-inspired modeling (e.g. artificial organs, artificial life)
- advanced methodologies
- data mining
- complex systems
- risk assessment methods & tools
- ...

# Nanocontainers in a life-cycle:

needed:

INTEGRATED RISK MANAGEMENT
(Over the life-cycle)!



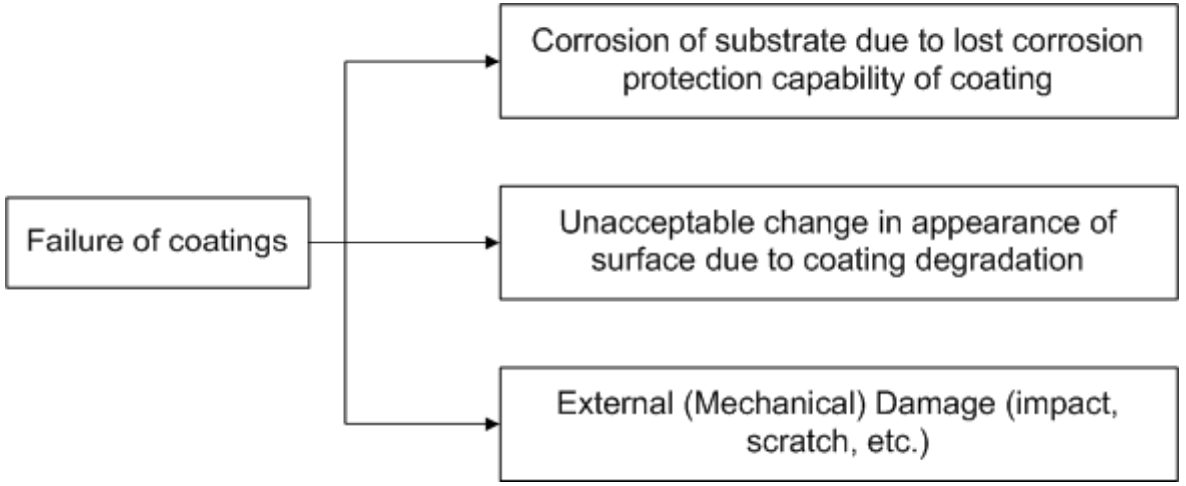
# … health … general:

- Health effect are:
  - not only “depositions” and “concentrations”, but more
  - how the people feel (“thick” or “well”!)
  - … if exposed to nanoparticles, nanomaterials, nanotechnologies …
- …and for industry and industrial safety it means the exposure of:
  - work force
  - users of their products
  - general population

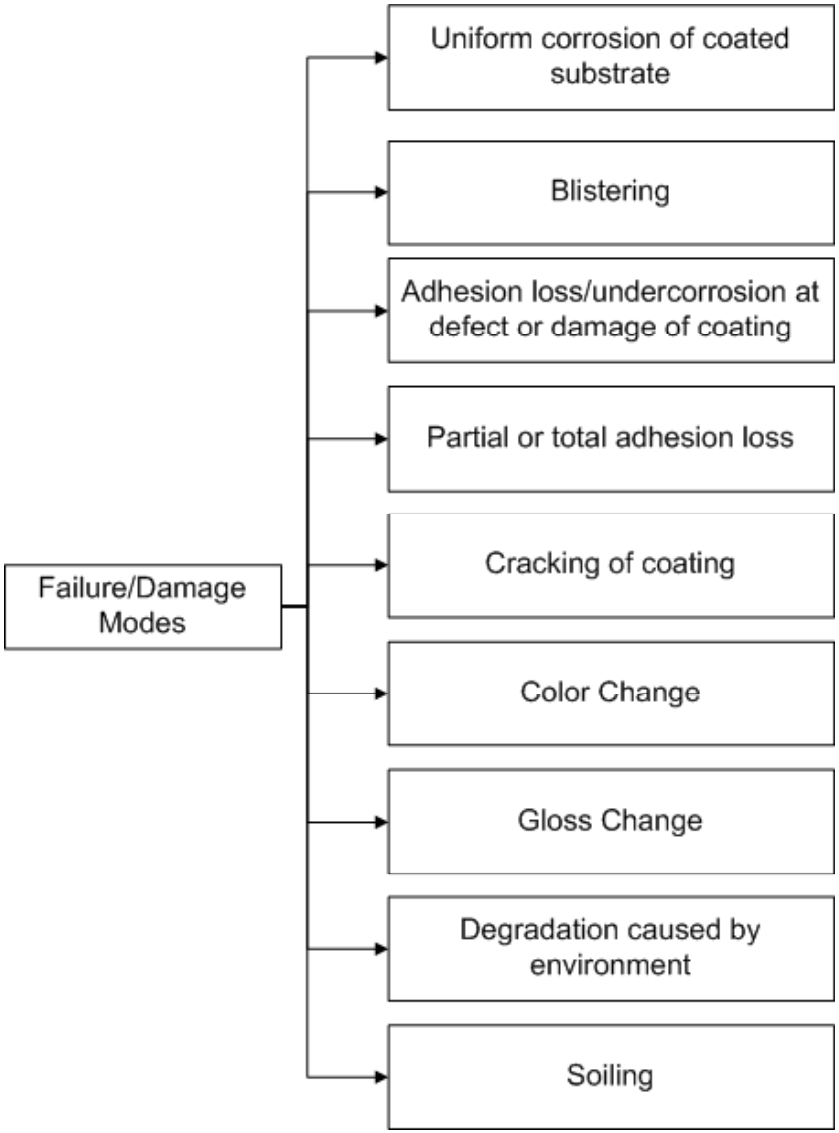
## Nanocontainers – what can go wrong?
## Non-performance….

- **Non-performance**: material properties
  - The properties are not as expected/foreseen – globally, locally, in time
- **Non-performance**: as part of the structure
  - difficult or impossible to inspect, monitor, maintain
- **Non-performance**: failure modes
  - Different/unforeseen failure modes … ?
- **Safety / Health/ Economic / business risk** of failure or non-performance?

# Example of Risk-analysis



# Example of Risk-analysis



# Example of Risk-analysis

| Severity/Consequences | RN | Likelihood | RN | Probability for detection | RN |
|---|---|---|---|---|---|
| **None** – there are no consequences known or possible upon event occurrence | 0-1 | **None** – the event cannot occur under no circumstances | 0-1 | **Obvious** - Failure which always is noted. Probability for detection > 99.99% | 0-1 |
| **Low** – the event can lead to short delays or small technical drawbacks that can be very fast mitigated; very small amount of additional resources needed. | 2-3 | **Low** – the event can occur only in very exceptional circumstances | 2-3 | **Very good detectable** - Normal probability for detection 99.7% | 2-3 |
| **Medium** – the event leads to the medium (couple of days to couple of weeks) delays or technical drawbacks that can be mitigated in the relatively short time; some amount of additional resources needed. | 4-5 | **Medium** – the event can occur and the cases of occurrence are known | 4-5 | **Good Detectable** - Certain probability for detection >95% | 4-5 |
| **Medium-high** – the event leads to the serious (up to 2 months) delays or technical drawbacks that require significant amount of work to be overcome; additional resources are needed. | 6-7 | **Medium-high** – the event can occur and the cases of occurrence have already been experienced by the risk assessors, it is common occurrence in the field of appraisal | 6-7 | **Detectable** - Probability for detection >50% | 6-7 |
| **High** – the event leads to the serious (up to 6 months) delays or technical drawbacks that require high amount of work to be overcome; significant additional resources are needed. | 8-9 | **High** – the event occurrence in the particular case is probable; the risk assessor identifies the elements/indicators that might lead to the occurrence | 8-9 | **Difficulty to Detect** - Probability for detection < 50% | 8-9 |
| **Very high** – the event might lead to total failure of the project or technical solution, technical drawback or additional work to overcome the problem is measured in years; doubling or more of the resources is needed. | 10 | **Very high** – the event occurrence in the particular case is very probable; the risk assessor identifies most of the elements/indicators that lead to the occurrence | 10 | **Not detectable** - Failures will not be found - cannot be tested or not feasible | 10 |

# Example of Risk matrix
# CEN CWA 15740:2008

| Examples of PoF scales | Descriptive | MTBF | PoF | |
|---|---|---|---|---|
| | Very probable | < 1 year | $>1\times10^{-1}$ | 5 |
| | Probable | 1-5 years | $1\times10^{-1}$ to $1\times10^{-2}$ | 4 |
| | Possible | 5-10 years | $1\times10^{-2}$ to $1\times10^{-3}$ | 3 |
| | Unlikely | 10-50 years | $1\times10^{-3}$ to $1\times10^{-4}$ | 2 |
| | Very unlikely | >100 years | $<1\times10^{-4}$ | 1 |

PoF category

| | | | | |
|---|---|---|---|---|
| | | | | **Very high risk** |
| | | | **High risk** | |
| | | **Medium risk** | | |
| | **Low risk** | | | |
| (Very Low, negligible risk) | | | | |

**CoF category**

| | A | B | C | D | E |
|---|---|---|---|---|---|
| ***Health (Long term visibility)*** | Warning issued No effect | Warning issued Possible impact | Temporary health problems, curable | Limited impact on public health, threat of chronical illness | Serious impact on public health, life threatening illness |
| ***Safety (Instant visibility)*** | No aid needed Work disruption | First aid needed No work disability | Temporary work disability | Permanent work disability | Fatality(ies) |
| ***Environment*** | Negligible impact | Impact (e.g. spill) contained | Minor impact (e.g. spill) | On-site damage | Off-site damage Long term effect |
| ***Business (€)*** | <10k€ | 10-100 k€ | 0.1-1 M€ | 1-10 M€ | >10 M€ |
| ***Security*** | None | On-site (Local) | On-site (General) | Off site | Society threat |
| ***Image Loss*** | None | Minor | Bad publicity | Company issue | Political issue |
| ***Public disruption*** | None | Negligible | Minor | Small community | Large community |

*Examples of CoF scales*

# Example of one item risk assessment

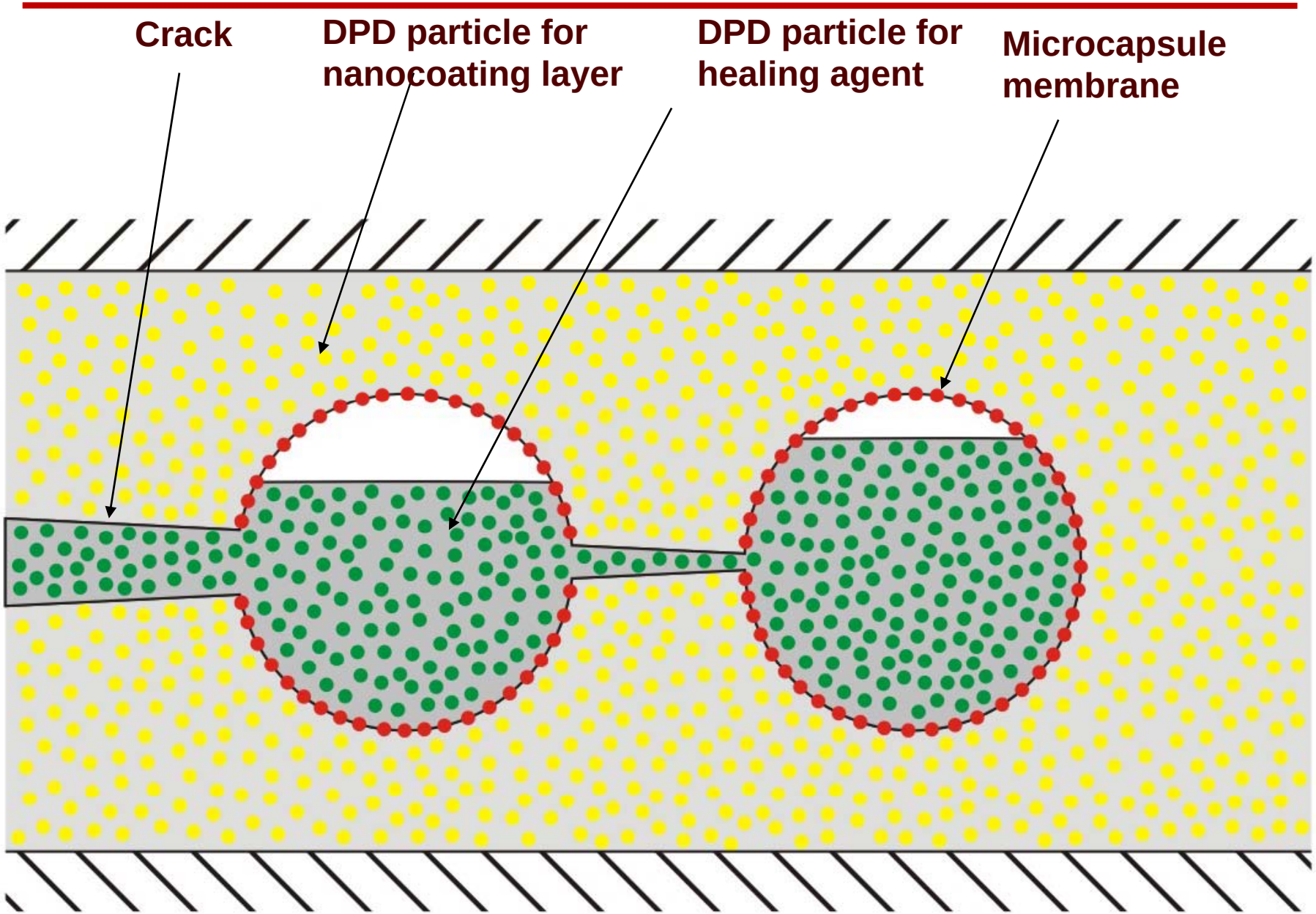
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 15 | Detection | detection? laser scatter? | Medium high | Low | Low | 1 | | | |
| | **Weighted Average** | **Weighted Average of ALL Risks** | **Medium** | **High** | **Medium** | | | | |

Insert New...

