Modeling nanoindentation of virus shells: Do substrate adhesion and geometry matter?

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Abstract

This article investigates the deformation of a shell representing a virus in the context of slow evolution linear elasticity and in contact of different substrates. In order to understand the influence of the adhesion forces in the deformation of the virus, we compare the virus binding in contact of a flat substrate with and without the adhesion forces derived from the Lennard-Jones potential. Finally, we study the influence of the geometry of the substrate by considering a support made of two circles. The numerical simulations use a finite elements discretization.

Keywords: virus binding, linear elasticity, unilateral contact, virus interaction with substrate, finite elements.

1 Introduction

Recent past has witnessed significant improvements in techniques for the measurement of forces at nanoscale [2] and an increased interest in the physical phenomena underlying the behavior of viruses as many-body molecular systems [18, 16]. As a consequence there is an increased demand on theoretical models for problems relating to the interaction of a virus with its environment.

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For example, viruses have to bind and cross the plasma membrane. It is well established that instances of multivalent virus binding to the host plasma membrane trigger signaling pathways in the cell which lead to virus endocytosis [15]. Similarly, binding to the endosomal membrane triggers in certain viruses profound conformational changes [25]. How is virus mechanics involved in translating the binding events into a chemical transformation cascade? This type of problem is important because virus deformation could be an integral part of various stages of the virus life cycle.

Numerous experimental studies of virus deformation using the mechanical probe of an atomic force microscope have already provided a wealth of information on the strength of a virus shell and on the dynamics of deformation under directional load; see e.g. [3, 8, 9, 10, 17, 20, 23, 24]. Theoretical treatments followed, from simple thin elastic shell approximations, through finite-element numerical simulations of continuum models, to coarse-grained molecular dynamics [19, 1, 5]. In all these models, the interaction between the substrate and the virus during compression by a mechanical probe is reduced to a rough contact and a hard-wall potential, i.e. the particle cannot slip and only very short-range repulsive interactions occur between the surface and the elements of the virus model.

However, in reality, viruses have to bind to the substrate surface to be immobilized for atomic force microscope (AFM) imaging. Attractive forces must exist between substrate and the virus shell. As the shell is pressed against the substrate by the AFM probe, adhesion increases. The question we address here is how might these attractive forces influence the force-displacement curve and the measurement of an elastic constant for the virus particle?

The mathematical model that we will use is based on linear elasticity theory with unilateral contact, first developed from a mathematical point of view by G. Fichera [7], J.-L. Lions and G. Stampacchia [14], and G. Duvaut and J.-L. Lions [6] and by N. Kikuchi and J. T. Oden from a numerical point of view [12]. We consider in the sequel an elastic shell representing the virus with initial shape Ω^0 and subjected to forces $\mathcal{F}$, combination of an imposed force $\mathbf{F}$ and substrate adhesion forces $\mathbf{f}_{adh}$ derived from the Lennard-Jones potential [11]. The shell is subjected to unilateral contact with a rigid support. We assume that the force $\mathbf{F}$ is progressively applied by small increments $\frac{\mathbf{F}}{N}$, where $N \in \mathbf{N}^*$, like in a slow evolution and that the body is subjected to a succession of equilibrium states and that it remains elastic all along. In particular we assume that the passage from the equilibrium under the force $\frac{n\mathbf{F}}{N}$, where $0 \leq n < N$, to the equilibrium under the force $\frac{(n+1)\mathbf{F}}{N}$ pertains to linear elasticity. Note that the “linear elasticity” behavior applies to the constitutive law only since the problem is nonlinear in any case due to the unilateral forces as described below.

This paper is organized as follows: in Section 2, we start by writing the set of inequations of linear elasticity modeling the deformation of a virus subject to an exterior force and in contact with a solid support. In a first approximation this rigid surface could represent the cell surface. Then we give some classical theoretical results regarding the existence and uniqueness of the solution for such a model. To avoid remeshing the domain at each increment of force, we chose to do all the calculations in the initial domain Ω^0 representing the

initial shape of the virus, thus implementing in fact an Euler-Lagrange representation. We proceed in Section 2.3 to a change of variables in order to express the variational formulation in terms of the variables in Ω^0 . In Section 3 we introduce the incremental algorithm and the discretization of the variational formulation using a finite elements method. Finally, Section 4 is dedicated to numerical simulations. We discuss some test cases representing the deformation of a virus in contact with a flat support and in contact with two circles with and without the adhesion force. The force-deformation figure (Figure 8), shows the highly non-linear behavior of the virus, even if we used a linear elasticity constitutive law. See [9] for discussions on the utilization of several different non-linear constitutive laws. We ourselves intend in future works to study the effect of using some nonlinear constitutive laws (nonlinear elasticity, plasticity possibly) and to compare the results to the current study.

2 Mathematical modeling

To model the virus deformation, the procedure is as follows: we start from a state Ω^n (which could be Ω^0) corresponding to a force $\frac{nF}{N}$. Then we apply a force $\frac{(n+1)F}{N}$. For practical (computational) reasons, we chose to make the numerical calculations in the undeformed state Ω^0 . We call φ^n the application mapping Ω^0 onto $\Omega^n = \varphi^n(\Omega^0)$. The incremental force treated in the realm of linear elasticity produces a “small” displacement $\mathbf{u}^n$. Then $\Omega^{n+1} = \{\mathbf{x} + \mathbf{u}^n(\mathbf{x}), \mathbf{x} \in \Omega^n\}$ and we call φ^{n+1} the application mapping Ω^0 onto Ω^{n+1} .

In summary we start with Ω^0 , $\varphi^0 = Id$ (Identity). When Ω^n and φ^n are known we compute $\mathbf{u}^n$ (the displacement starting from Ω^n), and φ^{n+1} by setting

$$\begin{aligned}\varphi^n(\mathbf{x}^0) &= \mathbf{x}^n, \quad \mathbf{x}^0 \in \Omega^0, \quad \mathbf{x}^n \in \Omega^n, \\ \varphi^{n+1}(\mathbf{x}^0) &= \mathbf{x}^n + \mathbf{u}^n(\mathbf{x}^n).\end{aligned}\tag{1}$$

At the end we obtain $\Omega^N = \Omega^\varphi$ and $\varphi^N = \varphi$ the final state and the final mapping $\Omega^\varphi = \varphi(\Omega^0)$ with displacement $\mathbf{u}(\mathbf{x}^0) = \varphi(\mathbf{x}^0) - \mathbf{x}^0$.

2.1 Equations

In order to write the model describing the deformation of the virus, we will first give some definitions of the physical parameters and quantities involved.

The initial domain is

$$\Omega^0 = \{r_1 \leq \sqrt{x^2 + y^2} \leq r_2\}$$

where $r_1 = 10 \text{ nm}$ and $r_2 = 15 \text{ nm}$, although, obviously, other geometrical domains can be considered. The inner and outer boundaries of Ω are denoted by Γ_1 and Γ_2 .

