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Mathematical modelling of pronuclei migration in the mammalian egg

At this time it remains unanswered how the embryonic-abembryonic axis of the mouse blastocyst is first established. Cell-fate is flexible in the sense that the development can recover from perturbations. However, the early mouse embryo is not merely a uniform ball. The cells show some preferences for adopting certain positions that will in turn govern their developmental decisions. Our main question is: When are these preferences established? Cell-fates could be decided completely at random but it is also possible that these decisions are guided by even as early contributing factors as the first cleavage of the egg. The orientation of the opposing pronuclei plays most likely a decisive role in the polarity of the developing embryo. Earlier studies of the mouse embryo development show deviating results of when patterning is initiated in the egg, [1]-[4], [6], [7]. Some of these studies that conclude that the pattern formation starts later in the embryo have however been conducted in 2D. We think it is important to see this as a three dimensional problem to reduce bias in the results. The purpose of introducing our model of the migration is to easier visualize the fertilization process to answer these questions. The usefulness of a mathematical model of the migration is not only a case for visualization, but could also be used to predict outcomes by simulating different scenarios, such as the dependence of the point of sperm entry. Also, values of model parameters can be used to quantify the effect of standard treatment or measurements of fertilized eggs in the lab. From the model we can make simulations of the migration process and plot the meeting positions for the pronuclei. As data we use stacks of confocal microscopy time-lapse images of the pronuclei migration, and realistic parameters in the models are identified by statistical methods. Given different distances between the sperm entry and the position of the second polar body, the estimated models are then used to produce distributions of orientations of the meeting plane between the pronuclei. Parameter values corresponding to the size of these forces are estimated from data of both eggs treated with a microtubule inhibitor and untreated eggs. The centralization force is modelled by two mechanisms of pushing and pulling of the microtubule exerted forces. The model is essentially based on two forces of attraction, a general migration directed towards the centre of the cell, and a second attraction force towards the other pronucleus. From this we have for example an indication that the pulling mechanism is more significant than the pushing.

References

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