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The effect of friction and impact angle on the spermatozoa–oocyte local contact dynamics

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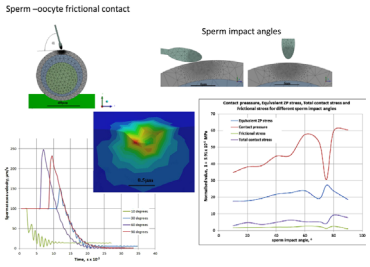
HIGHLIGHTS

- Sperm–oocyte local contact dynamics are studied trough biomechanical FEM analysis.
- Sperm–oocyte contact was defined as non-linear frictional contact.
- Deformations of ZP relative to different sperm impact angles (SIA) are discussed.
- An effect which resembles the "slip-stick" effect was identified.
- Favorable ZP-stress state for sperm penetration for different SIA are discussed.

GRAPHICAL ABSTRACT



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ABSTRACT

Although a large proportion of biomolecules involved in spermatozoa–oocyte interaction has been discovered so far, many details of fertilization mechanism remain unknown. Both biochemical and biomechanical components exist in the fertilization process. Mammalian sperm evolved a ZP (zona pelucida) thrust reduction penetration strategy probably in response to the ZP resilient elasticity.

Using a biomechanical approach and FEM analysis, local contact stress, ZP deformations during impact and attempt of sperm head penetration relative to different sperm impact angles (SIA) were studied. The sperm–oocyte contact was defined as non-linear frictional contact. A transient structural analysis at 37 °C revealed that, from the mechanical standpoint there are SIA that are more favorable for possible ZP penetration due to larger equivalent stress of ZP. An "slip-stick" resembling effect was identified for almost all examined SIA. The sperm head–ZP contact area increases as SIA decreases. Favorable ZP-stress state for sperm penetration regarding SIA are discussed.

1. Introduction

Fertilization process in mammals is a complex multiphase process that requires healthy oocyte and certain amount of functional spermatozoa. Classical concept of fertilization includes binding of spermatozoa to a 3D mesh-like extracellular structures of the oocyte–Zona pellucida (ZP) (Familiari et al., 2006; Martinova et al., 2008), the acrosome reaction and subsequent penetration of spermatozoa through ZP, binding and fusion of a spermatozoid with the oolemma, activation of the oocyte–cortical reaction, releasing the contents of the cortical vesicles into the perivitelline space and polyspermy block-consecuent prevention of other

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spermatozoa to fertilizing the oocyte (Talbot et al., 2003; Okabea and Cummins, 2007; Gaffney et al., 2011; Gadella, 2013).

During their chemotactical, rheotactical and thermotactical (Miki and Clapham, 2013) movement in female reproductive tract some spermatozoa will pass through complex metabolic and structural changes, becoming fertilization-competent. (Flesch and Gadella, 2000). Only a small fraction of a given sperm population (averaging around 10%) is responsive to different factors released from female reproductive tract and these represent capacitated spermatozoa (Eisenbach, 1999).

Sperm swimming velocity is a key determinant of male fertilization success (Malo et al., 2006). Mouse spermatozoa, as very vulnerable cells, develop strategies to survive long enough to reach and fertilize the oocytes. Spermatozoa of species with multiple partners mating system develop strategies to increase fertilization success by increasing the sperm swimming velocity by acquiring more energy for movements (longer midpiece, or longer flagella) (Anderson and Dixson, 2002; Firman and Simmons, 2010; Tourmente et al., 2011)

According to the classical fertilization concept, recognition and binding of spermatozoa to ZP will cause the acrosome reaction and consequent release of acrosome enzymes that will digest the ZP and ease the sperm penetration through it. Bedford (1998) argues that sperm penetration of ZP is only lytic event and that has also a biomechanical component that precludes lytic events.

When a spermatozoa fuse with oolema, ZP changes its structure and biomechanical properties – it becomes harder and resistant not only to proteolysis but also to mechanical forces (Sun et al., 2003; Papi et al., 2009).

Different computational techniques are used for modeling biological processes in reproductive system. Boundary element method for motion of a micromachine with a head and an elastic tail immersed in viscous media (Nasseri and Phan-Thien, 1997a, 1997b) could be applicable for sperm motion in viscous fluid with some limitations; finite element model to simulate multiple morphogenetic movements of a simplified ellipsoidal Drosophila embryo (Allena et al., 2010). To parametrize shell-like deformations inside membrane of Drosophila embryo a technique described by (Allena and Aubry, 2011) could be used. Finite elament method is also used in characterization of vibration properties of mouse embryo (Hedrih and Ugrcic, 2013).

