Metadata of the chapter that will be visualized online

Chapter Title	Transition in Oscillatory Behavior in Mouse Oocyte and Mouse Embryo Through Oscillatory Spherical Net Model of Mouse Zona Pellucida
Copyright Year	2014
Copyright Holder	Springer International Publishing Switzerland

Corresponding Author	Family Name	**Hedrih**
	Particle	
	Given Name	**Andjelka N.**
	Suffix	
	Division	Department for Bio-medical science
	Organization	State University of Novi Pazar
	Address	Vuka Karadzica bb, 36 300, Novi Pazar, Serbia
	Email	handjelka@hm.co.rs

Abstract	Zona pellucida, a 3D matrix that surrounds mammalian oocyte, dynamically changes its elasticity during the maturation and fertilization process. We consider fertilization as a biomechanical oscillatory phenomenon and hypothesized that mature oocyte and embryo are in different oscillatory states. Using an oscillatory spherical net model of mouse ZP [4], eigen circular frequencies of mouse oocyte and mouse embryo were calculated. Frequency analysis of circular frequencies of ZP under periodical external excitation force in the form of sperm cell impact was done for both states. To determine the conditions for dynamical absorption under impact of sperm cells on ZP of mouse oocyte and embryo, numerical analyses were done.

Transition in Oscillatory Behavior in Mouse Oocyte and Mouse Embryo Through Oscillatory Spherical Net Model of Mouse Zona Pellucida

Andjelka N. Hedrih

Abstract Zona pellucida, a 3D matrix that surrounds mammalian oocyte, dynamically changes its elasticity during the maturation and fertilization process. We consider fertilization as a biomechanical oscillatory phenomenon and hypothesized that mature oocyte and embryo are in different oscillatory states. Using an oscillatory spherical net model of mouse ZP [4], eigen circular frequencies of mouse oocyte and mouse embryo were calculated. Frequency analysis of circular frequencies of ZP under periodical external excitation force in the form of sperm cell impact was done for both states. To determine the conditions for dynamical absorption under impact of sperm cells on ZP of mouse oocyte and embryo, numerical analyses were done.

AQ1

1 Introduction

Zona pellucida (ZP), the outermost surface of the oocyte, dynamically changes its elasticity during the maturation and fertilization process [1,6,7]. The purpose of this structure is to protect the oocyte, to work as high selective structure for high-quality spermatozoa, to select the "right one," to ensure polyspermy block, and to guide the embryo through the oviduct. The final fertilization process occurs at ZP. Considering fertilization process as a biomechanical phenomenon we hypothesized that mature oocyte [3,5] and embryo are in different oscillatory states. If they are in different oscillatory states, what are oscillatory properties of mouse embryo that do not allow penetration of other sperm cells through ZP in fertilized oocyte?

If there is only an initial perturbation by kinetic and potential energy given to oscillatory structures, only free vibrations of ZP appear. In this case material particles at the initial moment obtain the initial displacement measured from their equilibrium positions and initial velocities. In order for free oscillations to appear, it is enough that only one mass particle position is perturbed from its equilibrium

A.N. Hedrih (✉)
Department for Bio-medical science, State University of Novi Pazar, Vuka Karadzica bb, 36 300 Novi Pazar, Serbia
e-mail: handjelka@hm.co.rs

J. Awrejcewicz (ed.), *Applied Non-Linear Dynamical Systems*, Springer Proceedings in Mathematics & Statistics 93, DOI 10.1007/978-3-319-08266-0_21

position or that only one mass particle at its equilibrium position obtains initial velocity. If we apply one or multifrequency external excitation forces to a ZP discrete net, it oscillates in multifrequency forced regime oscillations.

The aim of our study was to compare eigen circular frequencies of mouse oocyte and mouse embryo ZP as a property of the systems and to determine the conditions for dynamical absorption under impact of sperm cells on ZP of mouse oocyte and embryo through spherical surface net model of mZP [4].

