Synchronisation in oscillatory model of embryo's ZP molecules in context of polyspermy block

Julijana Simonovic* and Andjelka Hedrih**

* *Mechanical Faculty University of Nis, Nis, Serbia*

***Department for Bio-Medical Science, State University of Novi Pazar, Novi Pazar, Serbia*

Summary. After fertilization of mammalian oocyte, polyspermy block occurs- the reaction of the *Zona pellucida* (ZP) that prevents other sperm cells to penetrate the oocyte and gets "harder". This biological phenomenon ensures the quantity of genetic material in each generation. The aim of our research was to test if dynamics of oscillations of molecules in ZP of fertilised oocyte could explain this phenomenon of polyspermy block. To simulate the conditions of identical synchronisation (IS) of oscillations the model of ZP molecules coupled by visco-elastic non-linaear rheologic elements was presented. Structural model, a system of non-linear differential equations of Duffing type with non-linearity of third order, was numerically solved for multi parametric analysis.

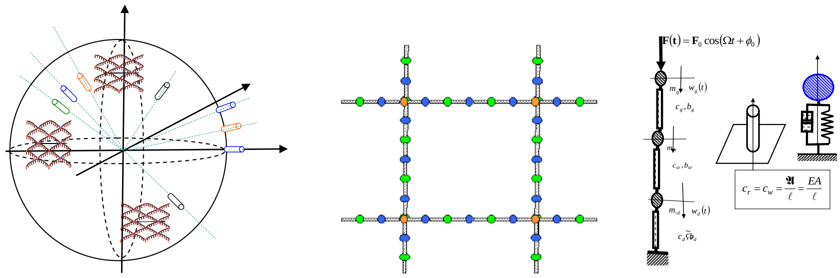
Results of numerical simulation show that for successful polyspermy block are of great importance: the position, direction and strength of spermatozoid impact but, also the coupling properties of mZP molecules-better viscosity and elasticity of ZP guaranty better synchronization of oscillatory molecules therefore better possibilities of polyspermy block.

Introduction

When one sperm cell successfully penetrates the *Zona pellucida (ZP)* of a mammalian oocyte, oocyte produces the cortical granules the content of which will help in chemical changes of ZP. ZP changes its physical properties, so that no other sperm can bind to the ZP and previously bind are drop out-phenomenon known as polyspermy block [1,2]. After fertilization ZP undergoes chemical and mechanical hardening. Precise molecular mechanisms of polyspermy block are still not known.

Treating the fertilization process as an oscillatory phenomenon [3], and using the oscillatory spherical net model of mouse ZP (mZP) [4] we modelled the oscillatory behaviour of knot molecules in the mZP of mouse embryo. For modal analysis one small part of mZP net that still preserves the molar ratio of mZP glycoproteins, was used. See Fig 1.

As oocyte and embryo are in different oscillatory states, our assumption is that ability of synchronization in oscillations of molecules in mZP could contribute to polyspermy block. To analyse under which conditions synchronisations of knot molecules of mZP is possible, we use non-linear discrete model [5].



a* b* c*

Figure 1. ***a**** Scheme of the mZP oscillatory spherical net model b* part of the mZP net that still preserves the molar ratio of mZP glycoproteins; Orange represents ZP1, blue ZP2, and green ZP3 mZP glycoproteins; **c*** Visco-elastic non-linear rheological element

Non-linear oscillatory model of mouse embryo's ZP

After fertilization, when series of spermatozoids continue impacts on the *ZP* causing initial perturbations of mass particle positions and their initial velocities in the *mZP* net model in comparison with natural equilibrium mass particle configurations system of mZP, oscillatory net is considered as non-linear and non-conservative system and oscillates in forced oscillatory regimes. Oscillatory behaviour of the mZP net for forced regime could be described by the system of non-linear differential equations of Duffing type with nonlinearity of third order. The net of eleven material particles coupled by non-linear visco elements, Fig.1.c*, was modeled in two orthogonal directions, Fig. 1.a*. The system of non-linear differential equations in circular (similarly in meridional) direction is presented in the following form:

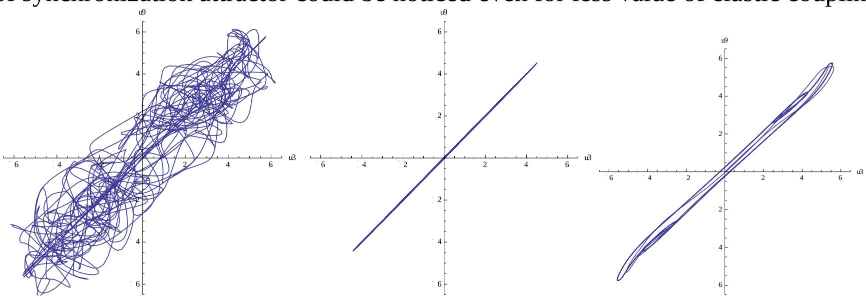
$$m\ddot{u}_{ij} = c_{(u)}\left(u_{i+1.j} - 2u_{i.j} + u_{i-1.j}\right) + \tilde{c}_{(u)}\left(u_{i+1.j} - u_{i.j}\right)^3 - \tilde{c}_{(u)}\left(u_{i.j} - u_{i-1.j}\right)^3 + k_{(u)}\left(\dot{u}_{i+1.j} - 2\dot{u}_{i.j} + \dot{u}_{i-1.j}\right) + h_{Ui,j}\cos\left(\Omega_{ij}t + \alpha_{ij}\right). \quad (1)$$

Where $u_{i.j}$, $i, j = 1,\dots 11.$ is mass displacements in circular direction, $k_{(u)}$ are coefficients of the damping force and $h_{Ui,j}$ are amplitude values of external excitations. For numerical experiment we approximate that coefficients of rigidity of linear $c_{(u)}$ and non-linear $\tilde{c}_{(u)}$ elastic properties are equal for all material particles and calculated it from the experimental data of Sun et al [6], molecular masses m of mZP glycoproteins were taken from [7].

To investigate identical synchronization (IS) conditions of mZP knot molecules in forced regime we use Mathematica ND Solver tool and very several parameters: linear and non-linear coefficient of elasticity, viscosity, intensity and position of external force. Synchronization threshold for vicinal knot molecules are discussed. The multi-parameters analyses were done by presentation of numerical simulation in the phase space of output variables of coupled particles, and through synchronization error diagrams.

Results

In chain systems with non-linear coupling the non-linearity brings the properties of exponentially divergence of trajectories of particles that starts from very close points in phase space, nevertheless even in that systems we may find synchronization, which is rather surprising detail [8,9]. In the general sense, the synchronization considers the correlation or mutual response in time behaviour of two or more processes. From all different cases of synchronization the IS, as a particular case of general synchronization, would be of interest in this paper. The IS could be bring off when particles are coupled with sufficient coupling strength so that their states are equal $u_i = u_j$ after transient changes [9]. This equality presents diagonal line of first and third quadrant in phase space. When the viscosity and non-linearity takes places in the coupling, then we have to consider multi parametric analysis of synchronization possibilities. For instance the Figs. 2 present synchronization diagrams for knot particles when excitation acts on central particles for different coefficient of linear stiffness and damping coefficient. The diagonal line is visible on Fig 2 a*, but only in the beginning period, otherwise the difference of knots displacements are significant. On Fig. 2b* is visible that for bigger values of coupling elastic coefficient the knots have the same displacement in particular direction, but in presence of damping, the form of synchronization attractor could be noticed even for less value of elastic coupling, Fig.2c*.



a* **b*** **c***

Figure 2. Synchronization diagrams on knot molecules of ZP model for different values of parameters: a* without damping for particular values of coefficient of linear and non-linear stiffnesses; b* increasing of coefficient of linear stiffness; c* increasing of damping coefficient

Conclusions

The presented analyses show that the synchronization effects of oscillating molecules of mouse embryo could be of crucial importance for polyspermy block effect. For successful polyspermy block are of great importance: the position, direction and strength of spermatozoid impact but, also the coupling properties of mZP molecules. This paper has investigated all those influences for possible synchronization of knot molecules in mZP model. The identically synchronized molecules are more likely to block future spermatozoid penetration. mZP of embryo is “harder” then mZP of oocyte [4,7], and our numerical experiment reveals that better viscosity and elasticity of ZP guaranty better synchronization of oscillatory molecules therefore better possibilities of polyspermy block.

Acknowledgement. The authors would like to thank to Prof. Katica (Stevanović) Hedrih from the Mathematical Institute of SASA, Belgrade, Serbia for help with useful consultations. Parts of this research were supported by the Ministry of Education, Science and Technological Development of Republic of Serbia through Grant ON174001.

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