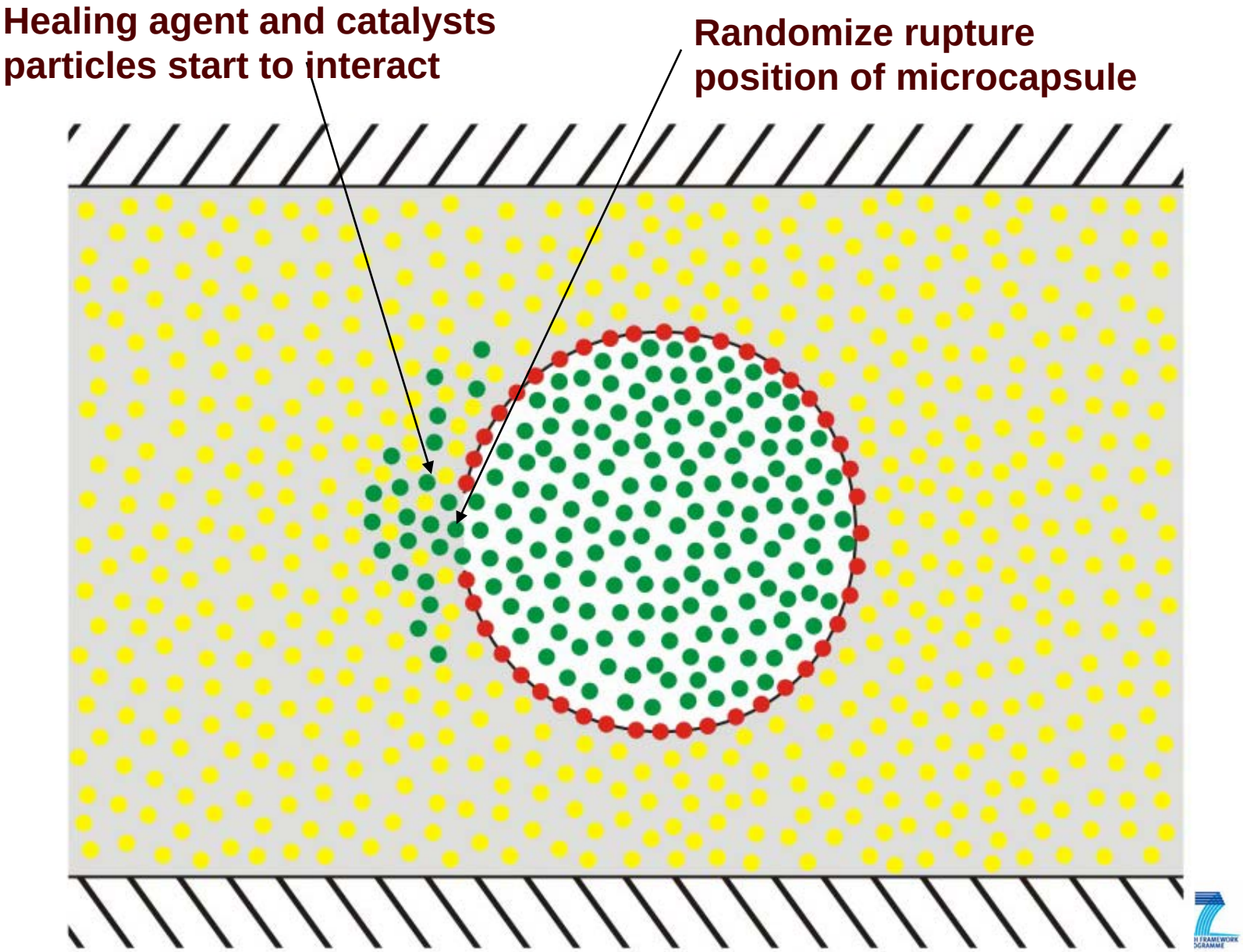
**Risk Matrix**

| LIKELIHOOD | | | | | | |
|---|---|---|---|---|---|---|
| | 5 | | | | | |
| | 4 | | | 2. Agglomeration of the nanocontainers | | |
| | 3 | 15. Detection | 1. Non-opening of the container<br>3. Not enough agent in the container | 14. Powder & Suspensions | | |
| | 2 | 4. Too fast release of the agent<br>5. Too slow release of the agent | | | 11. Quantities / use<br>**Weighted Average** | 10. Registration (REACH)<br>13. Safety |
| | 1 | | | | 6. The agent does not perform<br>8. Scale effects | 7. The agent has an opposite effect<br>9. Basic properties change<br>12. Toxicity problems |
| | | A | B | C | D | E |
| | | CONSEQUENCES | | | | |

# Basic DPD simulation concept for self-healing process



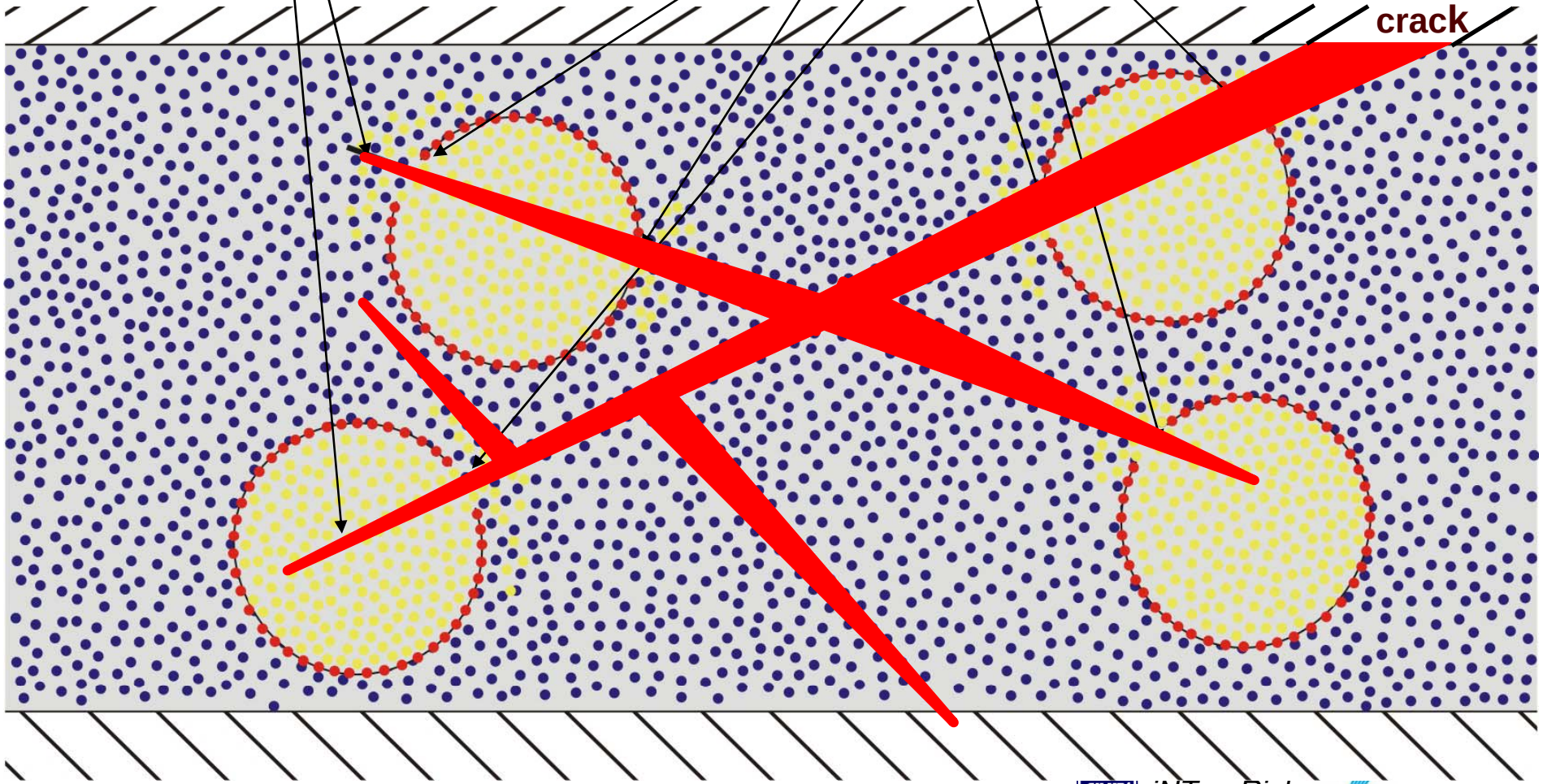
# DPD simulation for one microcapsule



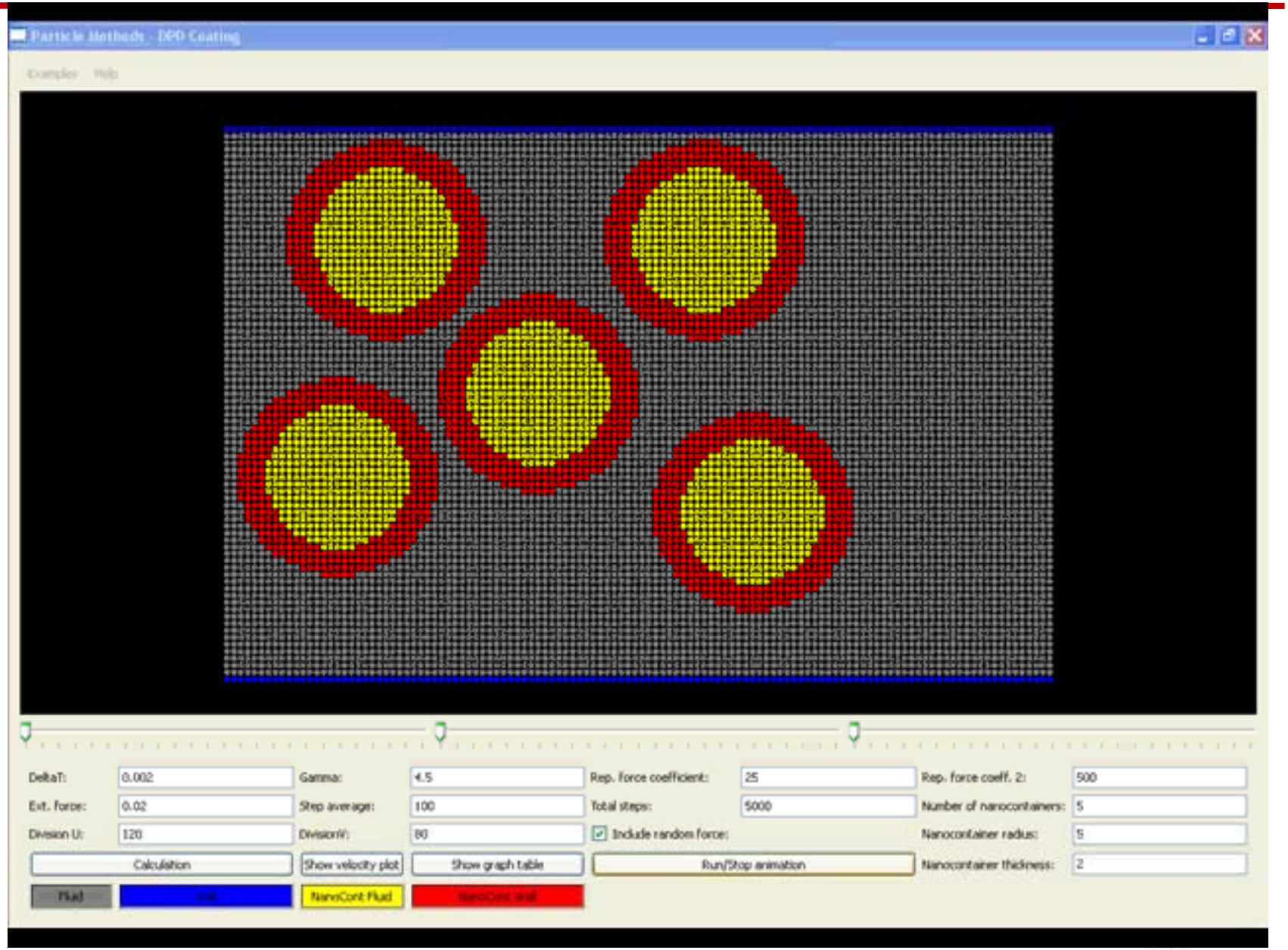
# DPD simulation for more nanocontainers: “Scenarios”

Crack lines are positioned randomly or according to the supposed “damage scenario”

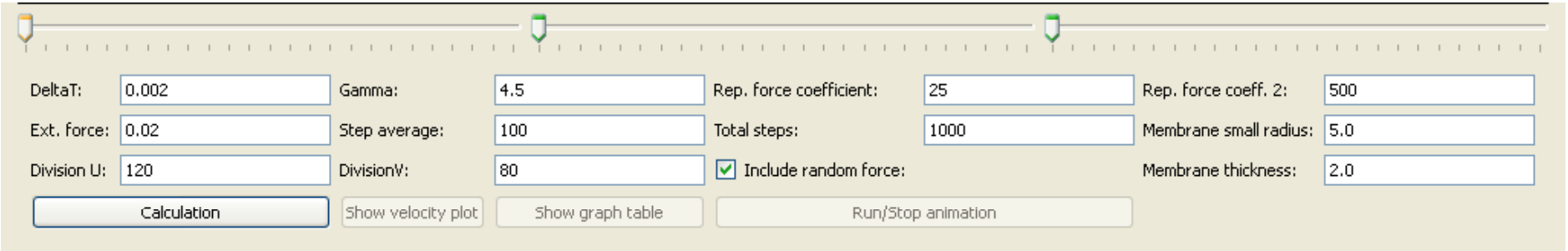
Rupture of nanocontainer



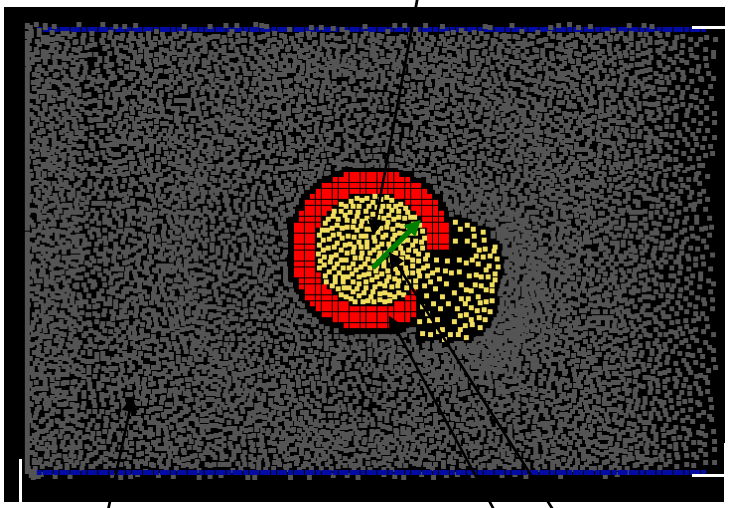
# User friendly software for DPD simulation of nanocoating with nanocontainers



# Basic parameters in DPD equations and main software dialog




Rep. force coefficient 2 – $a_{ij}$ repulsive coefficient for healing agent particles



Division V – initial number of particles in Y direction

Division U – initial number of particles in X direction

Membrane small radius

Membrane thickness

Rep. force coefficient – $a_{ij}$ repulsive coefficient for nanocoating layer particles