2 Determination of the Eigen Circular Frequencies

Using spherical surface net model of mZP [4] and a method of discrete continuum [2] we considered that the system of ZP oscillatory net oscillates in a free regime after ovulation without the presence of spermatozoa. In a spherical surface net model of mZP [4] ZP is modeled as a one-layer network that envelops the oocyte/embryo that we supposed that is solid, elastic, and rigid. The network consists of orthogonal chains of material particles interconnect with elastic massless springs on a specific manner. Material particles represent the ZP glycoproteins. See Fig. 1a. To do a frequency analysis of a part of spherical net model and to determine a particular set of the eigen circular frequencies of mZP, we use the smallest part of the mZP oscillatory spherical surface model (see Fig. 1b) that still preserves the molar ratio of the mZP glycoproteins (ZP1:ZP2–ZP3 is 1:5).

We applied one or multifrequency external excitation forces to a one knot molecule *ZP* discrete net (third in the chain or ninth in this chain using symmetry

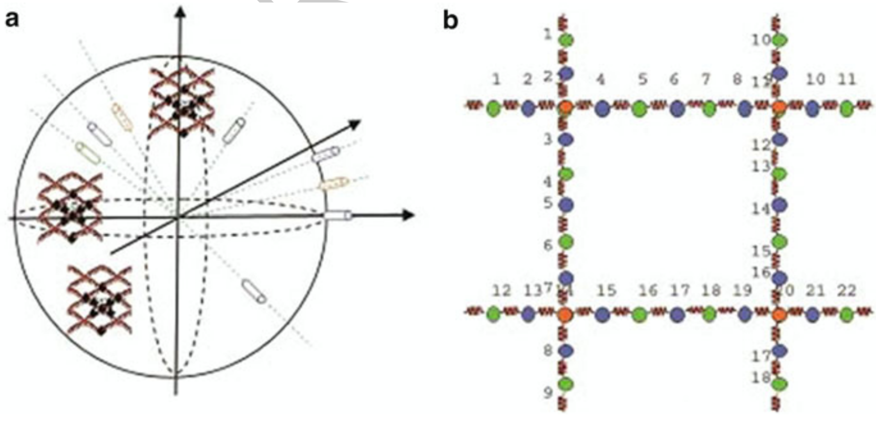
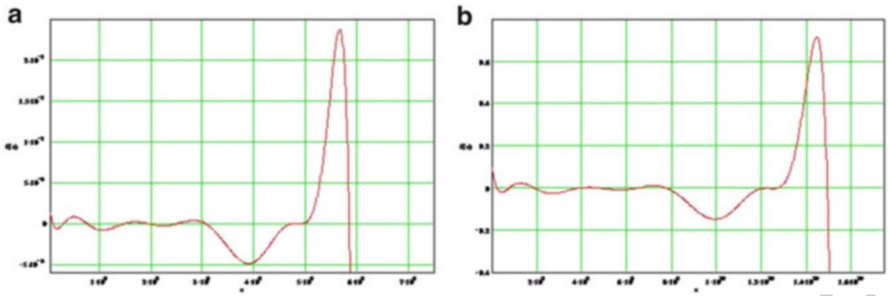


Fig. 1 (**a**) Model of *ZP* spherical surface that shows a radial direction of axis of constructive elements of the model—*ZP* proteins. *Axis* shows directions of movements of *ZP* proteins. Each *ZP* protein is connected to the sphere with elastic springs that can oscillate in radial direction. (**b**) Part of the *ZP* network on a part of the sphere (oocyte). *Orange* (*ZP*1), *blue* (*ZP*2), and *green* (*ZP*3) represent *ZP* proteins. The network is identical in both circular and meridian direction



AQ2 **Fig. 2** Presentation of two characteristic branches of the eleven degree polynomial function graphs along square of circular frequencies ω^2: (**a**) before and (**b**) after fertilization of ZP for different material parameters (module of elasticity and masses particles)

in order of eleven mass particles in chain). Frequency equation that describes the oscillations of the mZP glycoproteins is in the form of chain with eleven material particles. The frequency equation is an eleven degree polynomial function along square of possible circular frequencies ω^2 and is in the form

$$f\left(\omega^2\right) = \left|\mathbf{C} - \omega^2\mathbf{A}\right| = 0. \tag{1}$$