In the case of small deformations and displacements, the equation of the equilibrium of a deformable body subjected to a force $\mathbf{f}$ is given by:

$$\text{div}(\boldsymbol{\sigma}(\mathbf{u})) + \mathbf{f} = 0$$

where $\mathbf{u} = \begin{pmatrix} u_1(x, y) \\ u_2(x, y) \end{pmatrix}$, is the displacement and $\boldsymbol{\sigma} = 2\mu\boldsymbol{\varepsilon} + \lambda \text{Tr}(\boldsymbol{\varepsilon})\mathbf{Id}$ is the Cauchy stress tensor defined using the linear strain tensor

$$\varepsilon_{i,j} = \frac{1}{2}(u_{i,j} + u_{j,i}),$$

where $u_{i,j} = \frac{\partial u_i}{\partial x_j}$.

The physical parameters μ and λ are the Lamé coefficients and are defined by:

$$\mu = \frac{E}{2(1+\nu)} \text{nN/nm}$$

and

$$\lambda = \frac{E\nu}{(1-2\nu)(1+\nu)} \text{nN/nm}$$

where

- $E = 0.5$
- $\nu = 0.35$ (Poisson's ratio)

As described below, at each iteration n , when Ω^n and φ^n are known we suppose that we apply to the virus the force $\mathbf{F}^{n+1}$. We divide the outer boundary Γ_2^n of Ω^n in three non intersecting parts, Γ_D^n , Γ_P^n and Γ_C^n such that $\Gamma_2^n = \Gamma_D^n \cup \Gamma_P^n \cup \Gamma_C^n$; Γ_D^n is the part of Γ_2 where the displacement is imposed, Γ_P^n is the part of Γ_2 in contact with the punch and Γ_C^n is the part of Γ_2 in contact with the support. Finally, we suppose also the contact to be rigid; therefore the virus cannot penetrate the support, and we suppose that there is no friction with the contact. One can then propose the following set of equations and inequations, see e.g.[6], [12] and [22]:

$$\left\{ \begin{array}{ll} \boldsymbol{\sigma}_{ij,j}^n + \mathbf{f}_{adh,i}^n = 0, & \text{in } \Omega^n, \\ \mathbf{u}^n = \mathbf{u}_0, & \text{on } \Gamma_D^n, \\ \boldsymbol{\sigma}^n \mathbf{n} = 0, & \text{on } \Gamma_1^n, \\ \boldsymbol{\sigma}^n \mathbf{n} = \mathbf{F}^{n+1}, & \text{on } \Gamma_C^n, \\ \boldsymbol{\sigma}^n \mathbf{n} = 0, & \text{on } \Gamma_D^n \cup \Gamma_P^n, \\ \mathbf{u}_N^n - g^n = \mathbf{u}_i^n \mathbf{n}_i - g^n \leq 0, & \text{on } \Gamma_C^n, \\ \boldsymbol{\sigma}_N^n = \boldsymbol{\sigma}_{ij}^n \mathbf{n}_i \mathbf{n}_j \leq 0, & \text{on } \Gamma_C^n, \\ (\boldsymbol{\sigma}_T^n)_i = \boldsymbol{\sigma}_{ij}^n \mathbf{n}_j - \boldsymbol{\sigma}_N^n n_i = 0, & \text{on } \Gamma_C^n, \\ \boldsymbol{\sigma}_N^n (u_N - g^n) = 0, & \text{on } \Gamma_C^n. \end{array} \right. \quad \begin{array}{l} (2a) \\ (2b) \\ (2c) \\ (2d) \\ (2e) \\ (2f) \\ (2g) \\ (2h) \\ (2i) \end{array}$$

Here the vector $\boldsymbol{\sigma}^n \mathbf{n}$ is decomposed into the sum of its tangential and normal components:

$$\boldsymbol{\sigma}^n \mathbf{n} = \boldsymbol{\sigma}_T^n + \boldsymbol{\sigma}_N^n \mathbf{n},$$

with $\mathbf{n}$ the outward unit normal to the virus and $\boldsymbol{\sigma}_N^n = \sigma^n \mathbf{n} \cdot \mathbf{n}$. We impose a Dirichlet boundary condition on Γ_D^n and without lack of generality we will suppose $\mathbf{u}_0 = \mathbf{0}$. The force $\mathbf{F}^{n+1} = -\frac{(n+1)F}{N}\mathbf{n}$, where F is a constant, is applied on Γ_P^n and g^n is the distance between the zone of contact Γ_C^n and the rigid support. In our study we will suppose that $g^n = 0$. When $g^n > 0$, the virus is not in reality in geometrical contact with the support along Γ_C^n , and this is consistent with the biological context (see below the definition of $\mathbf{f}_{adh}^n$). We denote by $\mathbf{f}_{adh}^n$ the adhesion force from the contact that we define later in Section 2.3.3. We will now study briefly the system (2).

2.2 Variational formulation

In order to write the variational formulation of the system (2) we introduce the following function space and set:

$$K^n = \{\mathbf{v}^n \in \mathbf{V}^n : \mathbf{v}_N^n = \mathbf{v}^n \cdot \mathbf{n} \leq 0 \text{ on } \Gamma_C^n\}$$

where

$$\mathbf{V}^n = \{\mathbf{v}^n \in H^1(\Omega^n)^2 : \mathbf{v}^n = 0 \text{ on } \Gamma_D^n\}.$$

Now by multiplying the first equation of the system (2) by $\mathbf{v}^n - \mathbf{u}^n$ where $\mathbf{v}^n \in K^n$ and by integrating in Ω^n and in view of the Green formula and of the boundary conditions, we obtain:

$$\begin{aligned} & - \int_{\Omega^n} 2\mu \varepsilon_{ij}^n(\mathbf{u}^n) \varepsilon_{ij}^n(\mathbf{v}^n - \mathbf{u}^n) d\mathbf{x}^n - \int_{\Omega^n} \lambda \varepsilon_{kk}^n(\mathbf{u}^n) \varepsilon_{ii}^n(\mathbf{v}^n - \mathbf{u}^n) d\mathbf{x}^n \\ & + \int_{\partial\Omega^n} \sigma_{ij}^n n_j (v^n - u^n)_i d\sigma^n + \int_{\Omega^n} f_{adh,i}^n (v^n - u^n)_i d\mathbf{x}^n \leq 0, \end{aligned} \quad (3)$$

where the Einstein convention of summation of repeated indices has been used. Using the boundary condition (2d), we see that

$$\int_{\partial\Omega^n} \sigma_{ij}^n n_j (v_i^n - u_i^n) d\sigma^n = \int_{\Gamma_P^n} \mathbf{F}^{n+1} \cdot (\mathbf{v}^n - \mathbf{u}^n) d\sigma^n$$