## Basic DPD equation

$$\mathbf{F}_i = \sum_{j \neq i} \left( \mathbf{F}_{ij}^C + \mathbf{F}_{ij}^D + \mathbf{F}_{ij}^R \left( \Delta t \right)^{-1/2} \right) + \mathbf{F}^{ext}$$

DeltaT = $\Delta t$

Ext.force = $F^{ext}$

$$\mathbf{F}_{ij}^C = a_{ij}(1 - r_{ij} / r_c)\mathbf{r}_{ij}^0$$

$$\mathbf{F}_{ij}^D = -\gamma w_D(\mathbf{v}_{ij} \cdot \mathbf{e}_{ij})\mathbf{r}_{ij}^0$$

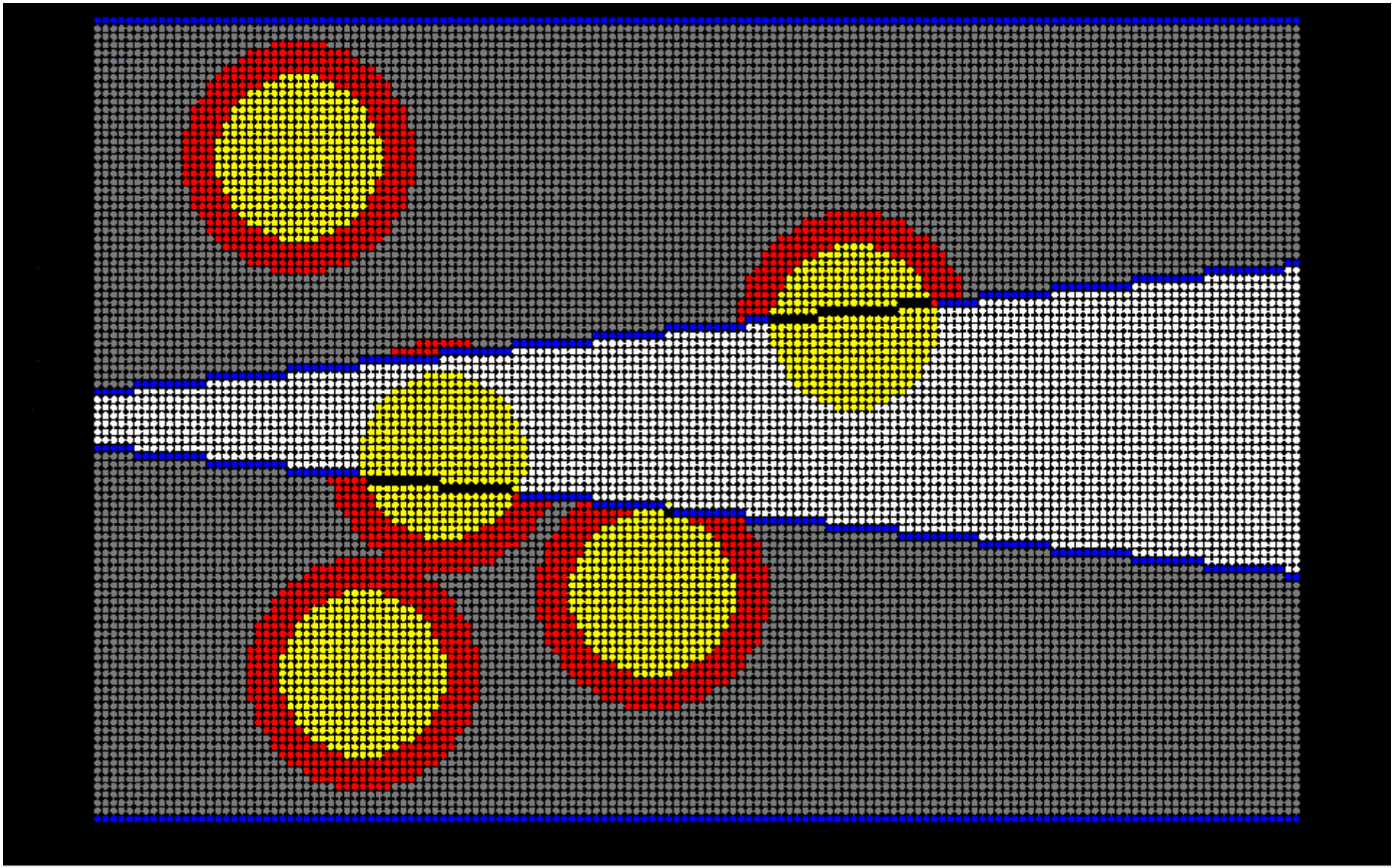
$$\mathbf{F}_{ij}^R = \sigma w_R \xi_{ij} \mathbf{r}_{ij}^0$$

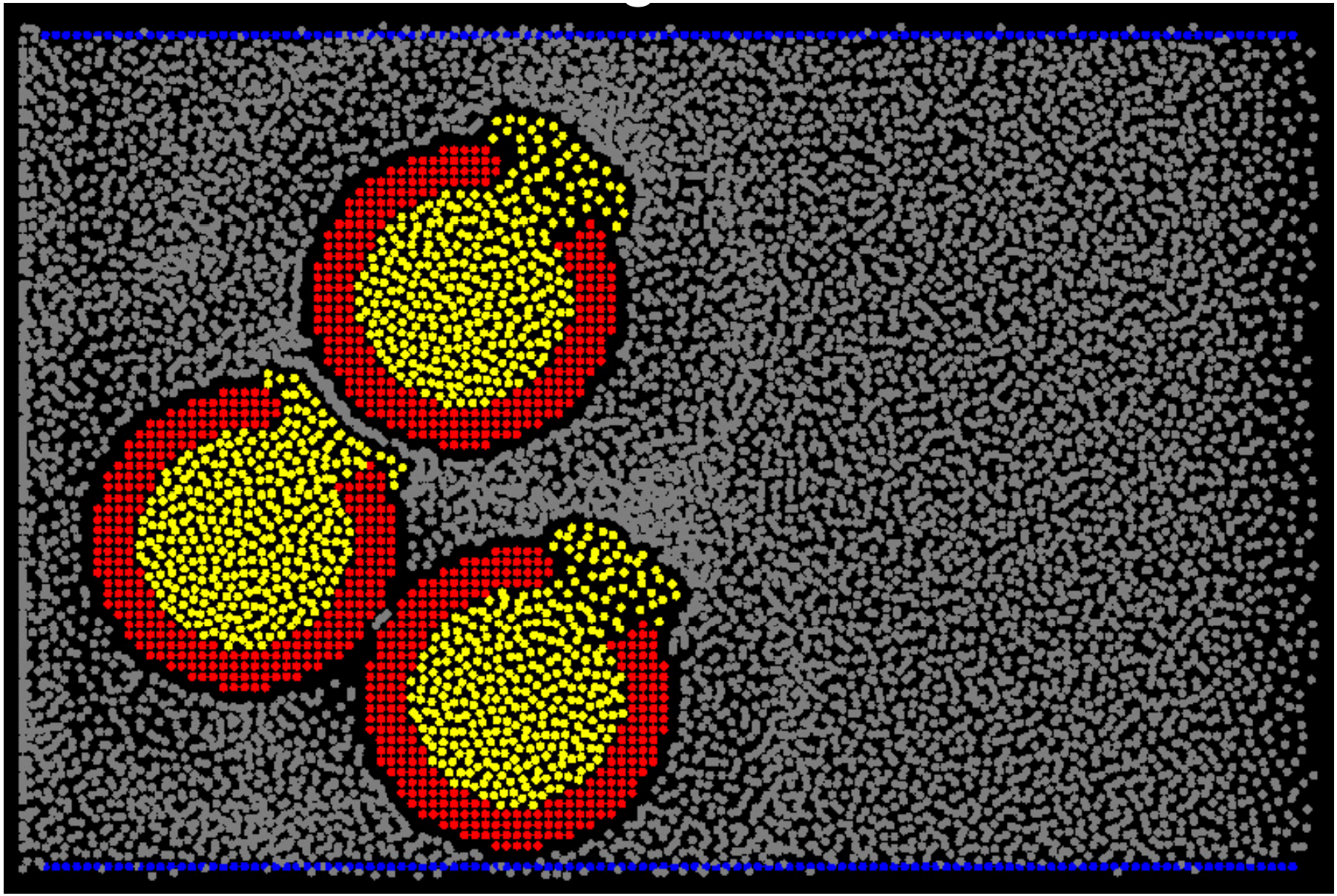
$F^C$ - conservative force

$F^D$ - conservative force

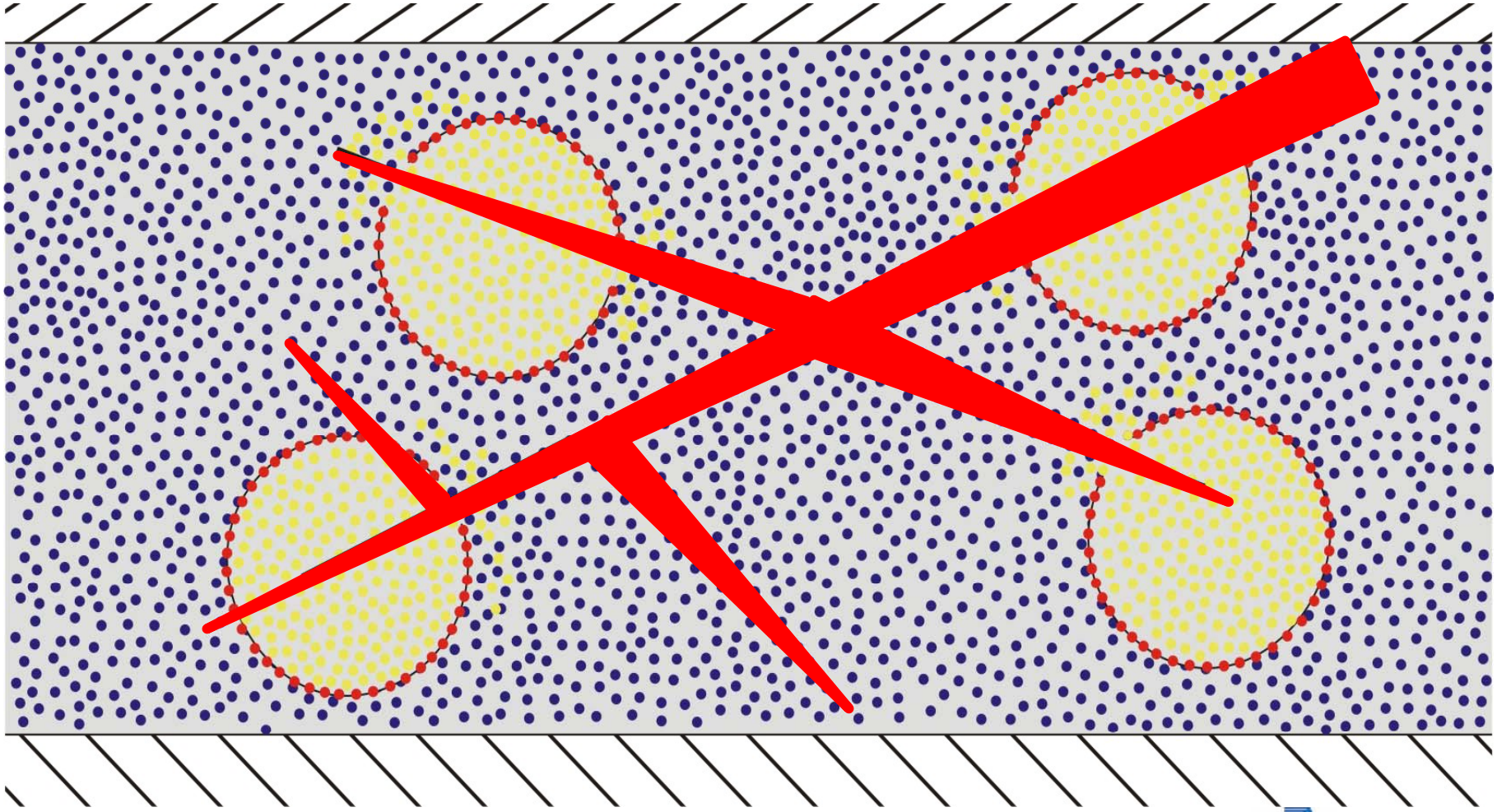
$F^R$ – random force

Gamma – $\gamma$ viscosity coefficient for dissipative force


Gamma:
4.5
Rep. force coefficient:
25
Rep. force coeff. 2:
Step average:
100
Total steps:
10000
Number of nanocontainers:
DivisionV:
100
Include random force:
Nanocontainer radius:



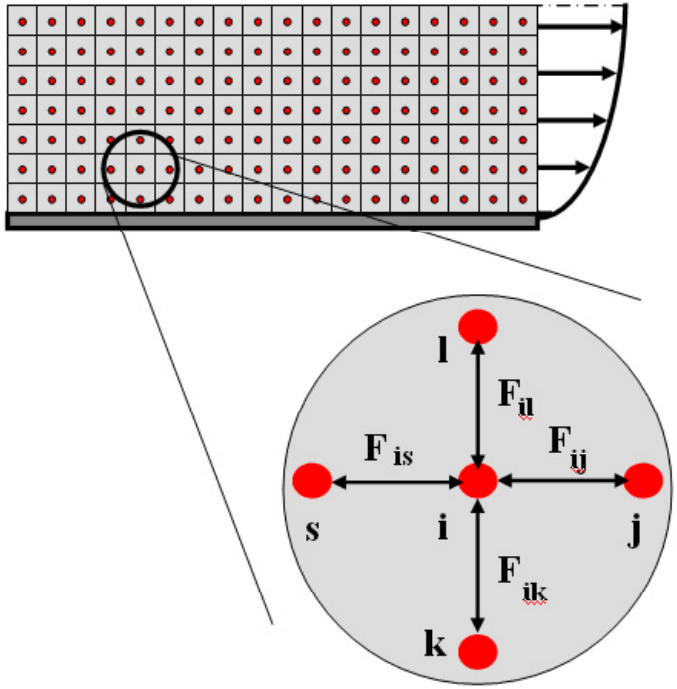
# Thank you very much!



