

Given a Spherical Cow...

What Do We Know About the Initial Symmetry of the Fertilized Egg?

(Extending “The Hierarchical Genome and Differentiation Waves” 1.01)

Presented in the Embryo Physics Course <http://www.embryophysics.org>

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By

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"The germ is a unit, in space and time. What we are interested in is... its fascinating struggle in escaping from... sphericity..." (Dalcq, 1938).

- Dalcq, A.M. (1938). *Form and Causality in Early Development*. Cambridge, Cambridge University Press

“...cows are spherical, and not just when they are meatballs” HG.

- HG = Gordon, R. (1999). The Hierarchical Genome and Differentiation Waves: Novel Unification of Development, Genetics and Evolution. Singapore & London, World Scientific & Imperial College Press <http://www.worldscibooks.com/lifesci/2755.html>.

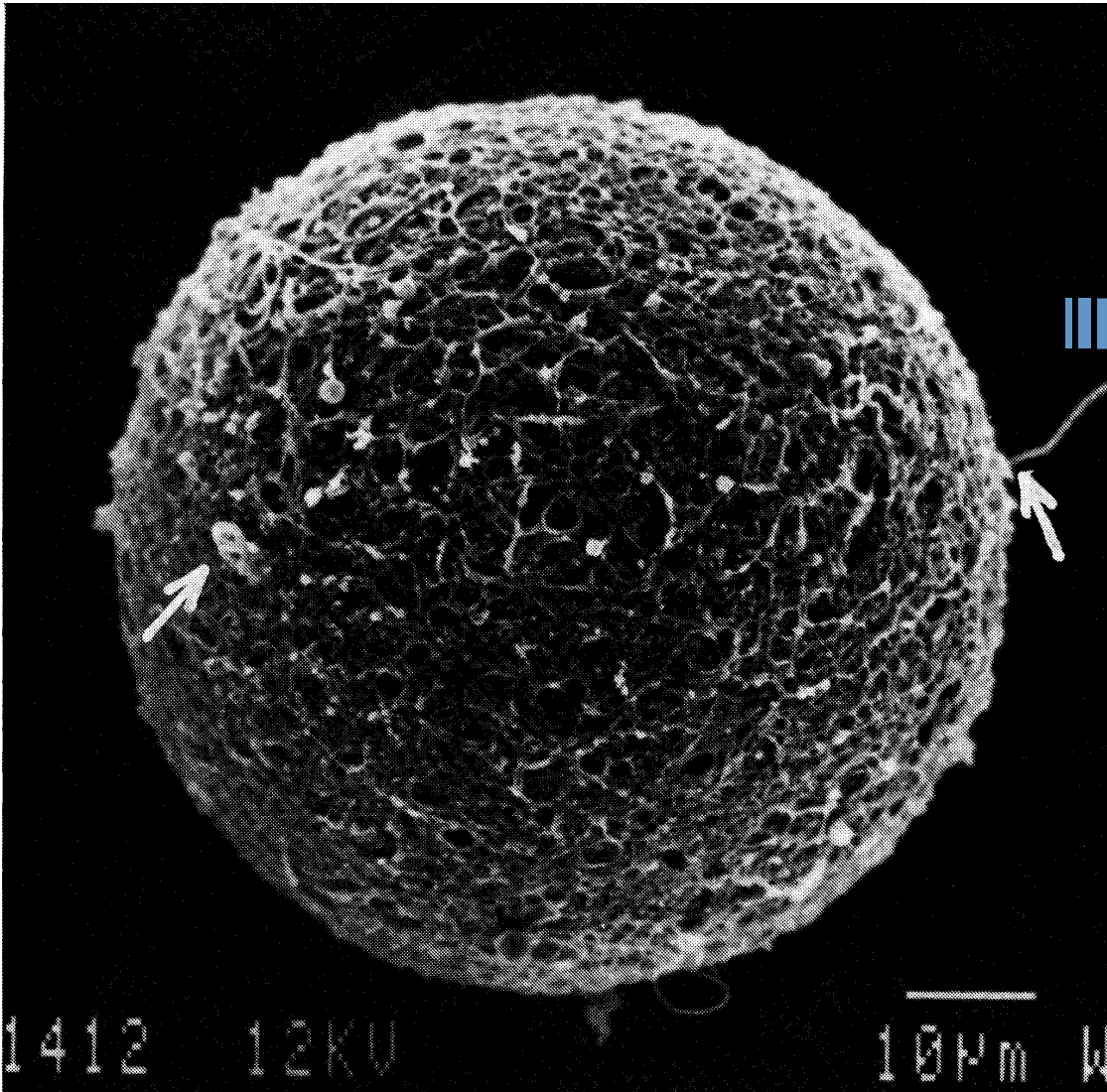


Spherical Cows



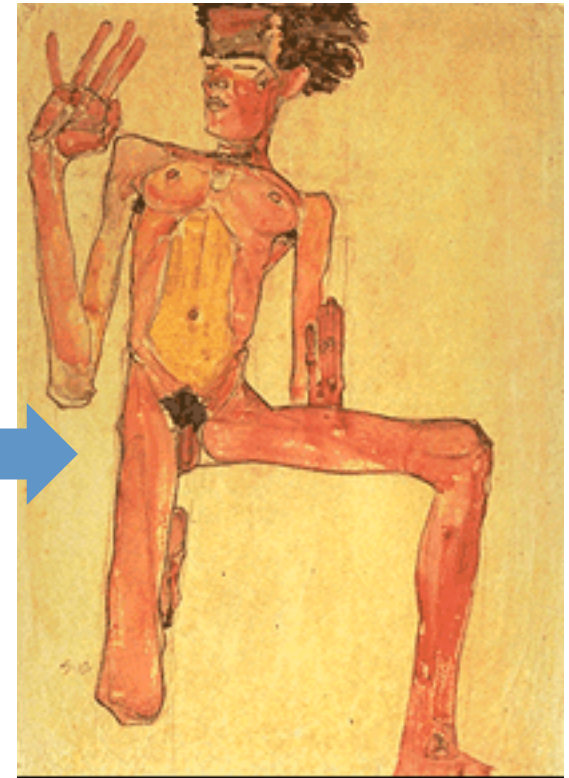
“...in biology we ascribe the same species name to every part of the life cycle of an organism. Thus a fertilized, spherical cow egg is a cow” HG

The Problem



Nikas, G., T. Paraschos, A. Psychoyos & A.H. Handyside (1994). The zona reaction in human oocytes as seen with scanning electron microscopy. *Hum. Reprod.* 9(11), 2135-2138.

?



1,000,000 μm = 1 meter

Egon Schiele
Kneeling Male Nude (Self-Portrait).
1910.

<http://www.moma.org/exhibitions/schiele/artistwork.html>

How did your spherically
symmetrical egg turn
into a highly
asymmetrical shape?