Therefore by defining

$$\begin{aligned} \mathbf{a}^n(\mathbf{u}^n, \mathbf{v}^n) &= \int_{\Omega^n} 2\mu \varepsilon_{ij}^n(\mathbf{u}^n) \varepsilon_{ij}^n(\mathbf{v}^n) d\mathbf{x}^n + \int_{\Omega^n} \lambda \varepsilon_{kk}^n(\mathbf{u}^n) \varepsilon_{ii}^n(\mathbf{v}^n) d\mathbf{x}^n, \\ \mathbf{l}^n(\mathbf{v}^n) &= \int_{\Gamma_P^n} \mathbf{F}^{n+1} \cdot \mathbf{v}^n d\sigma^n + \int_{\Omega^n} \mathbf{f}_{adh}^n \cdot \mathbf{v}^n d\mathbf{x}^n, \end{aligned} \quad (4)$$

the inequality (3) now reads:

$$\mathbf{a}^n(\mathbf{u}^n, \mathbf{v}^n - \mathbf{u}^n) \geq \mathbf{l}^n(\mathbf{v}^n - \mathbf{u}^n), \quad \forall \mathbf{v}^n \in K^n. \quad (5)$$

Then we have the following result:

Theorem 1 *If $\mathbf{f}_{adh}^n \in (L^2(\Omega^n))^2$ and $\mathbf{F}^{n+1} \in (L^2(\Gamma_P^n))^2$ are given and if $\text{meas}(\Gamma_D^n) \neq 0$ then the system (2) is well-posed and has a unique solution $\mathbf{u}^n \in K^n$ satisfying the variational inequality (5). Moreover $\mathbf{u}^n$ is solution of the following minimization problem:*

$$\min_{\mathbf{v} \in K^n} \mathcal{J}(\mathbf{v}),$$

where

$$\mathcal{J}(\mathbf{v}) = \frac{1}{2} \mathbf{a}^n(\mathbf{v}^n, \mathbf{v}^n) - \mathbf{l}^n(\mathbf{v}^n)$$

If $\text{meas}(\Gamma_D^n) = 0$, then $\mathbf{u}^n$ is unique up to a rotation.

Sketch of the proof: We will give here the outlines of the proof for the convenience of the reader. More details can be found in [12] and [6].

First we will prove the formal equivalence of the weak formulation (i.e (5)) and the strong solution (i.e (2a)-(2i)). More precisely we will prove that a regular solution of the variational inequality (5) is also a solution of the system (2). Suppose that the inequality (5) holds for a function $\mathbf{u}^n \in K^n$ and let us prove that $\mathbf{u}^n$ is then a solution of the system (2). Let us define:

$$\mathcal{D}(\Omega^n) = \{\Phi \in C^\infty(\Omega^n), \Phi \text{ has a compact support in } \Omega^n\}$$

Then $\mathbf{v}^n = \mathbf{u}^n \pm \Phi$, where $\Phi \in \mathcal{D}(\Omega^n)$, belongs to K^n and for such a $\mathbf{v}^n$, the inequality (5) reads:

$$\pm \int_{\Omega^n} 2\mu \varepsilon_{ij}^n(\mathbf{u}^n) \varepsilon_{ij}(\Phi) d\mathbf{x}^n \pm \int_{\Omega^n} \lambda \varepsilon_{kk}^n(\mathbf{u}^n) \varepsilon_{ii}(\Phi) d\mathbf{x}^n \pm \int_{\Omega^n} \mathbf{f}_{adh}^n \cdot \Phi d\mathbf{x}^n \geq 0$$

which implies:

$$\sigma_{ij,j}^n + f_{adh,i}^n = 0 \quad \text{in } \Omega^n. \quad (6)$$

Using (6) and the Green formula, the inequality (5) becomes: For all $\mathbf{v}^n \in K^n$:

$$\int_{\Gamma_P^n \cup \Gamma_C^n \cup \Gamma_1^n} \sigma_{ij}^n n_j (v_i^n - u_i^n) d\sigma^n \geq \int_{\Gamma_P^n} \mathbf{F}^{n+1} \cdot (\mathbf{v}^n - \mathbf{u}^n) d\sigma^n. \quad (7)$$

By choosing $\Phi \in V^n$ such that $\Phi = 0$ on $\Gamma_C^n \cup \Gamma_1^n$ and $\mathbf{v}^n = \mathbf{u}^n \pm \Phi$ we can deduce that:

$$\sigma \mathbf{n} = \mathbf{F}^{n+1} \quad \text{on } \Gamma_P^n,$$

and by using a similar argument we can show that:

$$\sigma \mathbf{n} = 0 \quad \text{on } \Gamma_1^n.$$

The inequality (7) can be now simplified using these two last equations and we obtain:

$$\int_{\Gamma_C^n} \sigma_{ij}^n n_j (v_i^n - u_i^n) d\sigma^n \geq 0.$$

Using the decomposition of the vector $\sigma^n \mathbf{n}$ as the sum of its tangential and normal components; $\sigma^n \mathbf{n} = \sigma_N^n \mathbf{n} + \sigma_T^n$ and by choosing $\mathbf{v}^n = \mathbf{u}^n + \Phi$ where $\Phi \in \{\Phi \in V^n : \Phi_N = \Phi \cdot \mathbf{n} = 0\}$, we obtain:

$$\int_{\Gamma_C^n} \sigma_{ij}^n n_j (v_i^n - u_i^n) d\sigma^n = \int_{\Gamma_C^n} (\sigma_N^n)(\mathbf{n} \cdot \Phi) d\sigma^n + \int_{\Gamma_C^n} \sigma_T^n \cdot \Phi d\sigma^n.$$

So we can deduce that $\int_{\Gamma_C^n} \sigma_T^n \cdot \Phi d\sigma^n \geq 0$ for all Φ such that $\Phi \cdot \mathbf{n} = 0$ and by doing the same calculations with $-\Phi$ we conclude that:

$$\sigma_T = 0 \quad \text{on } \Gamma_C^n.$$

Finally, let $\Phi \in V^n$ be such that $\Phi_N = \Phi \cdot \mathbf{n} \leq 0$ on Γ_C^n ; then we have $\mathbf{v}^n = \mathbf{u}^n + \Phi \in K^n$ and we obtain:

$$\int_{\Gamma_C^n} (\sigma_N^n)(\mathbf{n} \cdot \Phi) d\sigma^n \geq 0.$$

This implies that:

$$\sigma_N^n \leq 0 \quad \text{on } \Gamma_C^n,$$

which finishes the proof of the formal equivalence between the strong solution and the weak solution.

Now to prove the existence and uniqueness of a solution of the variational inequality (5), we will use the following theorem (Lions-Stampacchia [14]) and corollary (Stampacchia [21]).