# Discrete particle models of matrix with microcapsules

- Smoothed Particle Hydrodynamics (SPH)
- Discrete Particle Dynamics DPD
- Molecular Dynamics (MD)
- Multiscale modeling (bringing scale method)

# DPD Method – Theoretical background




$$\mathbf{F}_{ij} = \mathbf{F}_{ij}^{\text{Conservative}} + \mathbf{F}_{ij}^{\text{Disipative}} + \mathbf{F}_{ij}^{\text{Random}}$$

$$m_i \dot{\mathbf{v}}_i = \sum_j (\mathbf{F}_{ij}^C + \mathbf{F}_{ij}^D + \mathbf{F}_{ij}^R) + \mathbf{F}_i^{ext}$$

$$\mathbf{F}_{ij} = \mathbf{F}_{ij}^C + \mathbf{F}_{ij}^D + \mathbf{F}_{ij}^R$$

# Basic DPD equations

$$\mathbf{F}_{ij}^{C} = a_{ij}(1 - r_{ij} / r_c)\mathbf{r}_{ij}^{0}$$

$$\mathbf{F}_{ij}^{D} = -\gamma w_D(\mathbf{v}_{ij} \cdot \mathbf{e}_{ij})\mathbf{r}_{ij}^{0}$$

$$\mathbf{F}_{ij}^{R} = \sigma w_R \xi_{ij} \mathbf{r}_{ij}^{0}$$

$a_{ij}$ is the maximum repulsion force per unit mass

$r_{ij}$ is the distance between particles $i$ and $j$, is the unit vector pointing in direction from $j$ to $i$,

$\gamma$ is the friction coefficient

$\sigma$ is the amplitude of the random force.

$w_D$ and $w_R$ are the weight functions for dissipative and random forces

# Additional conditions for DPD equations

DPD fluid system possess a Gibbs–Boltzmann equilibrium state, the following relation between the amplitudes of the weight functions of dissipative and random forces,  and , must hold (Español 1995):

$$w_D = w_R^2$$

Also the amplitude of the random force $\sigma$ is related to the absolute temperature $T$,

$$\sigma = \left(2k_B T\gamma\right)^{1/2}$$

where  is the Boltzmann constant. The weight functions can be expressed in a form (Groot and Warren 1997) given as

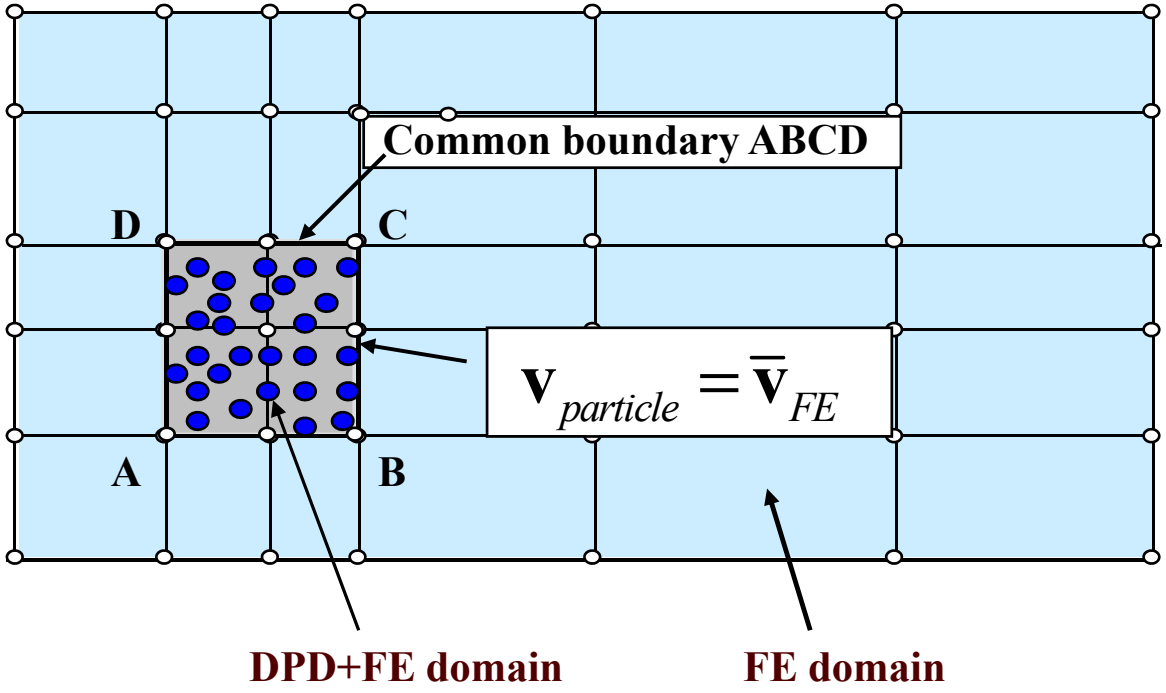
$$w_D = (1 - r_{ij}/r_c)^2 \qquad w_R = 1 - r_{ij}/r_c$$

# Multiscale Modeling FE + DPD

**Division of the flow domain into:**

**a) GLOBAL DOMAIN - Domain modeled by a continuum model (Finite Element) only**

**b) LOCAL DOMAIN - Domain modeled by both discrete particles (DPD) and FE**



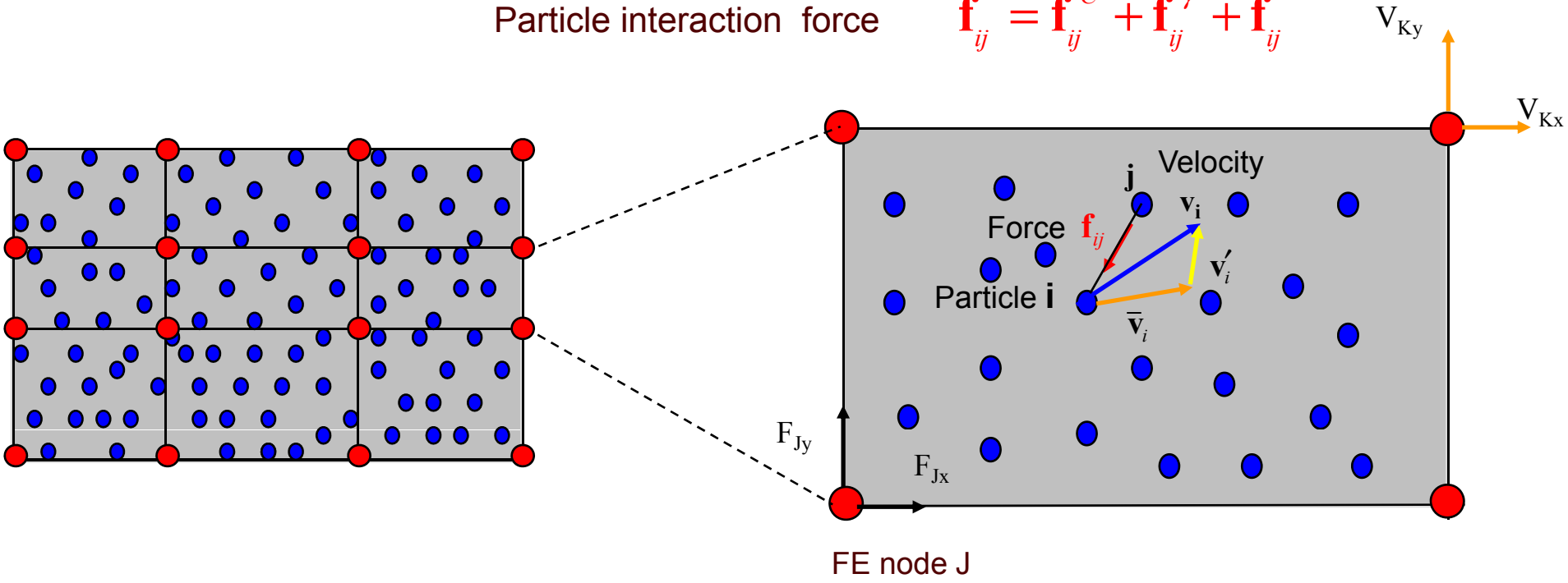

**Periodic boundary conditions – keep the number of particles constant within the local domain**

# Coupling the DPD and FE models

**1) Decomposition of particle velocities**

**2) FE nodal forces in terms of the particle interaction forces**

Particle interaction force $\mathbf{f}_{ij} = \mathbf{f}_{ij}^{C} + \mathbf{f}_{ij}^{\gamma} + \tilde{\mathbf{f}}_{ij}$



# MESOSCOPIC BRIDGING SCALE METHOD

## Mathematical interpretation of the coupling between discrete particle (DPD) and finite element (FE) models

**Kinetic energy**

$$E_k = \bar{E}_k + E'_k$$

$$E_k = \frac{1}{2}\mathbf{v}^T \mathbf{M}_A \mathbf{v} \qquad \text{DPD}$$

$$\bar{E}_k = \frac{1}{2}\bar{\mathbf{v}}^T \mathbf{M}_A \bar{\mathbf{v}} = \frac{1}{2}\mathbf{V}^T \mathbf{M}\mathbf{V}$$

$$E'_k = \frac{1}{2}\mathbf{v}'^T \mathbf{M}_A \mathbf{v}' \qquad \text{Fluctuating kinetic energy}$$

**Diff. Eqs. of Motion**

**Lagrangian Description**

$$\mathbf{M}_A \dot{\mathbf{v}} = \mathbf{f}^{ext} + \mathbf{f}^{\text{int}} \qquad \text{DPD}$$

$$\mathbf{M}\dot{\mathbf{V}} = \mathbf{F}^{ext} + \mathbf{F}^{\text{int}} \qquad \text{FE}$$

## Diff. Eqs. of motion

### Lagrangian description

$$\mathbf{M}_A\dot{\mathbf{v}}=\mathbf{f}^{ext}+\mathbf{f}^{\text{int}} \qquad \mathbf{M}\dot{\mathbf{V}}=\mathbf{F}^{ext}+\mathbf{F}^{\text{int}}$$

**Navier-Stokes FE eqs. of motion and Continuity**

$$\begin{bmatrix} \frac{1}{\Delta t}\mathbf{M}+{}^{t+\Delta t}\mathbf{K}^{(i-1)} & \mathbf{K}_{vp} \\ \mathbf{K}_{vp}^{T} & 0 \end{bmatrix} \begin{Bmatrix} \Delta\mathbf{V}^{(i)} \\ \Delta\mathbf{P}^{(i)} \end{Bmatrix} =$$

$$\begin{Bmatrix} {}^{t+\Delta t}\mathbf{F}_{\text{int}}^{(i-1)} \\ 0 \end{Bmatrix} + \begin{Bmatrix} {}^{t+\Delta t}\mathbf{F}_{ext}^{(i-1)} \\ 0 \end{Bmatrix} - \begin{bmatrix} \frac{1}{\Delta t}\mathbf{M}+{}^{t+\Delta t}\mathbf{K}^{(i-1)} & \mathbf{K}_{vp} \\ \mathbf{K}_{vp}^{T} & 0 \end{bmatrix} \begin{Bmatrix} {}^{t+\Delta t}\mathbf{V}^{(i-1)} \\ {}^{t+\Delta t}\mathbf{P}^{(i-1)} \end{Bmatrix} + \begin{Bmatrix} \frac{1}{\Delta t}\mathbf{M}^{t}\mathbf{V} \\ 0 \end{Bmatrix}$$

**Nodal internal forces**

$${}^{t+\Delta t}F_{Ki}^{\text{int}(i-1)} = -\int_V N_{K,j}\,{}^{t+\Delta t}\tau_{ij}^{(i-1)}\,dV$$

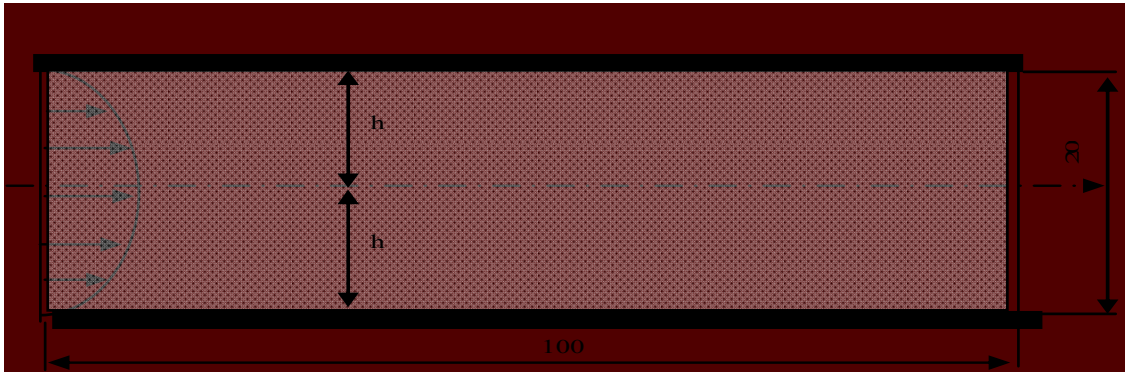
${}^{t+\Delta t}\tau_{ij}^{(i-1)}$ **Shear stresses**

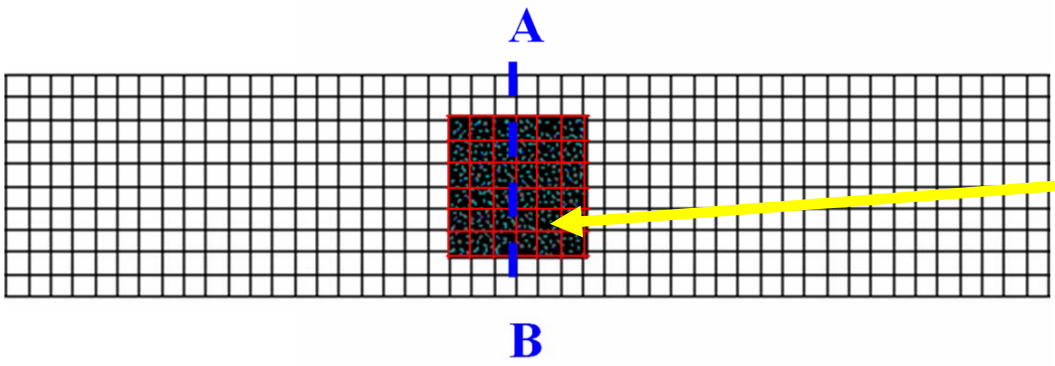
**Stress tensor**

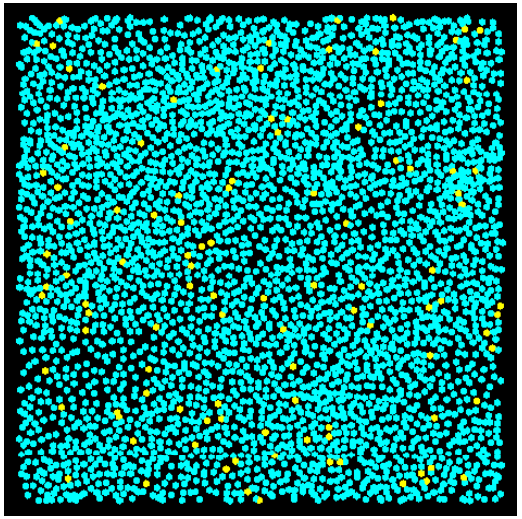
$$\boldsymbol{\sigma} = -n\left\langle \left[ \sum_i m_i \hat{\mathbf{v}}_i \otimes \hat{\mathbf{v}}_i + \frac{1}{2}\sum_i \sum_{j\neq i} \mathbf{r}_{ij} \otimes \mathbf{f}_{ij} \right] \right\rangle$$