C is matrix of coefficient of elasticity, and **A** is matrix of coefficient of mass inertia. For obtaining eigen circular frequencies we used graphical method and Mathcad software. See Fig. 2a, b. Relative molecular masses of the three mZP glycoproteins, Mr*ZP*1, 200,000 Da; Mr*ZP*2, 120,000 Da; and Mr*ZP*3, 83,000 Da transformed in kg, were used. The zeros (roots) in the frequency equations are squares of eigen circular frequencies ω_s^2. For considered nonhomogenous chains there are 11 squares of eigen circular frequencies: ω_s^2, $s = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11$.

AQ3

For our numerical experiment we approximate that coefficient of elasticity is equal for all material particles and calculated it from the experimental data of Sun et al. [9] according to the formula

$$c = \frac{E\left(R^2 - r^2\right)\pi}{2R} \tag{2}$$

E is Young module of elasticity, R is half diameter of the mouse oocyte/embryo, and r is internal radius of oocyte or is half diameter of the oocyte/embryo minus approximate thickness of mZP.

AQ4 For an oocyte: $E_o = 17.5$kPa; $2R_o = 56.2$ μm, average diameter of an oocyte from [9]; and $\delta_o = 4.8$ μm, approximate ZP thickness of the oocyt[illegible] = 0.253 N/m.

AQ5 For mouse embryo: $E_e = 42.2$kPa; $2R_e = 61$ μm, average diameter of an embryo from [9]; and $\delta_e = 5.34$ μm, approximate ZP thickness of the embry[illegible] $c_e = 0.646$ N/m.

For obtaining eigen circular frequencies we used graphical method and Mathcad software tool and correction factor 10^6.

AQ6 The obtained eigen circular frequencies for mouse oocyte, by use Mathcad software tool and in Fig 2. a presentation of characteristic branch of the eleven degree polynomial function graphs along square of circular frequencies ω_s^2, $s = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11$ before fertilization for corresponding material parameters (module of elasticity and masses particles) are: $\omega_{o1} = 9.318 \times 10^9$ rad, $\omega_{o2} = 1.72 \times 10^{10}$ rad/s, $\omega_{o3} = 2.707 \times 10^{10}$ rad/s, $\omega_{o4} = 3.856 \times 10^{10}$ rad/s, $\omega_{o5} = 4.379 \times 10^{10}$ rad/s, $\omega_{o6} = 5.011 \times 10^{10}$ rad/s, $\omega_{o7} = 5.522 \times 10^{10}$ rad/s, $\omega_{o8} = 6.887 \times 10^{10}$ rad/s, $\omega_{o9} = 6.952 \times 10^{10}$ rad/s, $\omega_{o10} = 7.024 \times 10^{10}$ rad/s, and $\omega_{o11} = 7.645 \times 10^{10}$ rad/s.

AQ7 The obtained eigen circular frequencies of mouse embryo, by use Mathcad software tool and in Figure 2.b presentation of characteristic branch of the eleven degree polynomial function graphs along square of circular frequencies ω_s^2, $s = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11$ for corresponding material parameters (module of elasticity and masses particles) are: $\omega_{e1} = 1.484 \times 10^{10}$ rad, $\omega_{e2} = 2.725 \times 10^{10}$ rad/s, $\omega_{e3} = 4.324 \times 10^{10}$ rad/s, $\omega_{e4} = 6.205 \times 10^{10}$ rad/s, $\omega_{e5} = 6.977 \times 10^{10}$ rad/s, $\omega_{e6} = 8.005 \times 10^{10}$ rad/s, $\omega_{e7} = 8.806 \times 10^{10}$ rad/s, $\omega_{e8} = 1.096 \times 10^{11}$ rad/s, $\omega_{e9} = 1.193 \times 10^{11}$ rad/s, $\omega_{e10} = 1.127 \times 10^{11}$ rad/s, and $\omega_{e11} = 1.221 \text{x}\ 10^{11}$ rad/s.