Theorem 2 (*Lions-Stampacchia [14]*) *Let V be a Hilbert space and $K \in V$ a nonempty, closed, convex subset of V .*

Let $A : V \rightarrow V'$, where V' denotes the dual of the space V , be a continuous and coercive linear operator, that is there exist $k, \alpha > 0$ such that:

$$\|Au - Av\| \leq k\|u - v\|, \quad \text{for all } u, v \in K,$$

$$\langle Au - Av, u - v \rangle \geq \alpha\|u - v\|^2, \quad \text{for all } u, v \in K.$$

Then for each $L \in V'$, there exists a unique solution $u \in K$ of the variational inequality

$$\langle Au - L, v - u \rangle, \quad \text{for all } v \in K.$$

As a consequence we have the following corollary (Stampacchia [21]):

Corollary 1 *Let V denote a real Hilbert space and $K \subset V$ a nonempty, closed, convex subset of V . Assume $a(\cdot, \cdot)$ is a continuous, coercive bilinear form on V and $L \in V'$. Then there exists a unique solution $u \in K$ of the variational inequality*

$$a(u, v - u) \geq \langle L, v - u \rangle, \quad v \in K.$$

As a next step we need to prove that K^n is a nonempty closed and convex set of V^n . In fact K^n is nonempty because it contains the null displacement. Let us consider $\mathbf{u}^n$ and $\mathbf{v}^n \in K^n$ and $0 < \alpha < 1$. We see that $\alpha \mathbf{u}_N^n \leq 0$ on Γ_C^n and $(1 - \alpha) \mathbf{v}_N^n \leq 0$ on Γ_C^n and we can deduce that $\alpha \mathbf{u}_N^n + (1 - \alpha) \mathbf{v}_N^n \leq 0$ on Γ_C^n and thus K^n is convex. To finish we prove that K^n is closed. Let $(\mathbf{u}_k^n)_{k \in \mathbb{N}} \in K^n$ and $(\mathbf{u}_k^n) \rightarrow \mathbf{u}^n$ in V^n which implies $\mathbf{u}_k^n \cdot \mathbf{n} \rightarrow \mathbf{u}^n \cdot \mathbf{n}$ in $L^2(\partial\Omega^n)$ by continuity of the trace. To finish this step one can use that if a sequence converges in $L^2(\partial\Omega^n)$ then one can extract a subsequence converging almost everywhere. As $u_k^n \cdot \mathbf{n} \leq 0$ on Γ_C^n one can conclude that $\mathbf{u}^n \cdot \mathbf{n} \leq 0$ on Γ_C^n and therefore the limit is in K^n .

Now to conclude, we need to prove that $a^n(\cdot, \cdot)$ is continuous and coercive. The continuity is straightforward and to prove the coercivity we need to assume that the tensor of elasticity $\mathbf{E}$ defined by $E_{ijkl} = \mu(I_{ik}I_{jl} + I_{il}I_{jk}) + \lambda I_{ij}I_{kl}$ is symmetric, it means $E_{ijkl} = E_{jikl} = E_{ijlk} = E_{klij}$, $1 \leq i, j, k, l \leq 2$, and elliptic. This last assumption means that there exists a constant $m > 0$ such that for all symmetric tensor ϵ the following inequality holds:

$$E_{ijkl} \epsilon_{ij} \epsilon_{kl} \geq m \epsilon_{ij} \epsilon_{kl}.$$

Finally by using the Korn inequality we can deduce the coercivity of $a^n(\cdot, \cdot)$ which finishes the proof of Theorem 1.

Remark 1 *For the numerical simulations we will transform the variational inequality (5) into a variational equation using the following observation (see [6]):*

If $\mathbf{w}^n \in K_0^n = \{\mathbf{v} \in K, \mathbf{v}^n = 0 \text{ on } \Gamma_C^n\}$ we can replace $\mathbf{v}^n$ by $\mathbf{u}^n \pm \mathbf{w}^n \in K^n$ and we find

$$\begin{aligned} & - \int_{\Omega^n} 2\mu \varepsilon_{ij}^n(\mathbf{u}^n) \varepsilon_{ij}(\mathbf{w}^n) d\mathbf{x}^n - \int_{\Omega^n} \lambda \varepsilon_{kk}^n(\mathbf{u}^n) \varepsilon_{ii}^n(\mathbf{w}^n) d\mathbf{x}^n \\ & + \int_{\partial\Omega^n} \sigma_{ij}^n n_j w_i^n d\mathbf{x}^n + \int_{\Omega^n} f_{adh,i}^n w_i^n d\mathbf{x}^n = 0, \quad \forall \mathbf{w}^n \in K_0^n. \end{aligned} \quad (8)$$

Changing notations we obtain:

$$\begin{aligned} & - \int_{\Omega^n} 2\mu \varepsilon_{ij}^n(\mathbf{u}^n) \varepsilon_{ij}(\mathbf{v}^n) d\mathbf{x}^n - \int_{\Omega^n} \lambda \varepsilon_{kk}^n(\mathbf{u}^n) \varepsilon_{ii}^n(\mathbf{v}^n) d\mathbf{x}^n \\ & + \int_{\partial\Omega^n} \sigma_{ij}^n n_j v_i^n d\mathbf{x}^n + \int_{\Omega^n} f_{adh,i}^n v_i^n d\mathbf{x}^n = 0, \quad \forall \mathbf{v}^n \in K_0^n. \end{aligned} \quad (9)$$

The equation (9) says that $\mathbf{u}^n \in K^n$ and

$$\mathbf{a}^n(\mathbf{u}^n, \mathbf{v}^n) = \mathbf{l}^n(\mathbf{v}^n), \quad \forall \mathbf{v}^n \in K_0^n. \quad (10)$$

2.3 Change of variables from $(x^n, y^n) \in \Omega^n$ to $(x^0, y^0) \in \Omega^0$

As we proceed by a slow, small increment of the force, the virus is deformed and occupies a new configuration at each step. In order to avoid remeshing the domain, we choose here to make all the calculations in the initial domain Ω^0 . We need then to make a change of

variables in the variational formulation (10). In the sequel we denote by $\tilde{\mathbf{u}}^n$ the displacement from Ω^0 to Ω^n . The variable will now be as follows:

$$\begin{aligned}\boldsymbol{\varphi}^n(\mathbf{x}^0) &= \mathbf{x}^n, \quad \mathbf{x}^0 \in \Omega^0, \quad \mathbf{x}^n \in \Omega^n, \\ \boldsymbol{\varphi}^{n+1}(\mathbf{x}^0) &= \mathbf{x}^n + \mathbf{u}^n(\mathbf{x}^n) = \mathbf{x}^0 + \tilde{\mathbf{u}}^n(\mathbf{x}^0),\end{aligned}\tag{11}$$

and we write:

$$\begin{aligned}\mathbf{a}^n(\mathbf{u}^n, \mathbf{v}^n) &= \mathbf{a}(\boldsymbol{\varphi}^n; \tilde{\mathbf{u}}^n, \tilde{\mathbf{v}}^n) = \langle \mathbf{A}(\boldsymbol{\varphi}^n) \tilde{\mathbf{u}}^n, \tilde{\mathbf{v}}^n \rangle_{\Omega^0}, \\ \mathbf{l}^n(\mathbf{v}^n) &= \mathbf{l}(\boldsymbol{\varphi}^n; \tilde{\mathbf{v}}^n) = \langle \mathbf{F}^{n+1}(\boldsymbol{\varphi}^n), \tilde{\mathbf{v}}^n \rangle_{\Gamma_P} + \langle \mathbf{f}_{adh}(\boldsymbol{\varphi}^n), \tilde{\mathbf{v}}^n \rangle_{\Omega^0}.\end{aligned}\tag{12}$$

The problem (10) becomes

$$\begin{aligned}\tilde{\mathbf{u}}^n &\in K \text{ and} \\ \mathbf{a}(\boldsymbol{\varphi}^n; \tilde{\mathbf{u}}^n, \tilde{\mathbf{v}}^n) &= \mathbf{l}(\boldsymbol{\varphi}^n; \tilde{\mathbf{v}}^n), \quad \forall \tilde{\mathbf{v}}^n \in K_0,\end{aligned}\tag{13}$$

and we will now make explicit each term in (13).