**From DPD**

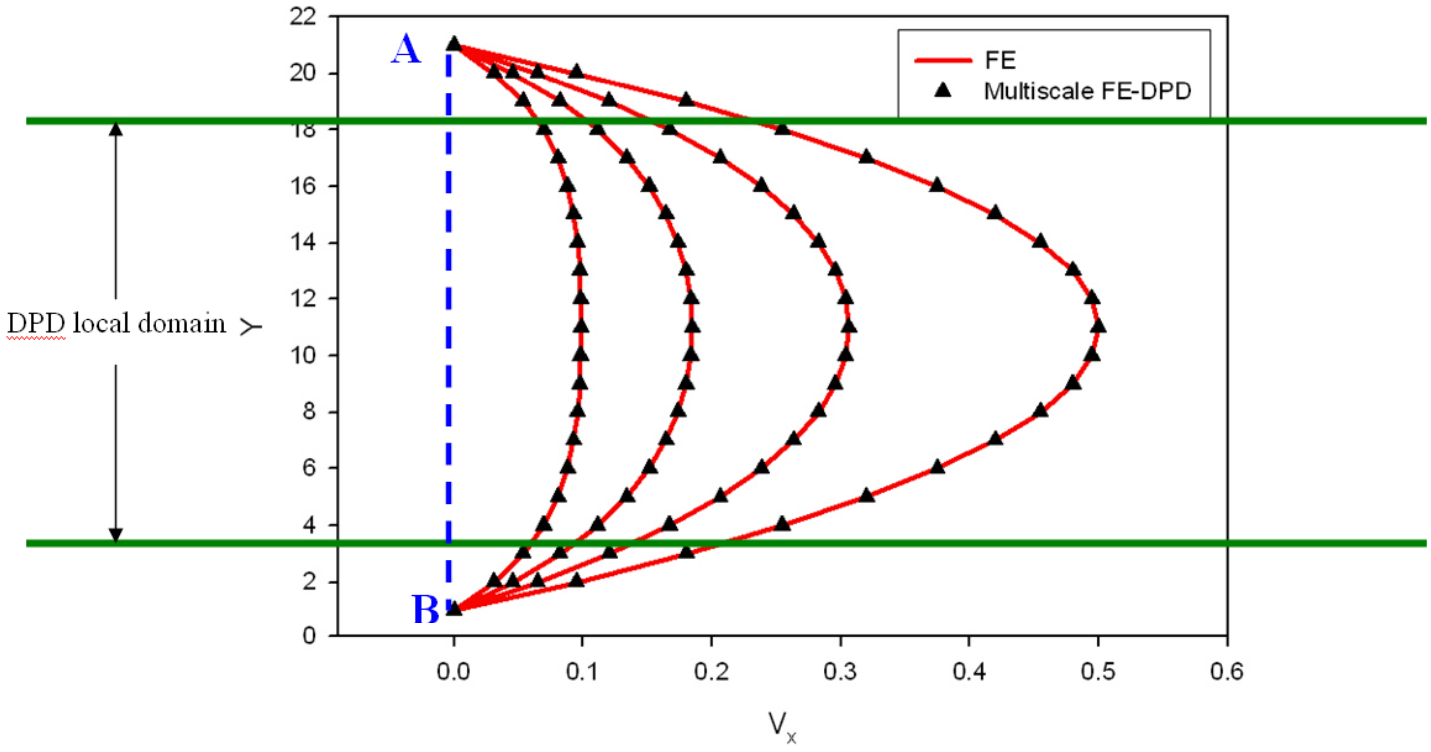
# Example 1: 2D Poiseuille fluid flow between two parallel plates