These two obtained sets of square of eigen circular frequencies of mZP ω_s^2, $s = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11$ before and after fertilization for corresponding material parameters (module of elasticity and masses particles) are also sets of resonant frequency squares of corresponding one frequency external excitation square of frequencies $\Omega_{rez,s}^2 = \omega_s^2$, $s = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11$.

3 Forced Oscillations

The system of ordinary differential equations of mass particles forced dynamics is in the following matrix form:

$$\mathbf{A}\{\ddot{x}\} + \mathbf{C}\{x\} = \{Q\} = \{F_0\}\cos\Omega t \tag{3}$$

Particular solution for kth mass particle in the chains, when one frequency external excitation is applied to the third mass particle in chain, is in the form

$$x_k\left(t, \Omega_3^2\right) = C_{(3)k}\left(\Omega_3^2\right)\cos\Omega_3 t \tag{4}$$

Amplitude $C_{(3)k}(\Omega_3^2)$ of particular solution for kth mass particle in chain forced vibration displacement under the one frequency external excitation applied to the third mass particle in chain is in the form

$$C_{(3)k}\left(\Omega_3^2\right) = \frac{\Delta_{(3)k}\left(\Omega_3^2\right)}{\Delta\left(\Omega_3^2\right)} \tag{5}$$

for $\Omega_3^2 \neq \omega_s^2$, $s = 1, 2, 3,, 4, 5, 6, 7, 8, 9, 10, 11$, and where determinant of the previous system is in the form

$$\Delta\left(\Omega_3^2\right) = \left|\mathbf{C} - \Omega_3^2 \mathbf{A}\right| \neq 0 \tag{6}$$

AQ8 and must be different from zero. Then $\Omega_3^2 \neq \omega_s^2$, $s = 1, 2, 3,, 4, 5, 6, 7, 8, 9, 10, 11$ conditions have to be fulfilled.

For obtaining amplitudes $C_{(3)k}(\Omega_3^2)$ of particular solutions, it is necessary to find
AQ9 sub-determinant $\Delta_{(3)}(\Omega_3^2)$. Corresponding sub-determinant $\Delta_{(3)}(\Omega_3^2)$ is possible to obtain by substitution corresponding 3th column by column containing nonzero element F_{03} and third element concerning that external excitation force is applied to the third mass particle of the chain system.

4 Conditions for Dynamical Absorption

Dynamical absorption is present in the systems with multiple degrees of freedom (in our case chain is system with 11 degrees of freedom) when external periodical force is applied to the system. Depending on the material properties and parameters of the oscillatory system structure (coefficient of elasticity, mass of material particles, external excitation frequencies, amplitudes) it is possible that under the influence of periodical external force one or more material particles don't oscillate in forced mode with external excitation frequency and that other mass particles are in this forced oscillatory mode. In the theory of oscillation [8] this phenomenon is known as dynamical absorption.

External excitation frequencies at which dynamical absorption occurs of mass particles on certain positions were read out from amplitude-frequency graphs for
AQ10 each mass particle in chain. For determine the amplitude of forced vibrations $C_k(\Omega_3^2)$, $k = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11$ for each mass particle, when third mass particles are loaded by external one frequency excitation through the impact of one sperm cell with frequency Ω_3, of each material particle in the chain when external periodical force is $F_3 = F_{03} \cos \Omega_3 t$. The required condition is

$$C_k\left(\Omega_3^2\right) = 0, \textit{for some of } k = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 \textit{ when } \Delta\left(\Omega_3^2\right) \neq 0 \tag{7}$$