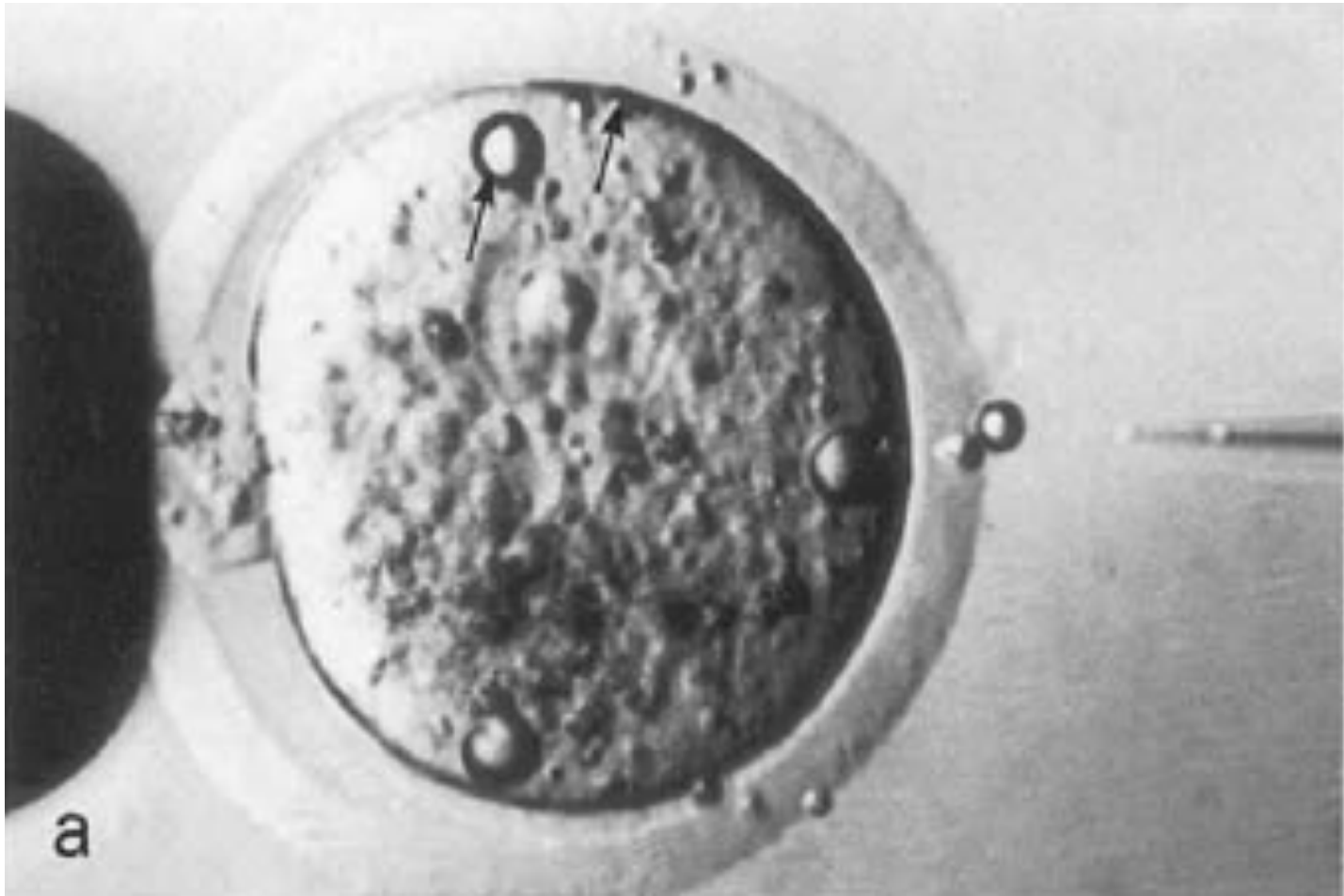
Spherical symmetry means that a spherical egg is the same in all directions from the center of the sphere. My guess is that the human egg is spherically symmetric. How do we know? We don't. The best we can say right now is that when the inside of a similar looking mouse egg was stirred around by Sergei Evsikov, using a miniature egg beater (actually a microscopic piezoelectric stirrer), while he was still in the Ukraine, he got a normal mouse. Sergei now works in reproductive technology in San Francisco.

Evsikov, S.V., L.M. Morozova & A.P. Solomko (1994).
Role of ooplasmic segregation in mammalian
development. *Roux's Arch. Dev. Biol.* **203**, 199-204.