2.3.1 Computation of $\mathbf{a}^n(\mathbf{u}^n, \mathbf{v}^n) = \mathbf{a}(\boldsymbol{\varphi}^n; \tilde{\mathbf{u}}^n, \tilde{\mathbf{v}}^n)$

We want to compute:

$$\int_{\Omega^n} \boldsymbol{\varepsilon}^n(\mathbf{u}^n) : \boldsymbol{\varepsilon}^n(\mathbf{v}^n) d\mathbf{x}^n = \int_{\Omega^n} 2\mu \varepsilon_{ij}^n(\mathbf{u}^n) \varepsilon_{ij}^n(\mathbf{v}^n) d\mathbf{x}^n + \int_{\Omega^n} \lambda \varepsilon_{kk}^n(\mathbf{u}^n) \varepsilon_{ii}^n(\mathbf{v}^n) d\mathbf{x}^n.\tag{14}$$

We have

$$\begin{aligned}\int_{\Omega^n} 2\mu \varepsilon_{ij}^n(\mathbf{u}^n) \varepsilon_{ij}^n(\mathbf{v}^n) d\mathbf{x}^n &= \mu \int_{\Omega^n} (u_{1,y^n}^n + u_{2,x^n}^n)(v_{1,y^n}^n + v_{2,x^n}^n) d\mathbf{x}^n \\ &\quad + \frac{\mu}{2} \int_{\Omega^n} (u_{1,x^n}^n v_{1,x^n}^n + u_{2,y^n}^n v_{2,y^n}^n) d\mathbf{x}^n, \\ \int_{\Omega^n} \lambda \varepsilon_{kk}^n(\mathbf{u}^n) \varepsilon_{ii}^n(\mathbf{v}^n) d\mathbf{x}^n &= \lambda \int_{\Omega^n} (u_{1,x^n}^n + u_{2,y^n}^n)(v_{1,x^n}^n + v_{2,y^n}^n) d\mathbf{x}^n.\end{aligned}\tag{15}$$

We compute each term

$$\mu \int_{\Omega^n} (u_{1,y^n}^n + u_{2,x^n}^n)(v_{1,y^n}^n + v_{2,x^n}^n) d\mathbf{x}^n = \mu \int_{\Omega^0} (u_{1,y^n}^n + u_{2,x^n}^n)(v_{1,y^n}^n + v_{2,x^n}^n) |\nabla \boldsymbol{\varphi}^n(\mathbf{x})| d\mathbf{x}\tag{16}$$

$$\frac{\mu}{2} \int_{\Omega^n} (u_{1,x^n}^n v_{1,x^n}^n + u_{2,y^n}^n v_{2,y^n}^n) d\mathbf{x}^n = \frac{\mu}{2} \int_{\Omega^0} (u_{1,x^n}^n v_{1,x^n}^n + u_{2,y^n}^n v_{2,y^n}^n) |\nabla \boldsymbol{\varphi}^n(\mathbf{x})| d\mathbf{x},\tag{17}$$

$$\lambda \int_{\Omega^n} (u_{1,x^n}^n + u_{2,y^n}^n)(v_{1,x^n}^n + v_{2,y^n}^n) d\mathbf{x}^n = \lambda \int_{\Omega^0} (u_{1,x^n}^n + u_{2,y^n}^n)(v_{1,x^n}^n + v_{2,y^n}^n) |\nabla \boldsymbol{\varphi}^n(\mathbf{x})| d\mathbf{x}.\tag{18}$$

We compute each derivative as follows:

$$\begin{aligned}u_{1,x^n}^n &= \tilde{u}_{1,x} \frac{\partial x}{\partial x^n} + \tilde{u}_{1,y} \frac{\partial y}{\partial x^n}, \quad u_{1,y^n}^n = \tilde{u}_{1,y} \frac{\partial y}{\partial y^n} + \tilde{u}_{1,x} \frac{\partial x}{\partial y^n} \\ u_{2,x^n}^n &= \tilde{u}_{2,x} \frac{\partial x}{\partial x^n} + \tilde{u}_{2,y} \frac{\partial y}{\partial x^n}, \quad u_{2,y^n}^n = \tilde{u}_{2,y} \frac{\partial y}{\partial y^n} + \tilde{u}_{2,x} \frac{\partial x}{\partial y^n}.\end{aligned}\tag{19}$$

Since $\frac{\partial(x^n, y^n)}{\partial(x, y)} = \nabla \boldsymbol{\varphi}^n$ we need to compute $(\nabla \boldsymbol{\varphi}^n)^{-1}$:

$$(\nabla \boldsymbol{\varphi}^n)^{-1} = \frac{1}{|\nabla \boldsymbol{\varphi}^n|} \begin{bmatrix} \varphi_{2,y}^n & -\varphi_{1,y}^n \\ -\varphi_{2,x}^n & \varphi_{1,x}^n \end{bmatrix}, \quad (20)$$

and therefore

$$\begin{aligned} \frac{\partial x}{\partial x^n} &= \frac{\varphi_{2,y}^n}{|\nabla \boldsymbol{\varphi}^n|}, & \frac{\partial x}{\partial y^n} &= -\frac{\varphi_{1,y}^n}{|\nabla \boldsymbol{\varphi}^n|} \\ \frac{\partial y}{\partial x^n} &= -\frac{\varphi_{2,x}^n}{|\nabla \boldsymbol{\varphi}^n|}, & \frac{\partial y}{\partial y^n} &= \frac{\varphi_{1,x}^n}{|\nabla \boldsymbol{\varphi}^n|}. \end{aligned} \quad (21)$$

Then (14) becomes:

$$\begin{aligned} < \mathbf{A}^n \mathbf{u}^n, \mathbf{v}^n >_{\Omega^n} = \mathbf{a}^n(\mathbf{u}^n, \mathbf{v}^n) = \mathbf{a}(\boldsymbol{\varphi}^n; \mathbf{u}^n, \mathbf{v}^n) = < \mathbf{A}(\boldsymbol{\varphi}^n) \tilde{\mathbf{u}}^n, \tilde{\mathbf{v}}^n >_{\Omega^0} = \\ & \int_{\Omega^0} \frac{\mu}{|\nabla \boldsymbol{\varphi}^n|} (-\tilde{u}_{1,x} \varphi_{1,y}^n + \tilde{u}_{1,y} \varphi_{1,x}^n + \tilde{u}_{2,x} \varphi_{2,y}^n - \tilde{u}_{2,y} \varphi_{2,x}^n) \\ & \quad (-\tilde{v}_{1,x} \varphi_{1,y}^n + \tilde{v}_{1,y} \varphi_{1,x}^n + \tilde{v}_{2,x} \varphi_{2,y}^n - \tilde{v}_{2,y} \varphi_{2,x}^n) d\mathbf{x} \\ & + \int_{\Omega^0} \frac{\mu}{2|\nabla \boldsymbol{\varphi}^n|} [(\tilde{u}_{1,x} \varphi_{2,y}^n - \tilde{u}_{1,y} \varphi_{2,x}^n)(\tilde{v}_{1,x} \varphi_{2,y}^n - \tilde{v}_{1,y} \varphi_{2,x}^n) \\ & \quad + (-\tilde{u}_{2,x} \varphi_{1,y}^n + \tilde{u}_{2,y} \varphi_{1,x}^n)(-\tilde{v}_{2,x} \varphi_{1,y}^n + \tilde{v}_{2,y} \varphi_{1,x}^n)] d\mathbf{x} \\ & + \int_{\Omega^0} \frac{\lambda}{|\nabla \boldsymbol{\varphi}^n|} (\tilde{u}_{1,x} \varphi_{2,y}^n - \tilde{u}_{1,y} \varphi_{2,x}^n - \tilde{u}_{2,x} \varphi_{1,y}^n + \tilde{u}_{2,y} \varphi_{1,x}^n) \\ & \quad (\tilde{v}_{1,x} \varphi_{2,y}^n - \tilde{v}_{1,y} \varphi_{2,x}^n - \tilde{v}_{2,x} \varphi_{1,y}^n + \tilde{v}_{2,y} \varphi_{1,x}^n) d\mathbf{x}. \end{aligned} \quad (22)$$

2.3.2 Computation of the virtual power of the punch force

The virtual power of the punch force for a virtual displacement $\mathbf{v}^n$ is:

$$< \mathbf{F}^{n+1}, \mathbf{v}^n >_{\Gamma_P^n} = < \mathbf{F}^{n+1}(\boldsymbol{\varphi}^n), \tilde{\mathbf{v}}^n >_{\Gamma_P} . \quad (23)$$

In our case $\mathbf{F}^{n+1} = -\frac{n+1}{N} F \mathbf{n}$, where $F = \text{constant}$ and $\mathbf{n}$ is the outward normal vector to Γ_P^n . Therefore, the equation yields

$$< \mathbf{F}^{n+1}, \mathbf{v}^n >_{\Gamma_P^n} = -\frac{n+1}{N} \int_{\Gamma_P^n} F \mathbf{n} \cdot \mathbf{v}^n d\mathbf{x}^n = -\frac{n+1}{N} F \int_{\Gamma_P} (\mathbf{n} \circ \boldsymbol{\varphi}^n) \cdot \tilde{\mathbf{v}}^n |\nabla \boldsymbol{\varphi}^n| d\mathbf{x}. \quad (24)$$

Thus we define

$$\mathbf{F}^{n+1}(\boldsymbol{\varphi}^n) = -\frac{(n+1)F}{N} (\mathbf{n} \circ \boldsymbol{\varphi}^n) |\nabla \boldsymbol{\varphi}^n|. \quad (25)$$

2.3.3 Computation of the virtual power of the adhesion forces

We give now the definition of the adhesion force resulting from the interaction between the molecules of the virus and the molecules of the contact surface. In this study we choose the adhesion force derived from the Lennard-Jones potential defined (see [11]) by:

$$U_{adh}^n := \int_{-\infty}^{-r_2-r_0} \int_{-\infty}^{+\infty} w(\mathbf{r}) dx^l dy^l, \quad (26)$$

where,

$$\begin{aligned} \mathbf{r} &= (x^l - x^\varphi, y^l - x^\varphi) \\ r_0 &= 0.5 \text{ nm}. \end{aligned} \quad (27)$$

The definition of $\mathbf{r}$ comes from the fact that we want $\|\mathbf{r}\| \geq r_0 = 0.5 \text{ nm}$, because the virus can not rest directly on the surface and it stays at the minimal distance r_0 from the surface. We set the origin at the center of the virus and define the support at $y = -r_2 - r_0$. Figure 1 shows the different coordinates.

Figure 1: Adhesion forces.

The function w is given by

$$w(\mathbf{r}) = \frac{A}{|\mathbf{r}|^{12}} - \frac{B}{|\mathbf{r}|^6}. \quad (28)$$

Remark 2 To find A and B we have to solve

$$\begin{aligned} |\mathbf{r}| = 0.5 &\implies \frac{dw}{d|\mathbf{r}|} = 0 \text{ and } w = -5.0 \cdot kT, \\ |\mathbf{r}| < 0.25 &\implies w \gg kT, \end{aligned}$$

where k is the Boltzmann constant and T is the temperature.

Therefore with $k = 1.3806488 \cdot 10^{-23} \text{ m}^2 \text{ kg s}^{-2} \text{ K}^{-1} = 1.3806488 \cdot 10^{-5} \text{ nm}^2 \text{ kg s}^{-2} \text{ K}^{-1}$, and $T = 310.1 \text{ K} (= 37 \text{ }^\circ\text{C})$ we want to solve

$$\begin{cases} -\frac{12A}{r_0^{12}} + \frac{6B}{r_0^6} = 0, \\ \frac{A}{r_0^{12}} - \frac{B}{r_0^6} = -5kT. \end{cases} \quad (29)$$

We obtain:

$$A = 5r_0^{12}kT, \quad B = 10r_0^6kT, \quad (30)$$

and w becomes

$$w(\mathbf{r}) = \frac{5r_0^{12}kT}{|\mathbf{r}|^{12}} - \frac{10r_0^6kT}{|\mathbf{r}|^6}. \quad (31)$$

Now to find the adhesion force we write the potential as

$$U_{adh}^n = \int_{-\infty}^{\infty} \left[\frac{A}{((x^l - x^n)^2 + (y^l - y^n)^2)^6} - \frac{B}{((x^l - x^n)^2 + (y^l - y^n)^2)^3} \right] dx^l. \quad (32)$$

So the adhesion force is

$$\mathbf{f}_{adh}^n := -\nabla U_{adh}^n = - \left(\frac{\partial U_{adh}^n}{\partial x^n}, \frac{\partial U_{adh}^n}{\partial y^n} \right)^t, \quad (33)$$

which reads

$$\mathbf{f}_{adh}^n := \begin{pmatrix} \int_{-r_2-r_0}^{-\infty} \int_{-\infty}^{\infty} \left[-\frac{12A(x^l - x^n)}{((x^l - x^n)^2 + (y^l - y^n)^2)^7} + \frac{6B(x^l - x^n)}{((x^l - x^n)^2 + (y^l - y^n)^2)^4} \right] dx^l dy^l \\ \int_{-r_2-r_0}^{-\infty} \int_{-\infty}^{\infty} \left[-\frac{12A(y^l - y^n)}{((x^l - x^n)^2 + (y^l - y^n)^2)^7} + \frac{6B(y^l - y^n)}{((x^l - x^n)^2 + (y^l - y^n)^2)^4} \right] dx^l dy^l \end{pmatrix}. \quad (34)$$

So we have:

$$\langle \mathbf{f}_{adh}^n, \mathbf{v}^n \rangle_{\Omega^n} = \int_{\Omega^n} \mathbf{f}_{adh}^n \cdot \mathbf{v}^n d\mathbf{x}^n. \quad (35)$$

By changing the variables we obtain:

$$\langle \mathbf{f}_{adh}^n(\boldsymbol{\varphi}^n), \tilde{\mathbf{v}}^n \rangle_{\Omega^0} = \int_{\Omega^0} (\mathbf{f}_{adh}^n \circ \boldsymbol{\varphi}^n) \cdot \tilde{\mathbf{v}}^n |\nabla \boldsymbol{\varphi}^n| d\mathbf{x}, \quad (36)$$

where $\tilde{\mathbf{v}}^n$ is a virtual displacement from Ω^0 to Ω^n .