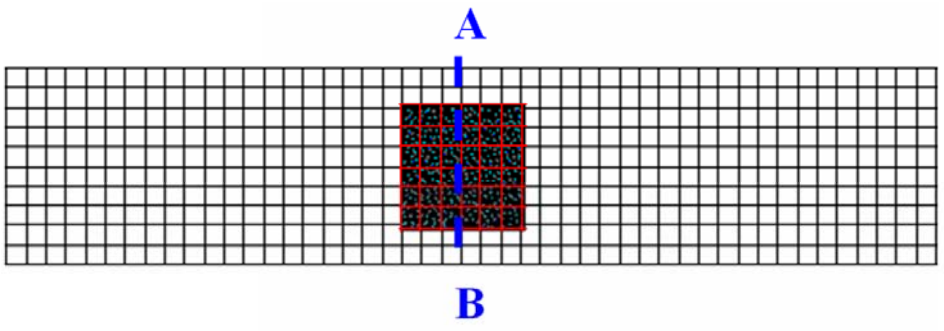


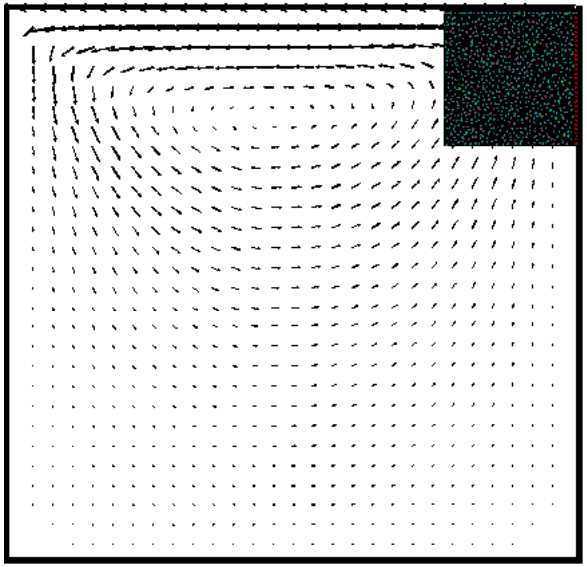



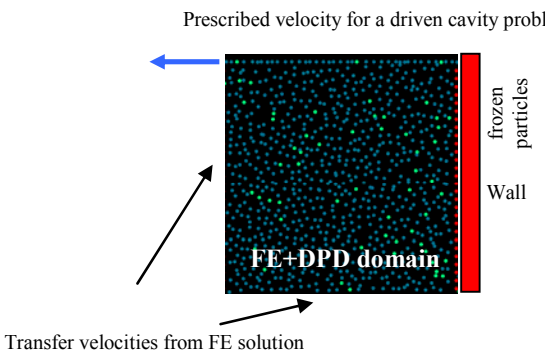
# 2D POISEUILLE FLOW

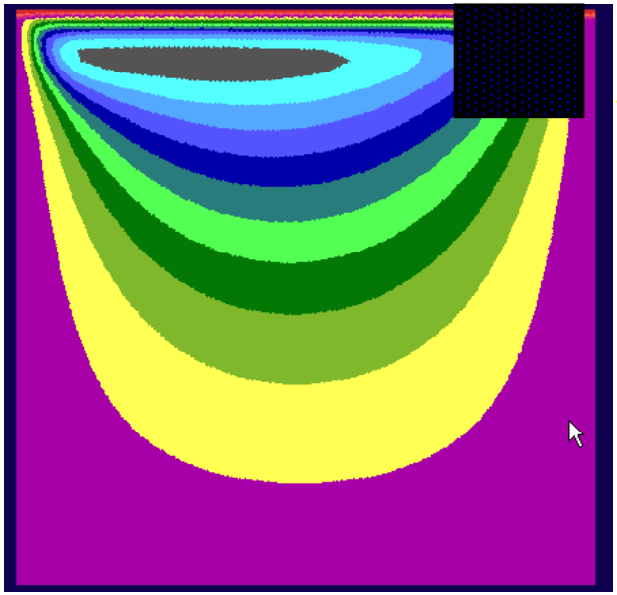


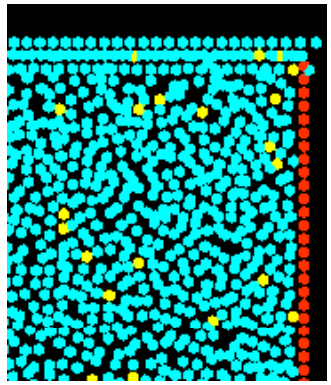



# Example 2: 2D flow inside a cavity

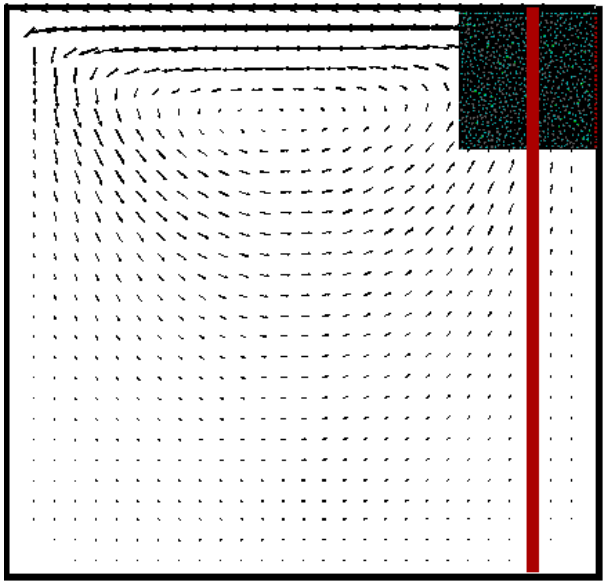


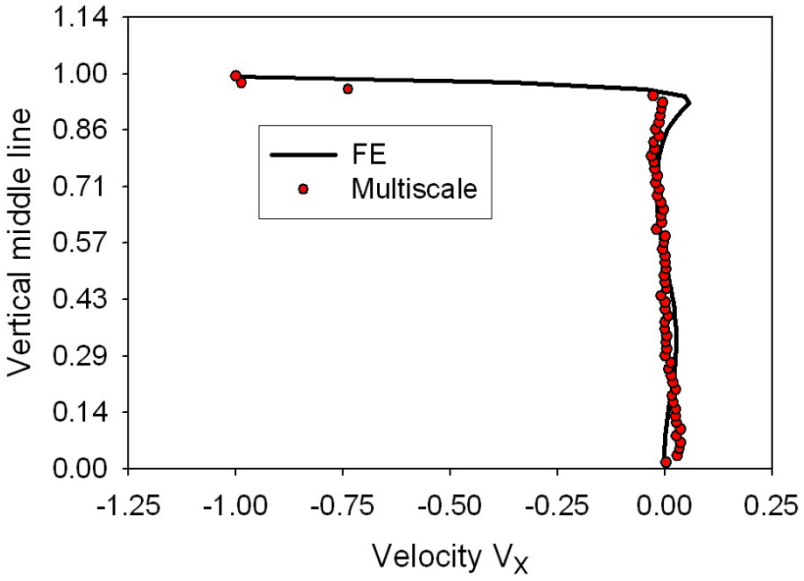


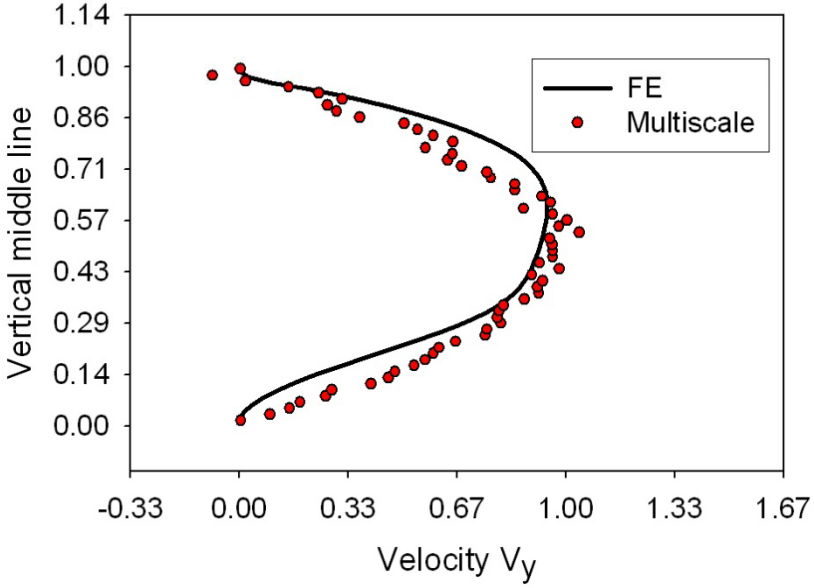





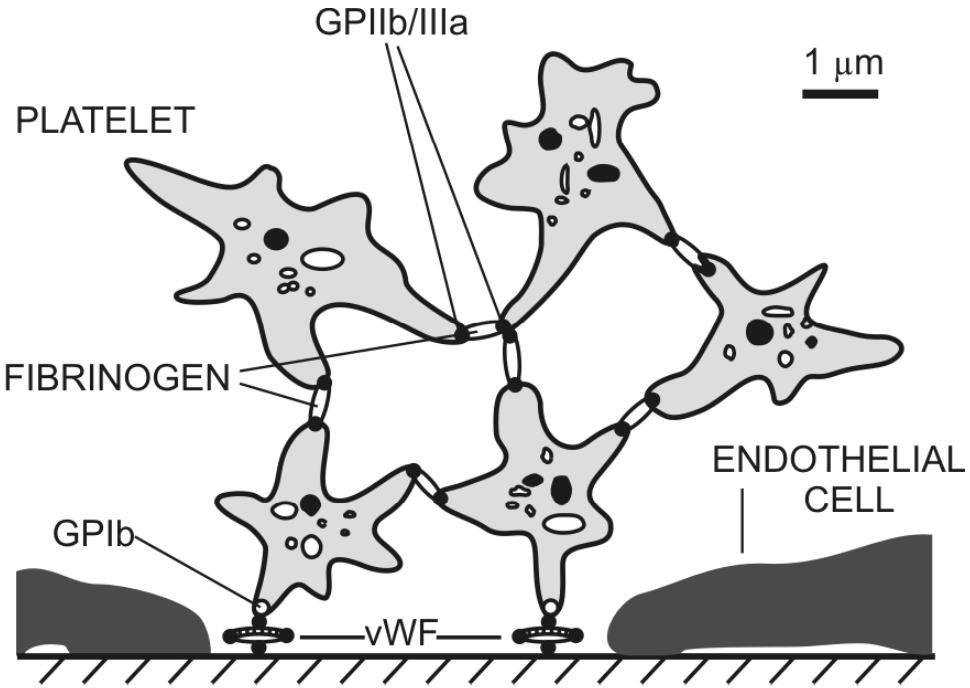
# Driven cavity problem: Results

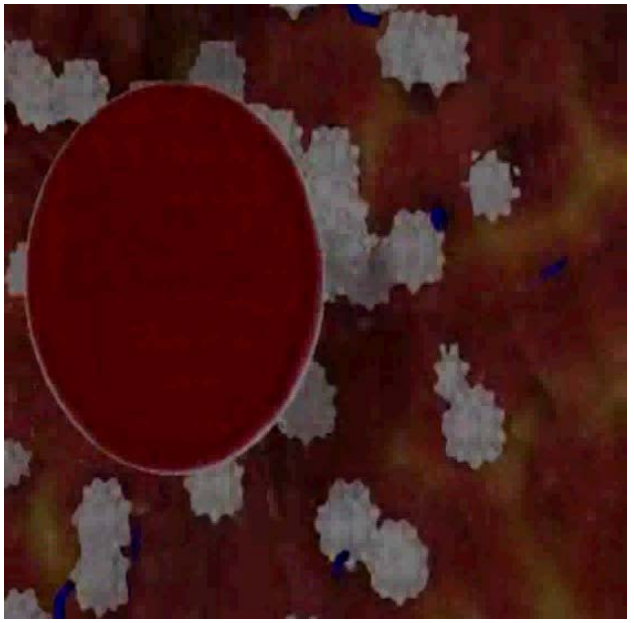




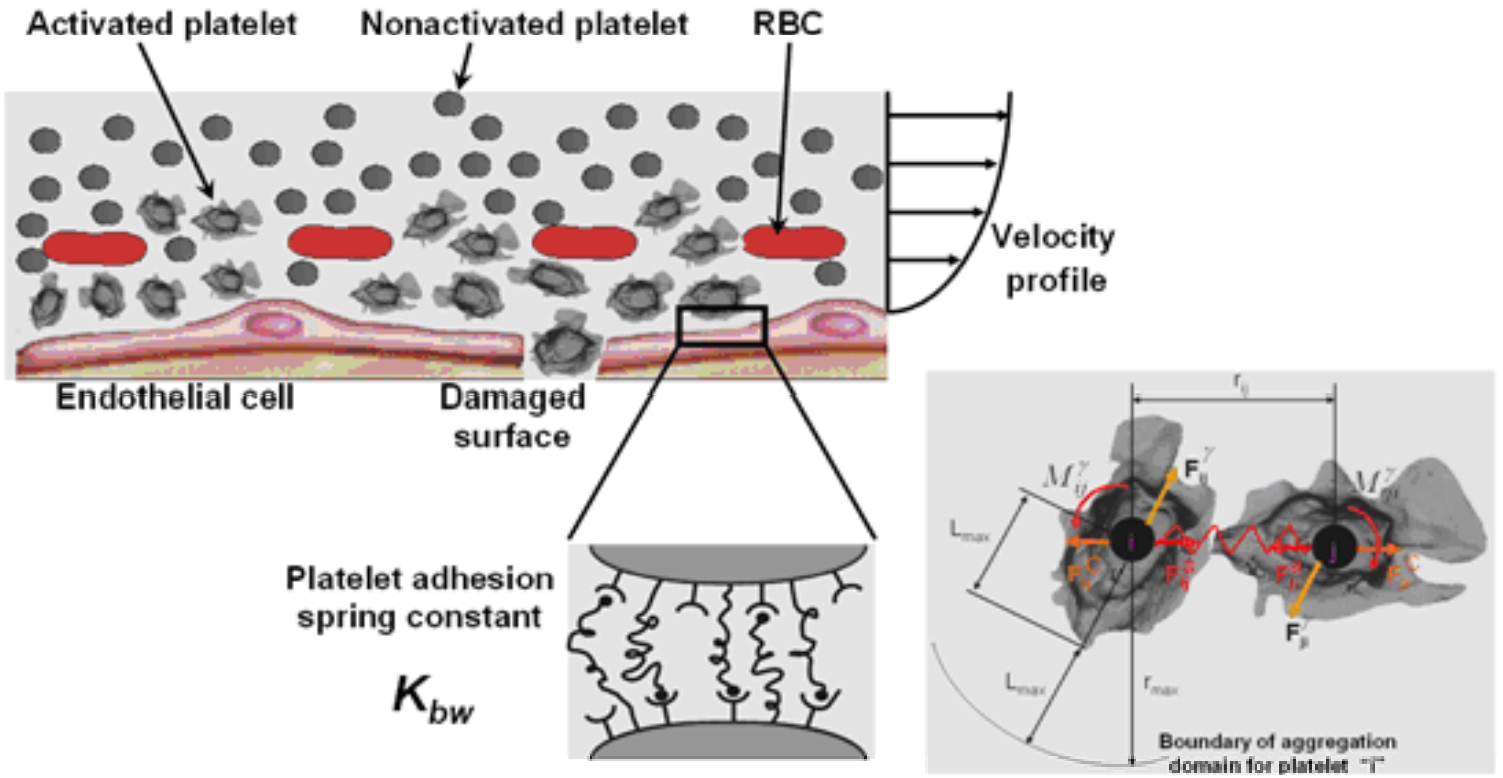
# DPD application in platelet adhesion and aggregation modeling



**Schematic representation of the mechanisms of platelet adhesion and aggregation in flowing blood**

# Additional forces in platelet aggregation and adhesion




Schematics of platelet aggregation and adhesion. Activated platelets in the vicinity of a injured wall epithelium and binding of platelets at the walls using springs. Interaction forces for two aggregated platelets .The domain of the interaction between platelets is denoted by $r_{max}$. (Filipovic et al. 2007)

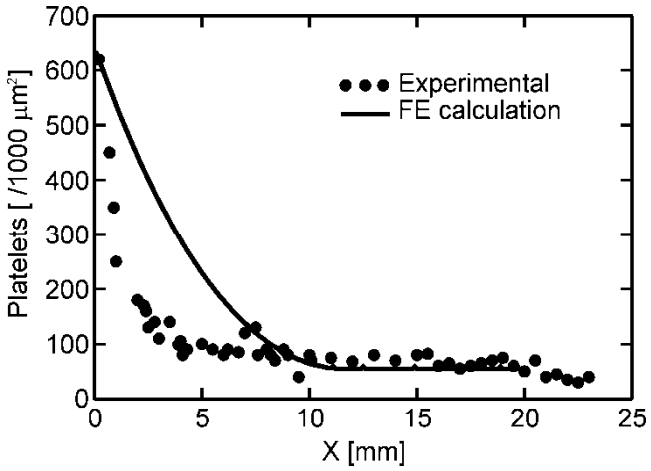
# Table of DPD parameters for thrombosis modeling

| Name of DPD parameter | What is used for platelet aggregation | Reference |
|---|---|---|
| Conservative force parameter | $a_{ij}$ = 25 | Groot, R.D., Warren, P.B., 1997. Dissipative particle dynamics: Bridging the gap between atomistic and mesoscopic simulation. J. Chem. Phys. 107, 4423-4435. |
| Friction coefficient | $\gamma$ = 4.5 | Groot, R.D., Warren, P.B., 1997. Dissipative particle dynamics: Bridging the gap between atomistic and mesoscopic simulation. J. Chem. Phys. 107, 4423-4435. |
| Spring constant for platelet binding | $k_{bw}$ = 50 N/m | Filipovic, N., Ravnic, D.J. Kojic, M., Mentzer, S.J., Haber, S. Tsuda, A., Interactions of Blood Cell Constituents: Experimental investigation and Computational Modeling by Discrete Particle Dynamics Algorithm, *Microvascular Research*, 75, 279-284, 2008. |

# Table of DPD parameters for thrombosis modeling

| | | |
|---|---|---|
| Relation between the weight functions of dissipative and random forces | $w_D = w_R^2$ | Groot, R.D., Warren, P.B., 1997. Dissipative particle dynamics: Bridging the gap between atomistic and mesoscopic simulation. J. Chem. Phys. 107, 4423-4435. |
| Boltzmann constant | $k_B = 1.3806504 \times 10^{-23}$ J/K | |
| Weight function of dissipative force | $w_D = (1 - r_{ij} / r_c)^2$ | |
| Weight function of random force | $w_R = 1 - r_{ij} / r_c$ | |
| Random number with zero mean and unit variance | $\xi_{ij}$ | The Random Number Generator which I used is based on the algorithm in a FORTRAN version published by George Marsaglia and Arif Zaman, Florida State University; At the fhw (Fachhochschule Wiesbaden, W.Germany), Dept. of Computer Science,<br>This random number generator originally appeared in "Toward a Universal Random Number Generator" by George Marsaglia and Arif Zaman. Florida State University Report: FSU-SCRI-87-50 (1987) It was later modified by F. James and published in "A Review of Pseudo-random Number Generators"<br>THIS ALGORITHM IS PUBLISHED IN TRANSACTIONS ON MATHEMATICAL SOFTWARE, VOL. 18, NO. 4, DECEMBER, 1992, PP. 434-435. |

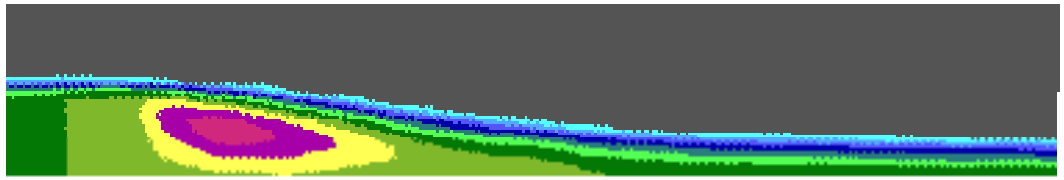
# Platelet aggregation in blood flow between two parallel plates

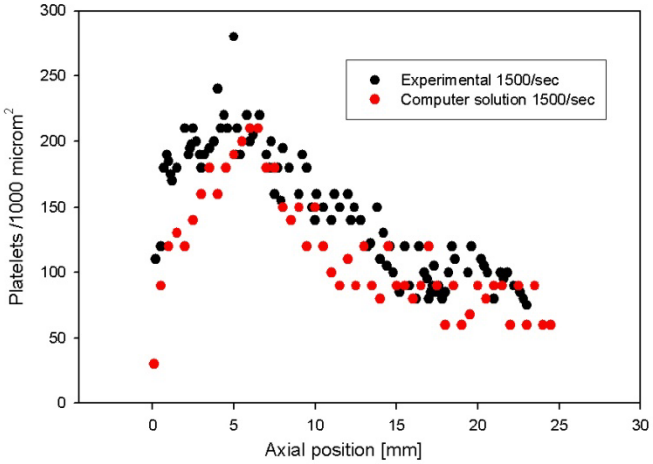



**Filipovic, N.**, Ravnic, D.J. Kojic, M., Mentzer, S.J., Haber, S. Tsuda, A., Interactions of Blood Cell Constituents: Experimental investigation and Computational Modeling by Discrete Particle Dynamics Algorithm, *Microvascular Research*, 75, 279-284, 2008.

**Filipovic, N.**, Haber, S., Kojic, M., Tsuda, A., Dissipative particle dynamics simulation of flow generated by two rotating concentric cylinders: II. Lateral dissipative and random forces, *J. Phys. D: Appl. Phys.* 41 035504 , 2008

# DPD simulation of Karino's example blood flow through expanded tube

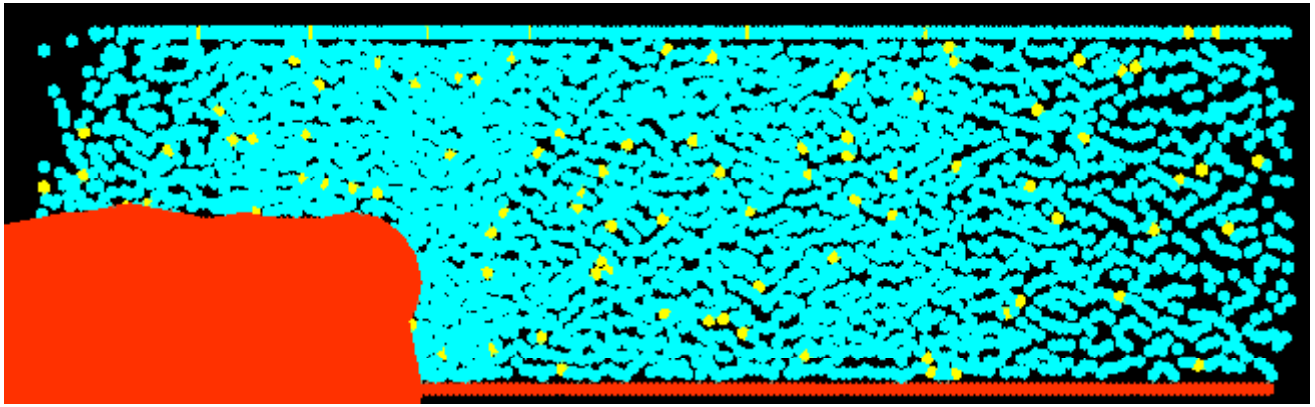


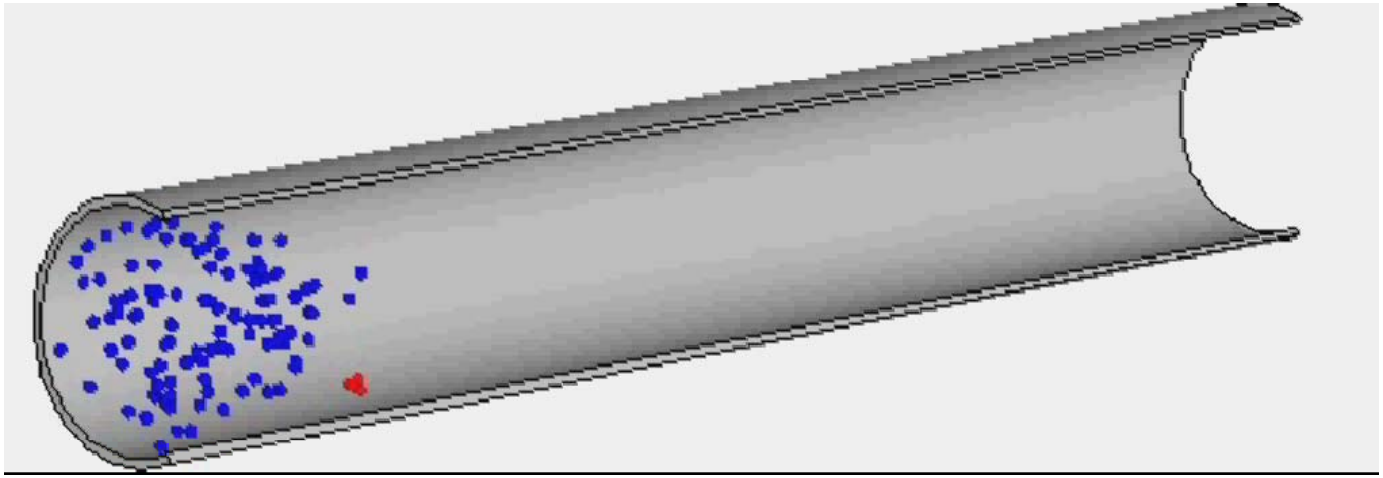



T. Karino, H.L. Goldsmith, Adhesion of human platelets to collagen on the walls distal to a tubular expansion, Microvascular Research 17, 238-269, 1977.