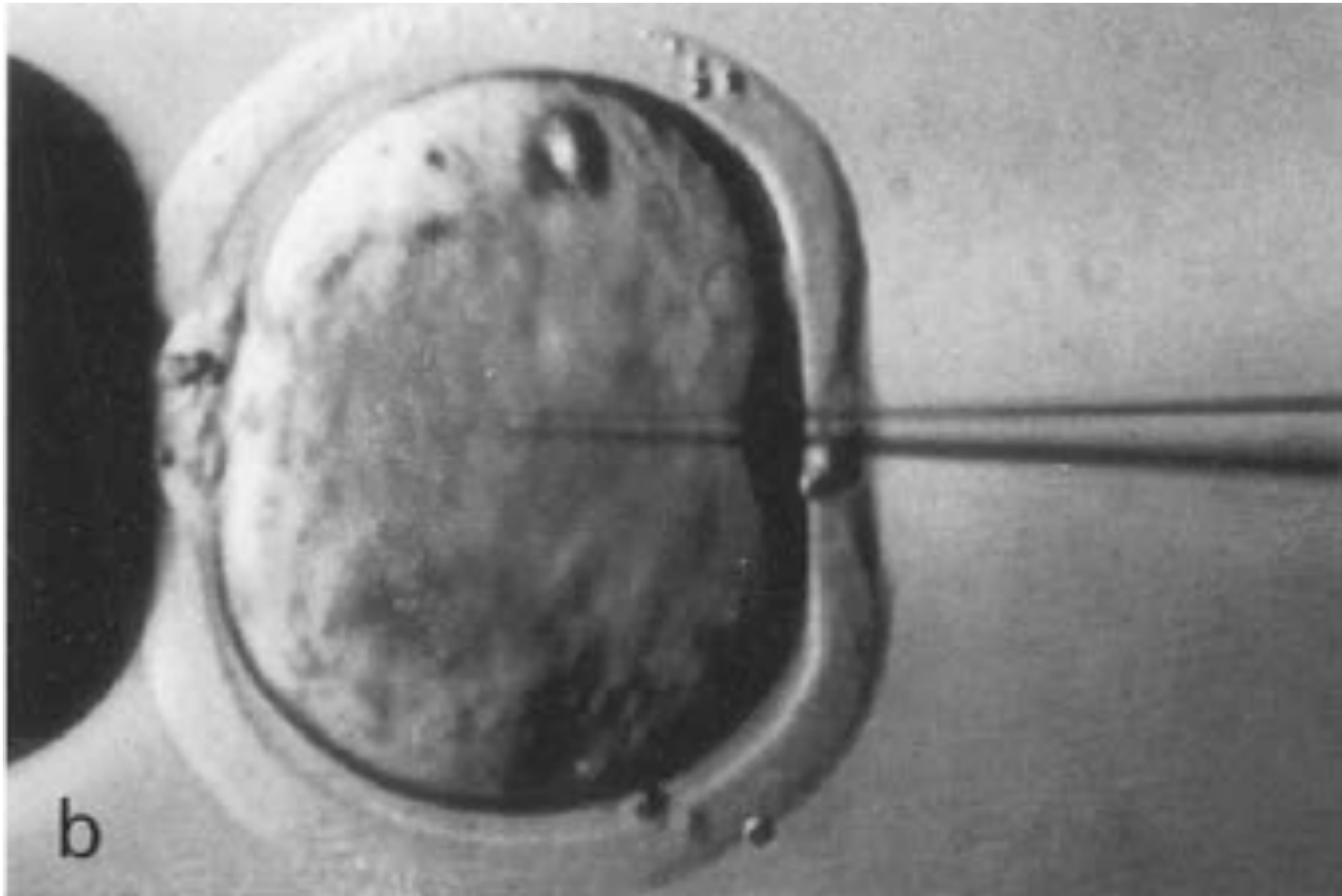
Sergei Evsikov's Evidence

- oil droplets injected beneath the plasma membrane were used as markers of the cortical regions of the zygote's cytoplasm
- 80-90 kHz voltage was applied to the piezoelement using a needle with a piezocrystal pressed to its side, with a 3 μm (micron) swing of the tip