3 Numerical approximation

Let us recall the equation we are solving at each step n , for $0 \leq n < N$:

$$\begin{aligned} \langle \mathbf{A}(\boldsymbol{\varphi}^n) \tilde{\mathbf{u}}^n, \tilde{\mathbf{v}} \rangle_{\Omega^0} = & \langle \mathbf{F}^{n+1}(\boldsymbol{\varphi}^n), \tilde{\mathbf{v}} \rangle_{\Gamma_P} + \langle \mathbf{f}_{adh}(\boldsymbol{\varphi}^n), \tilde{\mathbf{v}} \rangle_{\Omega^0}, \\ & \forall \tilde{\mathbf{v}} \in K_0. \end{aligned} \quad (37)$$

In the following section we will present the discrete version of this equation.

3.1 Finite elements

In this section we will drop the index n to construct the finite element basis and we will write the discrete version of the operator $\mathbf{A}$. Let $\mathcal{T}_h$ be a triangulation of Ω^0 , containing N_T triangles and N_v vertices, as in the example shown in Figure 2. Let

Figure 2: Example of triangulation of Ω

$$\mathcal{V}_h = \{ \boldsymbol{\psi}_h \in H^1(\Omega) \mid \boldsymbol{\psi}_h|_{\tau} \in \mathbb{P}_1 \quad \forall \tau \in \mathcal{T}_h \}; \quad (38)$$

then we define the basis of $\mathcal{V}_h$ $\{\boldsymbol{\psi}_i\}_{1 \leq i \leq N_v}$. For $\mathbf{u}_h \in \mathcal{V}_h$, we can write the discretized version of $\mathbf{a}(\boldsymbol{\varphi})$ and $\mathbf{l}(\boldsymbol{\varphi})$ on Ω^0 , that is for $\boldsymbol{\varphi}_h \in \mathcal{V}_h$ and $\mathbf{u}_h \in \mathcal{V}_h$

$$(\mathbf{A}(\boldsymbol{\varphi}_h) \mathbf{u}_h, \mathbf{u}_h) = \mathbf{a}(\boldsymbol{\varphi}_h; \mathbf{u}_h, \mathbf{u}_h),$$

therefore $\mathbf{A}_{ij}(\boldsymbol{\varphi}_h) = \mathbf{a}(\boldsymbol{\varphi}_h; \boldsymbol{\psi}_i, \boldsymbol{\psi}_j)$, and we also define

$$\mathbf{b}(\boldsymbol{\varphi}_h) = \mathbf{l}(\boldsymbol{\varphi}_h; \mathbf{u}_h).$$

Remark 3 *The construction of the basis is done as follows. Let $\{T_i\}_{1 \leq i \leq B_T}$ be the triangles of Ω^0 and we suppose that we have N_v vertices. We write $\mathbf{x}_i = (x_i, y_i)$. Then we have:*

$$\boldsymbol{\psi}_i^1 = (0, \boldsymbol{\psi}_i), \text{ for } 1 \leq i \leq N_v,$$

$$\boldsymbol{\psi}_i^2 = (\boldsymbol{\psi}_i, 0), \text{ for } 1 \leq i \leq N_v.$$

Therefore

$$\mathbf{u} = (u^1, u^2) := \sum_{i=1}^{N_v} u_i^1 \boldsymbol{\psi}_i^1 + \sum_{j=1}^{N_v} u_j^2 \boldsymbol{\psi}_j^2.$$

Now to define $\boldsymbol{\psi}$ on a triangle T_k , we define the three vertices of this triangle by the indices 1, 2, 3 and from [13] we have

$$H_1 = \frac{1}{2|T_k|} [(x_2 y_3 - x_3 y_2) + (y_2 - y_3)x + (x_3 - x_2)y],$$

$$H_2 = \frac{1}{2|T_k|} [(x_3 y_1 - x_1 y_3) + (y_3 - y_1)x + (x_1 - x_3)y],$$

$$H_3 = \frac{1}{2|T_k|} [(x_1 y_2 - x_2 y_1) + (y_1 - y_2)x + (x_2 - x_1)y],$$

where

$$|T_k| = \frac{1}{2} \det \begin{bmatrix} 1 & x_1 & y_1 \\ 1 & x_2 & y_2 \\ 1 & x_3 & y_3 \end{bmatrix}.$$

With these definitions we have

$$u^1|_{T_k} = u_1^1 H_1(x, y) + u_2^1 H_2(x, y) + u_3^1 H_3(x, y);$$

same for $u_2^1, u_3^1, u_1^2, u_2^2$, and u_3^2 .

For our numerical simulations we will use two different stands: one flat stand, see Figure 3, and a stand made of two circles of 60 nm radius, see Figure 4.

Figure 3: Domain Ω^0 with puncher and flat stand.

Figure 4: Domain Ω^0 with puncher and circle stands.

On the flat stand we have to impose the displacement and the rotation at one point in order to have a unique solution; on the two circles stand we fix the displacement at two points which will also fix the rotation. In the following we explain which points we choose.

In the case of the flat support, we fix the vertex that is in contact with the support at iteration 0 and we fix the horizontal translation of the point in contact with the puncher at iteration 0. Let us assume that (x_i, y_i) , for $1 \leq i \leq N_v$ are the vertices of our mesh on Ω^0 .

We define

$$i_{top} = \operatorname{argmax}(y_i), \quad i_{bottom} = \operatorname{argmin}(y_i). \quad (39)$$

We then fix the point at i_{bottom} and fix the horizontal translation in x at i_{top} .