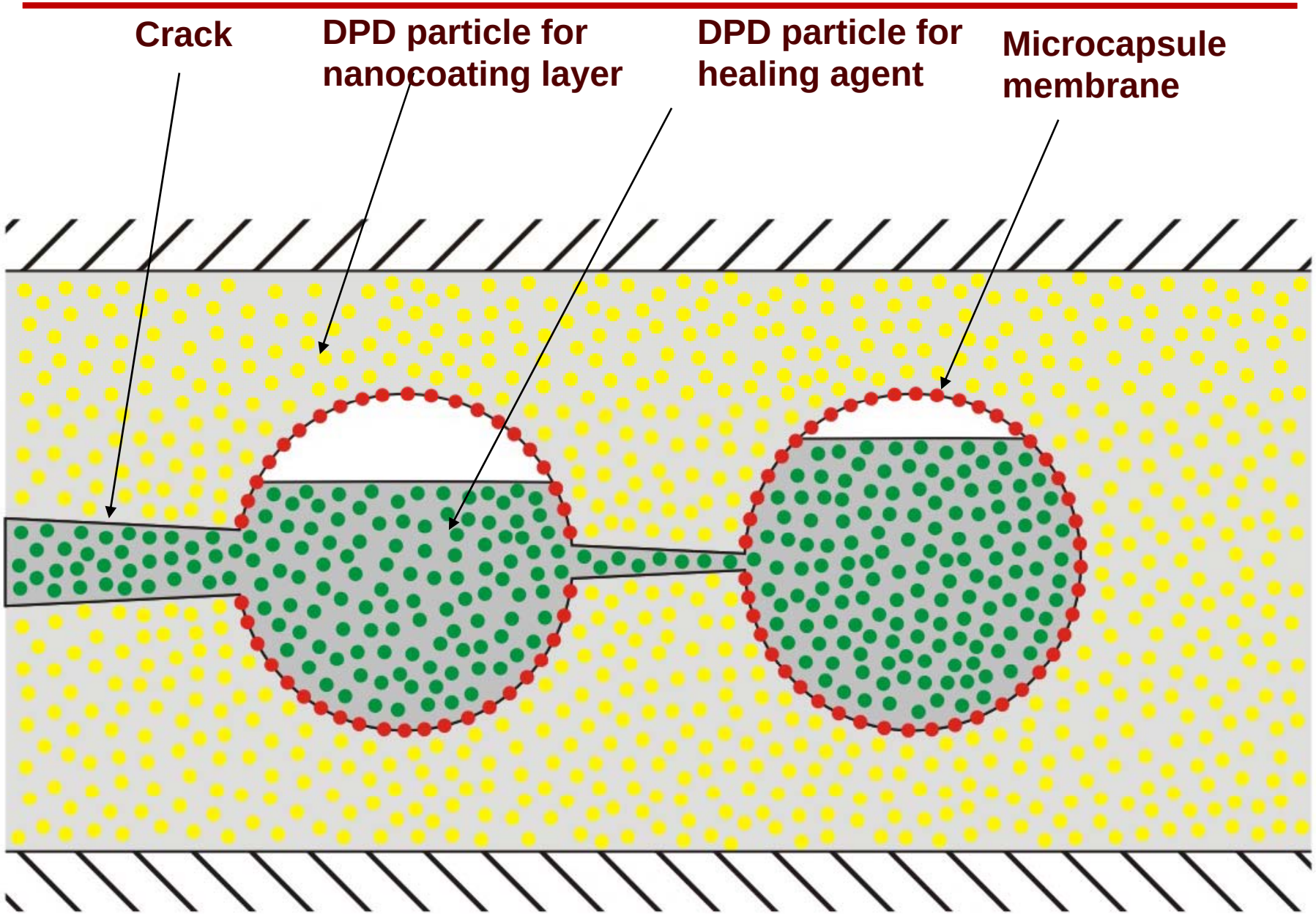
Filipovic, N., Kojic, M., Tsuda, A., Modeling thrombosis using dissipative particle dynamics method, Phil Trans Royal, A 366(1879), 2008

# Deposition of platelets, computer simulations





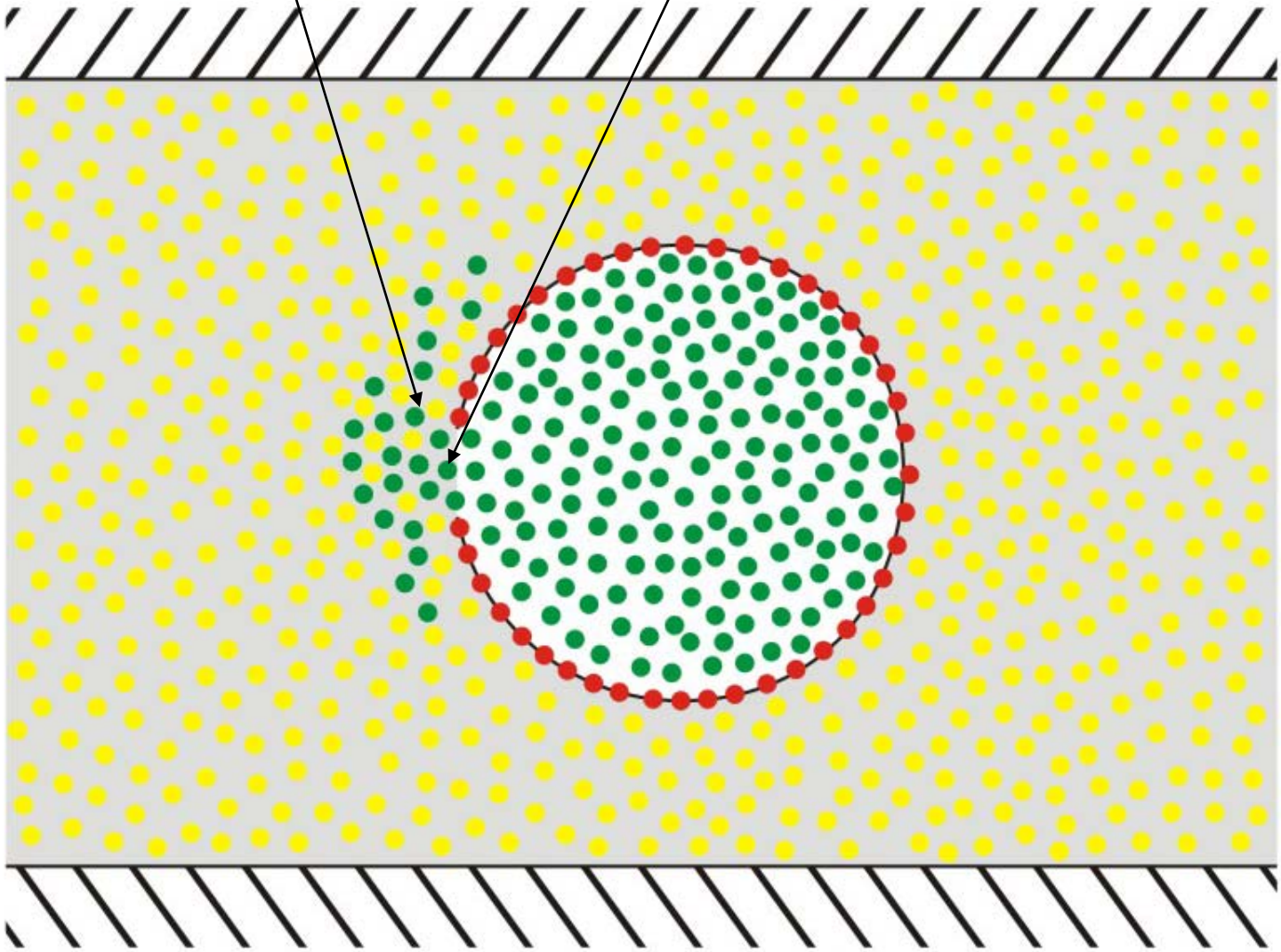
# Basic DPD simulation concept for self-healing process



# DPD simulation for one microcapsule

Healing agent and catalysts particles start to interact

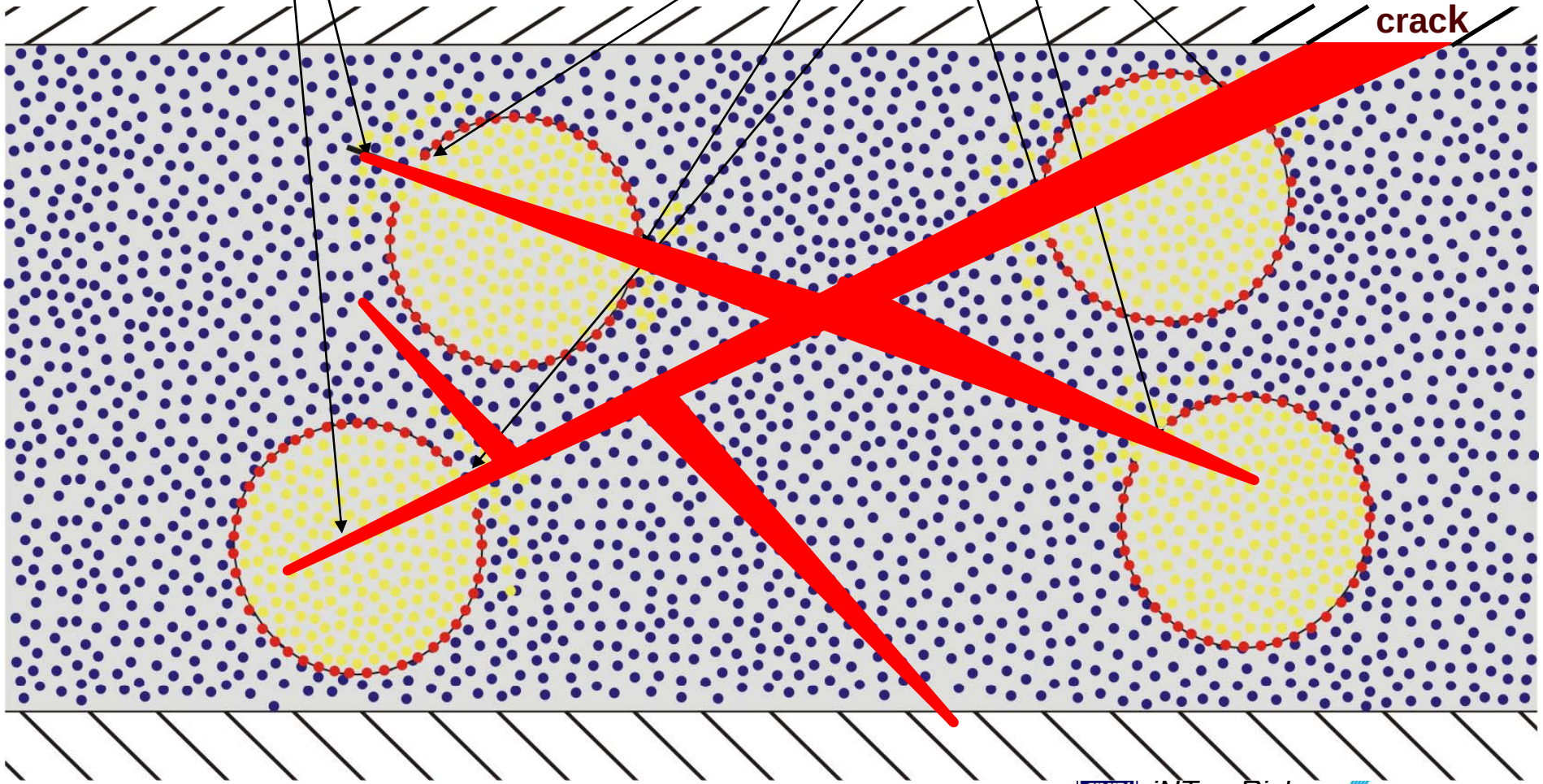
Randomize rupture position of microcapsule



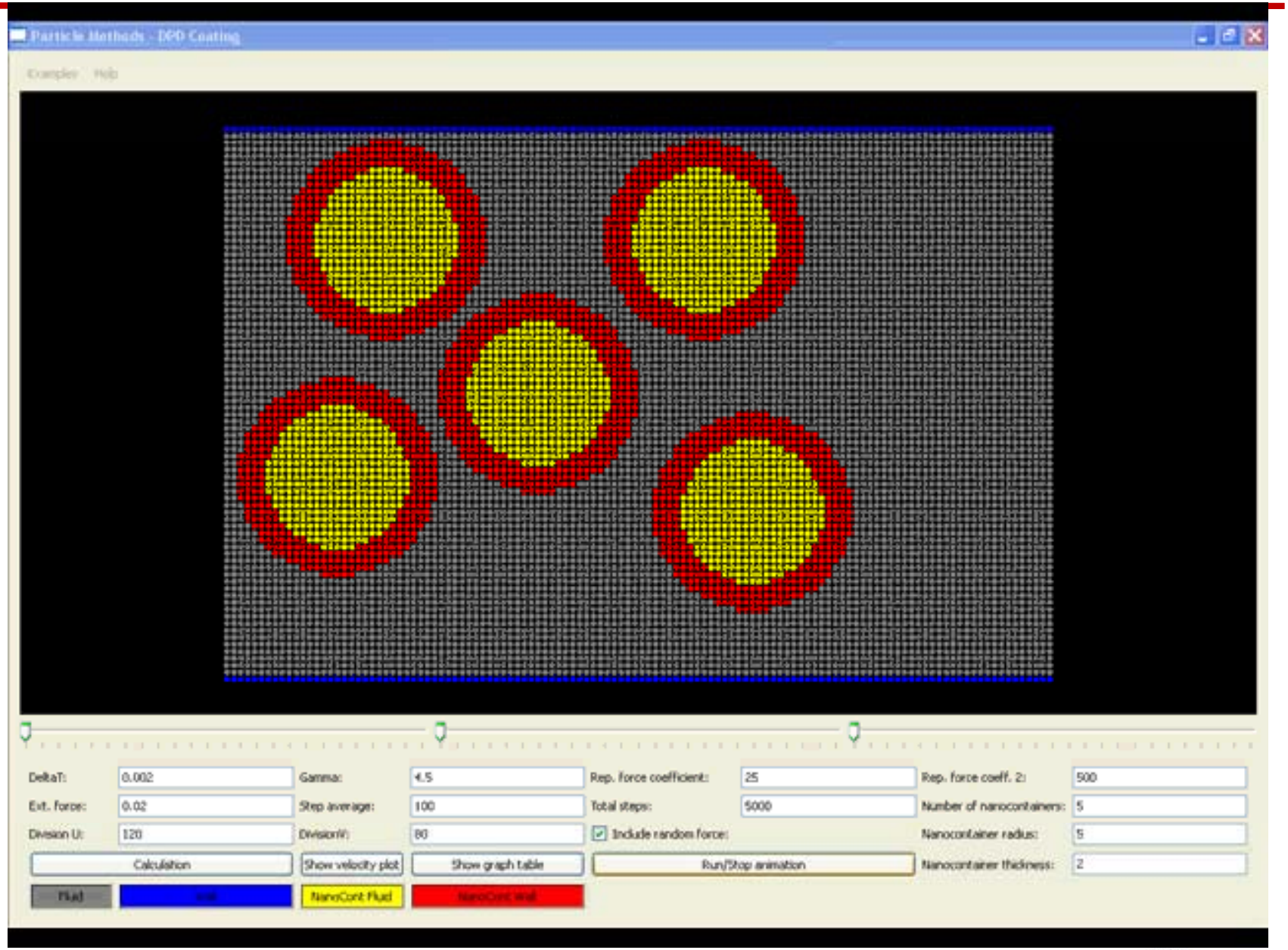
# DPD simulation for more nanocontainers: “Scenarios”