There several biomechanial models of fertilization proces that are based on sperm–egg interaction (Gefen, 2010; Kozlovsky and Gefen, 2012, 2013; Hedrih et al., 2013, 2015). First three are based on contact mechanics and other two are oscillatory models.

Using contact mechanics based modeling Gefen (2010) modeled relationship between sperm velocity and pressures applied to the ZP during early sperm–oocyte penetration. The analysis showed that sperm velocity has higher impact on pressure generated on the ZP surface than sperm head density. Kozlovsky and Gefen (2012) predicted that during the early stage of penetration into the ZP, biochemical binding forces acting on spermatozoa, are smaller than the mechanically-generated propulsive forces. “Hyperactivation of the spermatozoid and the sharpness of the spermatozoid head are all important factors that govern successful sperm penetration into the ZP” (Kozlovsky and Gefen, 2013). According to their analysis ZP hardening process as well as ZP thickness had a negligible effect on the maximum contact pressures, and the maximum penetration of the head of the spermatozoon.

Boccaccio et al. (2012) developed a hybrid procedure to investigate the biomechanical behavior of ZP membranes extracted from mature and fertilized bovine oocytes. The authors developed new hybrid model in order to increase the understanding of mechanisms that may lead to the biomechanical hardening of ZP, as well as to determine it's elastic properties. The hybrid model combines atomic force microscopy (AFM) nanoindentation measurements, nonlinear finite element analysis and nonlinear optimization algorithms. The displacement values measured by AFM nanoindentation measurements were compared with the corresponding results of FE analysis. The optimization algorithm was defined in order to extract parameters of material model for which there is a matching of experimental and FE data. Authors used three widely used hyperplastic models: Mooney–Rivlin, neo-Hookean and Arruda–Boyce eight-chain model for a constitutive model of the ZP. During FE modeling, Boccaccio et al. (2012) used axisymmetric finite element (FE) model: blunt conical indenter was treated as a rigid body and the ZP membrane was modeled as incompressible hyperelastic slab with 60 μm diameter and 10 μm thickness. Contact between AFM tip and ZP was assumed to be frictionless and analysis accounted for nonlinearity due to large deformations. During analysis the authors established that the hyperelastic behavior of the ZP membrane was always driven mainly by shear modulus, regardless of the constitutive model considered. Moreover, they established that the Arruda–Boyce model showed best results in capturing the biomechanical behavior of the ZP.

The strain-hardening behavior of an incompressible ZP membrane in AB model is predicted by using two constants: the shear modulus and the distensibility. Non-linear optimization softer compare results of computed force-indentation curves in FE analysis with experimental data, computed the error function and perturbed material parameters to minimize the error. Using this method they extract the elastic parameters of ZP membrane by using formulation of the inverse problem (Boccaccio et al., 2012). The qualitative results of Boccaccio et al. (2012) are in concordance with previous results that ZP gets harder upon fertilization and the inner ZP layer is harder compare to outer ZP layer in fertilized oocyte that is in concordance with ultra-structural experiments that inner ZP layers have more densely packed ZP glycoproteins (Martinova et al., 2008). The value of this paper is in hybrid procedure, FE model of ZP that is adequate for AFM probing experiments they used and usage of AB eight chain model instead of modified Hertzian model.

Using the same hybrid procedure (nonlinear FE analysis and nonlinear optimization) Boccaccio et al. (2014) developed optimization-based algorithm for extracting ZP linear viscoelastic properties in experiments with ZP of mature porcine oocyte: shear modulus, distensibility, Prony constant and relaxation time constant. The first two parameters describe the hyperelastic properties of ZP and the second two the viscous properties. This viscoelastic model of ZP describes the viscous response of the porcine ZP under different indentation speeds of AFM tip (from 0.5 to 10 μm/s) that simulates spermatozoa with different velocities. “As the indentation rate increases, viscous effects dominate and neglecting them leads to significant errors” (Boccaccio et al., 2014; Papi et al., 2013).

None of the models investigate the frictional contact between the spermatozoa head and the ZP, neither the sperm impact angle on stress and deformation generated in the ZP during sperm penetration process. Furthermore, noted models do not consider impact of spermatozoa on the ZP surface.

Bedford (2006) examined the problem of why the penetrating sperm creates an oblique path in the ZP, as ultrastructural analysis of mammal ZP by transmission electronic microscopy showed that the spermatozoid ZP penetration path has an oblique form (Bedford, 1998). He also discussed the benefits of this path for the developing embryo: “A small radially directed hole enlarges significantly as the zona stretches and thins during expansion of the trophoblast, which then tends to protrude or herniate” (Bedford, 2006).