Graphs of amplitude-frequency stationary forced regimes for forced vibration of $C_3(\Omega_3^2)$ third, $C_6(\Omega_6^2)$ sixth, and $C_9(\Omega_3^2)$ ninth material particle in chain excited by external excitation $F_3 = F_{03} \cos \Omega_3 t$ force with amplitude F_{03} and frequency Ω_3 applied to third mass particle in chain in mZP net model of oocyte and embryo are given in Figs. 3, 4, and 5, respectively. When external excitation $F_3 = F_{03} \cos \Omega_3 t$ force with amplitude F_{03} and frequency Ω_3 is applied to third mass particle in chain, frequencies under which dynamical absorption occurs in forced oscillatory regimes in the third material particle oscillatory displacement in the chain are:

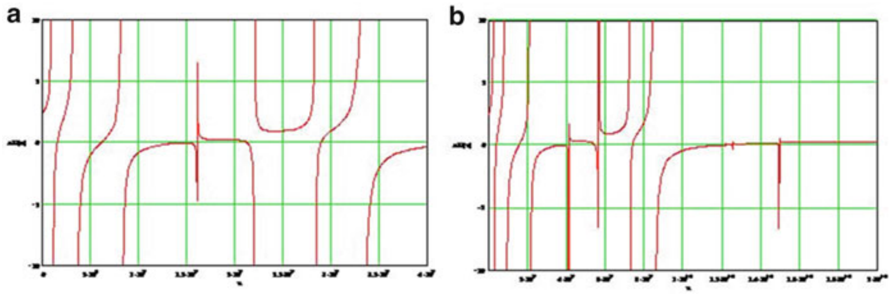


Fig. 3 Amplitude-frequency stationary forced regimes for forced oscillations of $C_3(\Omega_3^2)$ third material particle in chain excited by external excitation $F_3 = F_{03}\cos\Omega_3 t$ force with amplitude F_{03} and frequency Ω_3 applied to third mass particle in chain; $x = \Omega^2$. for (**a**) oocyte, (**b**) embryo

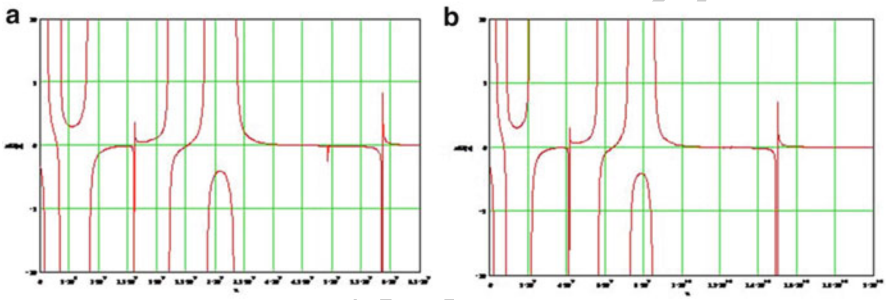


Fig. 4 Amplitude-frequency stationary forced regimes for forced oscillations of $C_3(\Omega_3^2)$ sixth material particle in chain excited by external excitation $F_3 = F_{03}\cos\Omega_3 t$ force with amplitude F_{03} and frequency Ω_3 applied to third mass particle in chain; $x = \Omega^2$.for (**a**) oocyte, (**b**) embryo

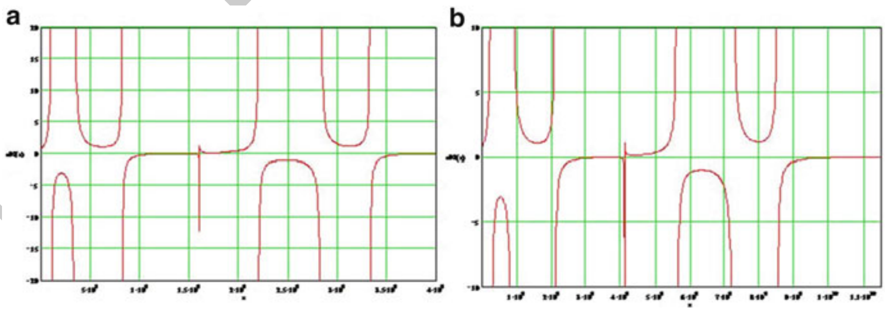


Fig. 5 Amplitude-frequency stationary forced regimes for forced oscillations of $C_3(\Omega_3^2)$ ninth material particle in chain excited by external excitation $F_3 = F_{03}\cos\Omega_3 t$ force with amplitude F_{03} and frequency Ω_3 applied to third mass particle in chain; $x = \Omega^2$. for (**a**) oocyte, (**b**) embryo. It is visible that there is no dynamical absorption

For mouse oocyte: 1.233×10^{10}rad/s, 2.49×10^{10}rad/s, 4.605×10^{10}rad/s, and 5.38×10^{10}rad/s.