In the case of circles support, we fix the two vertices in contact with each circle at iteration 0. Let $(x_l, y_l) = (-\frac{75}{\sqrt{2}}, -\frac{75}{\sqrt{2}})$ be the center of the left circle and let $(x_r, y_r) = (\frac{75}{\sqrt{2}}, -\frac{75}{\sqrt{2}})$ be the center of the right circle. We then fix the displacement at

$$i_{left} = \operatorname{argmin}(\sqrt{(x_i - x_l)^2 + (y_i - y_l)^2}), \quad i_{right} = \operatorname{argmin}(\sqrt{(x_i - x_r)^2 + (y_i - y_r)^2}). \quad (40)$$

3.2 Algorithm

As explained before in order to solve the equations with a linear model we are proceeding by increments of the constant F (and therefore the vector $\mathbf{F}$). Let N be the total number of increments; we recall that the force exerted by the puncher on Γ_P^n is

$$\mathbf{F}^{n+1} = -\frac{n+1}{N} F \mathbf{n}, \quad \text{for } 1 \leq n \leq N, \quad (41)$$

where $\mathbf{n}$ is the outer normal vector and Ω^n is the domain at iteration n , $\boldsymbol{\varphi}_h^n$ is the deformation from Ω^0 to Ω^n , and $\tilde{\mathbf{u}}_h^n$ is the displacement from Ω^0 to Ω^n . Recall that we have $\boldsymbol{\varphi}_h^{n+1} = \mathbf{x}_0 + \tilde{\mathbf{u}}_h^n$, where $\mathbf{x}_0$ is the identity function on Ω_0 . With these notation in mind we have at each step $n = 0, \dots, N-1$:

$$\begin{aligned} \langle \mathbf{A}(\boldsymbol{\varphi}_h^n) \tilde{\mathbf{u}}_h^n, \tilde{\mathbf{v}}_h \rangle_{\Omega^0} &= \langle \mathbf{F}^{n+1}(\boldsymbol{\varphi}_h^n), \tilde{\mathbf{v}}_h \rangle_{\Gamma_P} + \langle \mathbf{f}_{adh}(\boldsymbol{\varphi}_h^n), \tilde{\mathbf{v}}_h \rangle_{\Omega^0}, \\ &\quad \forall \tilde{\mathbf{v}}_h \in \mathcal{V}_h. \end{aligned} \quad (42)$$

For the sake of notational simplicity, we set

$$\begin{cases} \mathcal{F}^{n+1}(\boldsymbol{\varphi}_h^n) = F^{n+1}(\boldsymbol{\varphi}_h^n) & \text{on } \Gamma_P, \\ \mathcal{F}^{n+1}(\boldsymbol{\varphi}_h^n) = 0 & \text{on } \Omega^0 \setminus \Gamma_P \end{cases} \quad (43)$$

Now our algorithm proceeds as follows: $\boldsymbol{\varphi}_h^0 = \mathbf{Id}$ is known. Then for $n = 0, \dots, N-1$, we assume that $\boldsymbol{\varphi}_h^n$ is known and compute $\tilde{\mathbf{u}}_h^n$:

1. Fix $\boldsymbol{\varphi}_h^n$ and compute $\tilde{\mathbf{u}}_h^n$ using a Restart GMRES method on

$$\mathbf{A}(\boldsymbol{\varphi}_h^n) \mathbf{u}_h^{n+1} = \mathcal{F}^n(\boldsymbol{\varphi}_h^n) + \mathbf{f}_{adh}(\boldsymbol{\varphi}_h^n). \quad (44)$$

2. Then we compute $\boldsymbol{\varphi}_h^{n+1} = \mathbf{x}_0 + \tilde{\mathbf{u}}_h^n$.

We are then ready to compute the next step starting from $\boldsymbol{\varphi}_h^{n+1}$.

4 Numerical simulations

In this section, we present the results of 3 simulations. Simulations 1 and 2 are done on the flat stands, but for Simulation 1 the adhesion forces are 0 so that the virus deforms only because of $\mathbf{F}$ and for Simulation 2 the adhesion forces are present. Simulation 3 is done on the two circles without any adhesion forces. Adhesion was not included at this point to allow the separate analysis of the influence of substrate geometry.

4.1 Simulation 1: on the flat support without adhesion forces

Our first simulation, on a flat support, is done with $F = 0.022$ nN, $\mathbf{f}_{adh} = 0$ and $N = 30$. Figure 5 shows the results of the shape of the virus for the values of $F = 0.00514$, 0.01027 , 0.0154 , 0.02054 nN.

Figure 5: Shape of the shell at iteration 0, 15, 30, and 38 on a flat support. This corresponds to $F = 0.00514$, 0.01027 , 0.0154 , 0.02054 nN.

4.2 Simulation 2: on the flat support with adhesion forces

The following simulation is done on a flat support with $F = 0.006$, $\mathbf{f}_{adh}$ is defined as in (34). Figure 6 shows the results of the shape of the virus shell for the value of $F = 0.00514, 0.01027, 0.0154, 0.02054$ nN.

Figure 6: Shape of the shell at iteration 0, 2, 4, and 6 on a flat support with adhesion forces. This corresponds to $F = 0.00514, 0.01027, 0.0154, 0.02054$ nN.

4.3 Simulation 3: on the two circles support without adhesion forces

This simulation is done on two circles as support with $F = 0.03$ nN, $\mathbf{f}_{adh} = 0$, and $N = 30$. Figure 7 shows the results of the shape of the virus that correspond to the values for $F = 0.06, 0.012, 0.018, 0.024$ nN.

Figure 7: Shape the virus at iteration 0, 15, 30, and 36 on circles support. This corresponds to $F = 0.06, 0.012, 0.018, 0.024$ nN.

Remark 4 *Alternatively we may see the transformation $\Omega^0 \longrightarrow \Omega = \Omega^N$ as a whole, where the unknowns are both the final state (given by $\varphi = \varphi^N$, $\varphi(\Omega^0) = \Omega$ with displacements $\mathbf{u}(\mathbf{x}^0) = \varphi(\mathbf{x}^0) - \mathbf{x}^0$), and the distribution of stresses σ in Ω (expressed in either Ω^0 or Ω). Here the mechanical equations are meant to be written in the deformed space $\Omega = \Omega^N$ which is unknown. We leave this problem for future studies as it pertains to nonlinear elasticity with large deformation [4], or possibly to some other model of nonlinear mechanics.*

For example, we can also deal directly with a nonlinear model for which

$$\varepsilon_{i,j} = \frac{1}{2}(u_{i,j} + u_{j,i} + u_{k,i}u_{k,j}), \quad (45)$$

and in our algorithm we would consider

$$\varepsilon_{i,j} = \frac{1}{2}(u_{i,j}^n + u_{j,i}^n + u_{k,i}^n u_{k,j}^{n-1}). \quad (46)$$

Figure 8 shows how much the virus has been displaced with respect to the force $\mathbf{F}$ for the three simulations considered. For reasonable adhesion magnitude and the flat stand, the displacement – force curves are very similar overall between the case with and without adhesion. Only the initial deformation and the area of contact with the flat support are somewhat different because of the adhesion forces. However, the force-displacement curve from simulation of indentation on a substrate modeled by two adjacent circles is significantly different from that of the flat stand.

5 Conclusion

In conclusion, we have performed finite-element simulations of the deformation of an elastic shell on a substrate with emphasis on the role on the substrate–shell interaction. For the first time, adhesion interactions between the substrate and the shell being indented by a normal distributed force were considered in a model applicable to recent experiments of AFM indentation of virus particles. For typical nanoparticle-substrate adhesion forces, with the exception of small differences at initial indentations, the force–displacement curves are similar with and without adhesion. Therefore, adhesion on a flat surface is not expected to affect measurements of the elastic constant for viruses in any appreciable way. However, when the substrate is not flat, like in the case of the virus shell being lodged in a circular cusp, the apparent stiffness measured by indentation is expected to be significantly different.

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Figure 8: The height displacement of the virus in our three simulations.

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