Crack lines are positioned randomly or according to the supposed “damage scenario”

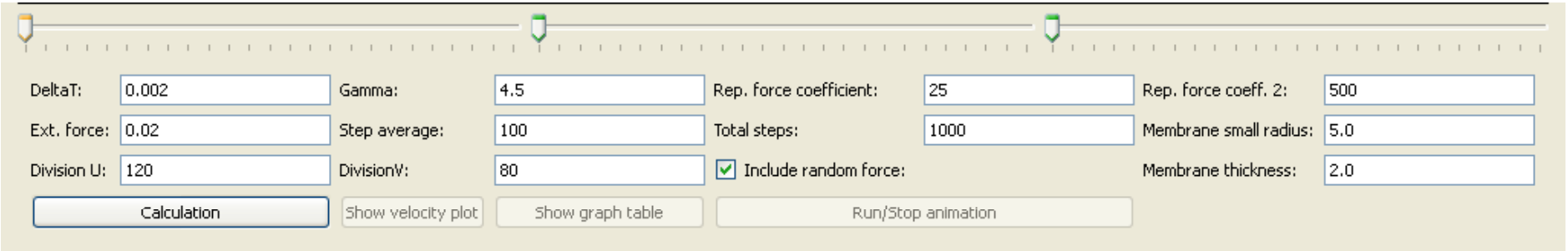
Rupture of nanocontainer



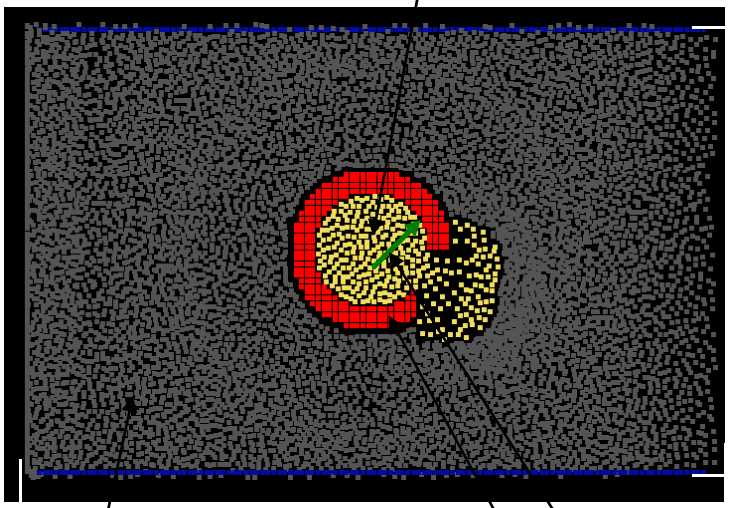
# User friendly software for DPD simulation of nanocoating with nanocontainers



# Basic parameters in DPD equations and main software dialog




Rep. force coefficient 2 – $a_{ij}$ repulsive coefficient for healing agent particles



Division V – initial number of particles in Y direction

Division U – initial number of particles in X direction

Membrane small radius

Membrane thickness

Rep. force coefficient – $a_{ij}$ repulsive coefficient for nanocoating layer particles

## Basic DPD equation

$$\mathbf{F}_i = \sum_{j \neq i} \left( \mathbf{F}_{ij}^C + \mathbf{F}_{ij}^D + \mathbf{F}_{ij}^R \left( \Delta t \right)^{-1/2} \right) + \mathbf{F}^{ext}$$

DeltaT = $\Delta t$

Ext.force = $F^{ext}$

$$\mathbf{F}_{ij}^C = a_{ij}(1 - r_{ij} / r_c)\mathbf{r}_{ij}^0$$

$$\mathbf{F}_{ij}^D = -\gamma w_D(\mathbf{v}_{ij} \cdot \mathbf{e}_{ij})\mathbf{r}_{ij}^0$$

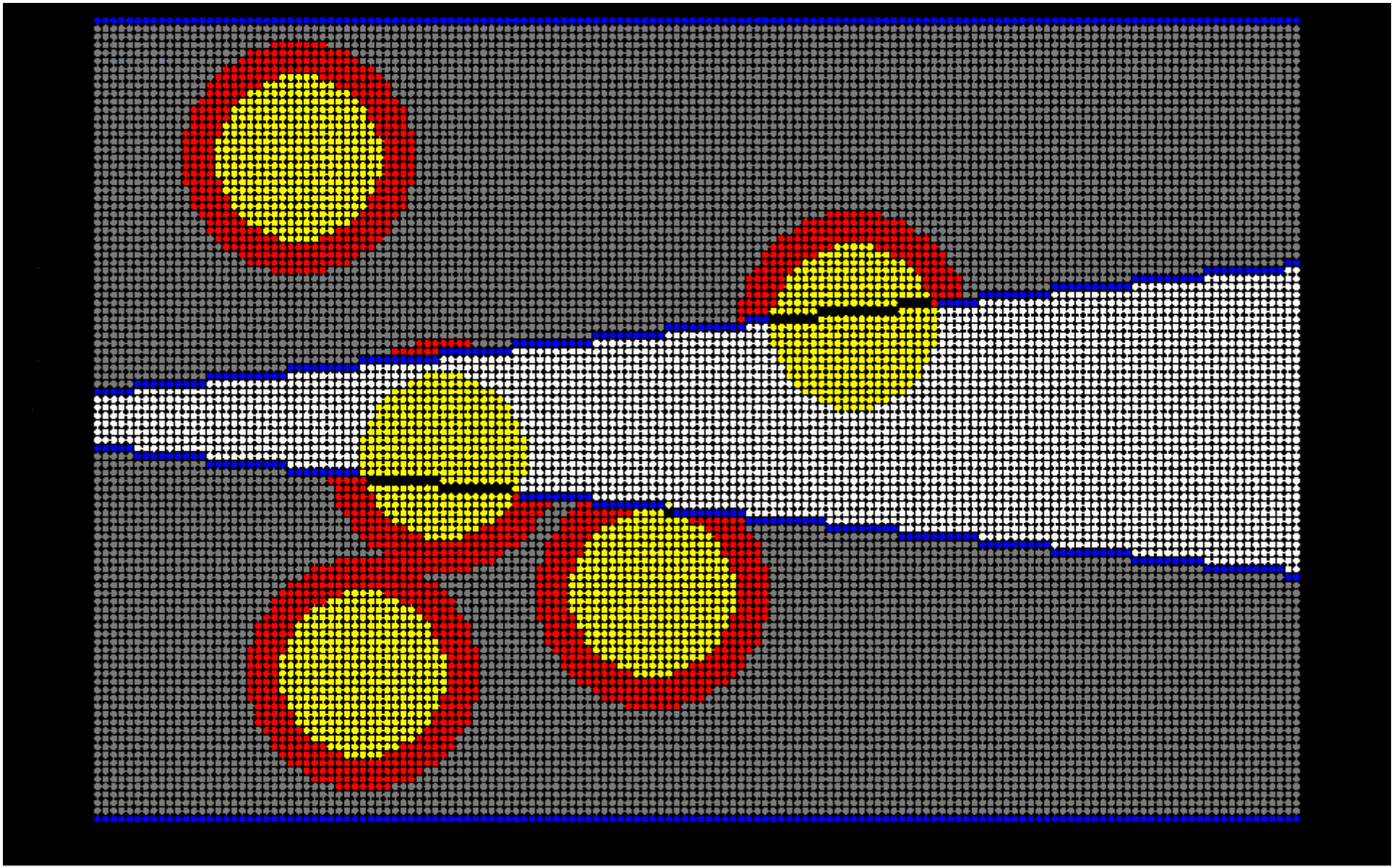
$$\mathbf{F}_{ij}^R = \sigma w_R \xi_{ij} \mathbf{r}_{ij}^0$$

$F^C$ - conservative force

$F^D$ - conservative force

$F^R$ – random force

Gamma – $\gamma$ viscosity coefficient for dissipative force


Gamma:
4.5
Rep. force coefficient:
25
Rep. force coeff. 2:
Step average:
100
Total steps:
10000
Number of nanocontainers:
DivisionV:
100
Include random force:
Nanocontainer radius:

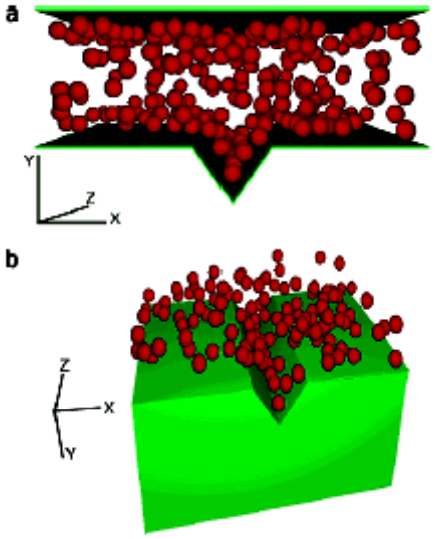
# Alternative and comparison: MD method for nanocomposite coating for healing surface defects

- Thin film of polimers and nanoparticles
- Polimers are modeled as bead-spring chains
- Each chain is composed of 50 Lennard-Jones (LJ) spheres that are connected by anharmonic springs

$$U_{LJ}(r) = \begin{cases} 4\varepsilon_{ij}\left[\left(\frac{\sigma_m}{r}\right)^{12} - \left(\frac{\sigma_m}{r}\right)^{6} - \left(\frac{\sigma_m}{r_c}\right)^{12} + \left(\frac{\sigma_m}{r_c}\right)^{6}\right] & r \le r_c \\ 0 & r > r_c \end{cases}$$

$$\sigma_m = \left(\sigma_i + \sigma_j\right)/2 \qquad r_c = 2^{1/6}\sigma_m$$

where $\sigma_m$ is the characteristics interaction energy between spheres *i* and *j*, $r_c$ is cut off radius




Geometry of the system used in the molecular dynamics (MD) simulations.
(a) full simulation box
(b) view from a different angle

**Adjoining spheres along a chain interact through a finite extendable nonlinear elastic (FENE) potential given as**

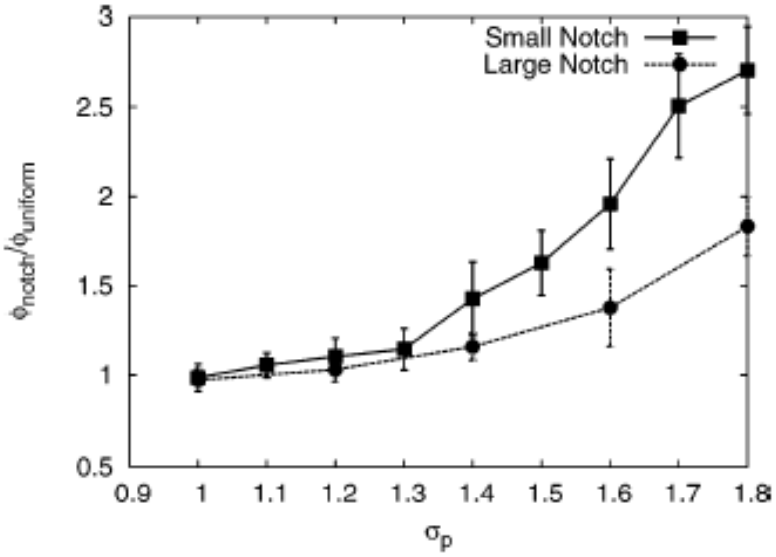
$$U_{FENE}(r) = \begin{cases} -0.5\kappa R_0^2 \ln\left[1-\left(\frac{r}{R_0}\right)^2\right] & r < R_0 \\ \infty & r \geq R_0 \end{cases}$$

$$\kappa = 30\varepsilon/\sigma^2 \qquad R_0 = 1.5\sigma \qquad T^* = kT/\varepsilon$$

**where κ is spring constant, $R_0$ is radius, $T^*$ is constant temperature maintained by a Brownian thermostat**

**Nanoparticles are added to the system at random positions, resulting in a configuration where monomers and nanoparticles overlap. This overlaping is define as**

$$U_{soft}(r) = \begin{cases} A\left[1+\cos\left(\frac{\pi r}{r_c}\right)\right] & r \leq r_c \\ 0 & r > r_c \end{cases}$$




**Average volume fraction of particles inside the notch (notch/uniform) as a function of particle size for two different notch sizes. [*Tyagi et al, Macromolecules 37, 9160-9168, 2004*]**

## References


1. Filipovic, N., Ravnic, D., Kojic, D., Mentzer, S.J. Haber, S. Tsuda, A. Platelet adhesion to a collagen wall: Experimental investigation and computer modeling by Dissipative Particle Dynamics Method, *Microvascular Research*, 75, 279-284, 2008.
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10. Tyagi, S., *et al.*, *Macromolecules,* 37, 9160, 2004.
11. Smith, K. A., *et al.*, *Macromolecules,* 38, 10138, 2005.