And for the embryo: 2.145×10^{10}rad/s, 3.95×10^{10}rad/s, 7.335×10^{10}rad/s, 8.602×10^{10} rad/s, 1.22×10^{11}rad/s, and 1.118×10^{11}rad/s.

We can see that in the forced regime one mode of forced oscillatory displacement of this third mass particle does not exist at a number of external excitation frequencies—frequencies of dynamical absorptions upon that mass particle are loaded. Other mass particles are not directly loaded and are in forced oscillatory regimes at these frequencies of dynamical absorption of third loaded mass particle. This is a dynamical paradox that this mass particle is loaded by external single frequency force and that loaded mass particle is not in the forced oscillatory regime and that other mass particles in chain oscillate in forced regimes at these frequencies. Amplitude of external excitation has no influence on the appearance of dynamical absorption. Only external excitation frequency in relation with chain material properties (system structure properties like eigen circular frequencies, coefficients of elasticity/rigidity, and masses of material particles) influenced the appearance of dynamical absorption.

When external excitation $F_3 = F_{03} \cos \Omega_3 t$ force with amplitude F_{03} and frequency Ω_3 is applied to third mass particle in chain, frequencies under which dynamical absorption occurs for the sixth material particle in the chain are:

For mouse oocyte: 1.672×10^{10} rad/s and 1.596×10^{10} rad/s

For the embryo: 2.683×10^{10} rad/s and 8.655×10^{10} rad/s

Under these conditions there is no dynamical absorption on the ninth material particle in the chain either in oocyte or in embryo.

5 Conclusions

Due to limited length of the paper we did not analyze the forced oscillations of knot molecules in ZP net; we analyzed only the phenomenon of dynamical absorption for certain molecules in the model. We did the analysis on a part of spherical surface net of mZP in the system with finite number of degree of freedom. In the real system of ZP there are a lot of molecules and almost indefinite eigen circular frequencies.

Young module of elasticity of mouse ZP in mature oocyte (before fertilization) has 2.5 times higher value compared to ZP of mouse embryo (after fertilization) [9]. Sperm cells could not penetrate the ZP of embryo. From a biological point of view after fertilization occurs polyspermy block-new sperm cells could not attach to the ZP and the already attached have been rejected. This process is receptor and enzymatic mediated and includes repulsive electric charge between ZP and sperm cells.

We tried to perceive these events from the aspect of theory of oscillations. Sperm cells have impact on a ZP in the form of multifrequency external excitation forces. We applied external excitation to the one knot molecule *ZP* discrete net (third in the chain). According to the spherical surface net model of mouse ZP, our numerical analysis shows that eigen circular frequencies of mouse embryo ZP have higher values compared to eigen circular frequencies of mouse oocyte ZP. This indicates that for potential penetration through mouse embryo, sperm cells will require more energy. In the living system this is not possible owing to sperm energy loss with time. After fertilization there are no sperm cells capable to respond to these increased demands.

On amplitude-frequency graphs zeros correspond to dynamical absorptions in forced oscillatory regime. On these frequencies certain material particle is not oscillating and external force has no effect on it. For the same molecules, frequencies when dynamical absorption occurs are higher for ZP of mouse embryo then for ZP of mouse oocyte. For sixth molecule in the chain in case of embryo there are six frequencies where dynamical absorption is possible, and for the case of oocyte, for the same molecule in the case of the oocyte there are four. All these results confirm that oocyte and embryo are in different oscillatory states and that these oscillatory states have biological purpose. As in biological systems this transition is an irreversible process; further investigations of conditions under which this irreversible process is possible should be done. If small nonlinearities are included in the system it is possible to determine the dependence of frequencies on initial conditions as well as resonant jumps in the system.

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

References

1. Familiari, G., Heyn, R., Relucenti, M., Sathananthan, H.: Structural changes of the zona pellucida during fertilization and embryo development. Frontier Biosci. **13**, 6730–51 (2008)
2. Hedrih (Stevanović), K.: Discrete continuum method, symposium, recent advances in analytical dynamics control, stability and differential geometry. In: Proceedings of the Mathematical institute SANU Edited by Vladan Djordjević, p. 151, pp. 30–57, 2002. ISBN 86-80593-32-X. http://www.mi.sanu.ac.yu/publications.htm
3. Hedrih, A.: Frequency analysis of knot mass particles in oscillatory spherical net model of mouse zona pellucida. In: Lecture Session, Short Paper, Abstract book of 23rd International Congress of Theoretical and Applied Mechanics, (IUTAM ICTAM Beijing 2012), Beijing, China, SM01-049, p. 209, 19–24 Aug 2012. ISBN 978-988-16022-3-7
4. Hedrih, A.: Modeling oscillations of zona pellucida before and after fertilization. ENOC Young Scientist Prize Paper. *EUROMECH* Newsletter 40. Europian Mech. Soc. **40**, 6–14. 2011

5. Hedrih, A., Lazarevic, M., Mitrovic-Jovanovic, A.: Fertilization as a biomechanical oscillatory phenomenon in mammals. In: Proceedings of the Fourth Serbian (29th Yu) Congress on Theoretical and Applied Mechanics, Vrnjacka Banja, Serbia, pp. 579–584, 4–7 June 2013
6. Murayama, Y., Mizuno, J., Kamakura, H., Fueta, Y., Nakamura, H., Akaishi, K., Anzai, K., Watanabe, A., Inui, H., Omata, S.: Mouse zona pellucida dynamically changes its elasticity during oocyte maturation, fertilization and early embryo development. Hum. Cell **19**, 119–125 (2006)
7. Papi, M., Sylla, L., Parasassi, T., Brunelli, R., Monaci, M., Maulucci, G., Missori, M., Arcovito, G., Ursini, F., De Spirito, M.: Evidence of elastic to plastic transition in the zona pellucida of oocytes using atomic force spectroscopy. Appl. Phys. Lett. **94**, 153902 (2009)
8. Rašković, P.D.: Teorija oscilacija (Theory of Oscillations). Beograd, Naučna knjiga (1965)
9. Sun, Y., Wan, K.T., Roberts, K.P., Bischof, J.S., Nelson, B.J.: Mechanical property characterization of mouse zona pellucida. IEEE T Nanobiosci. **2**(4), 279–286 (2003)

AUTHOR QUERIES

AQ1. Please check if "external excitation force" is okay as edited.
AQ2. Please note that the Figs. 1–5 texts are too thick and are not clear. So please supply new figures.
AQ3. Please check if edit to sentence starting "Relative molecular masses . . . " is okay.
AQ4. Please check if edit to sentence starting "For an oocyte . . . " is okay.
AQ5. Please check if edit to sentence starting "For mouse embryo . . . " is okay.
AQ6. Please check sentence starting "The obtained eigen . . . " for clarity.
AQ7. Please check sentence starting "The obtained eigen . . . " for clarity.
AQ8. Please check sentence starting "Then . . . " for clarity.
AQ9. Please check sentence starting "Corresponding sub-determinant . . . " for clarity.
AQ10. Please check sentence starting "For determine the . . . " for sense.
AQ11. Please check sentence starting "From a biological . . . " for clarity.
AQ12. Please check if "certain material particle is" should be changed to "certain material particles are".
AQ13. Please check sentence starting "For sixth molecule . . . " for clarity.
AQ14. Note that the references are sorted in alphabetical order in the reference list. Please check and confirm.