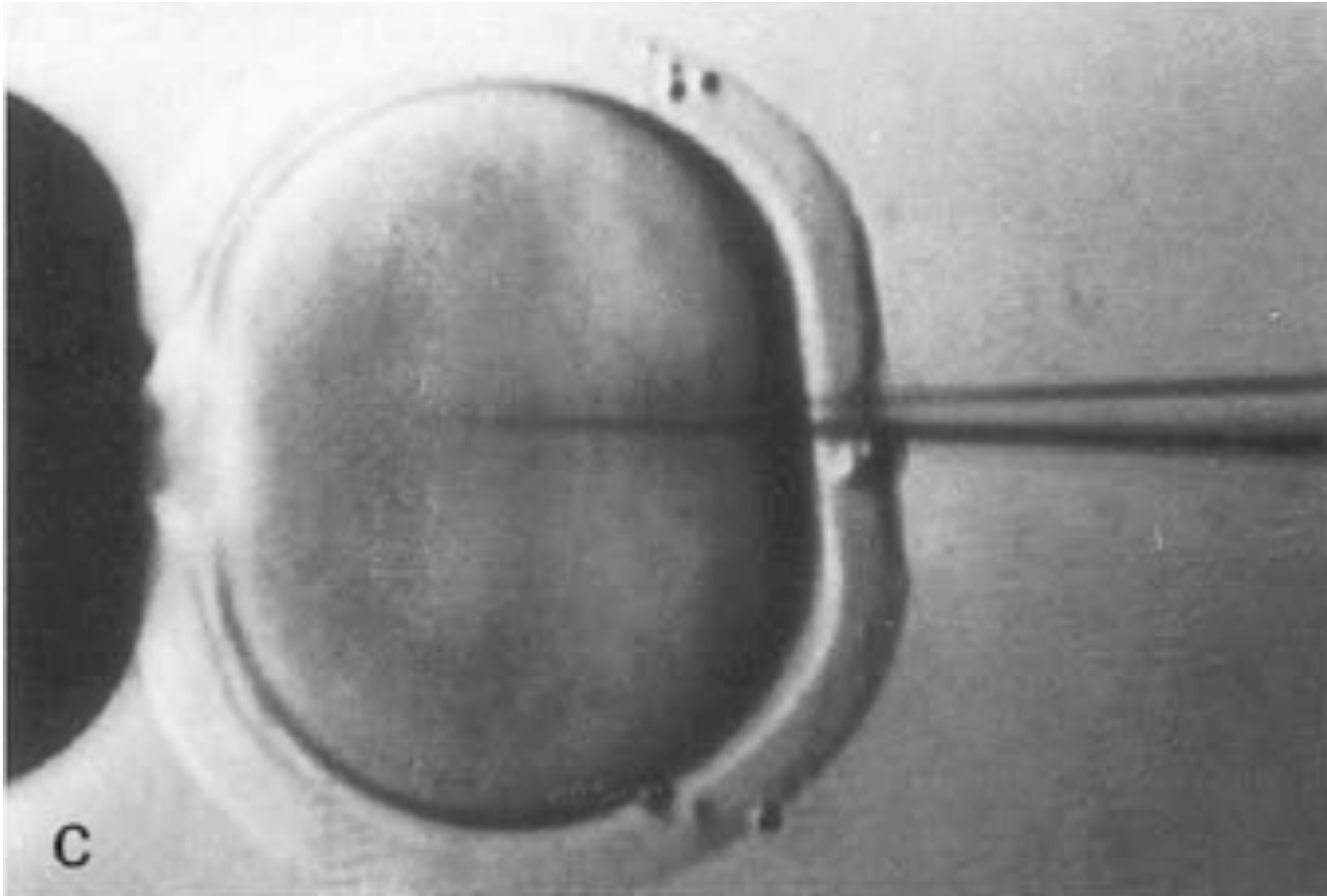
Starting Condition, with oil droplets



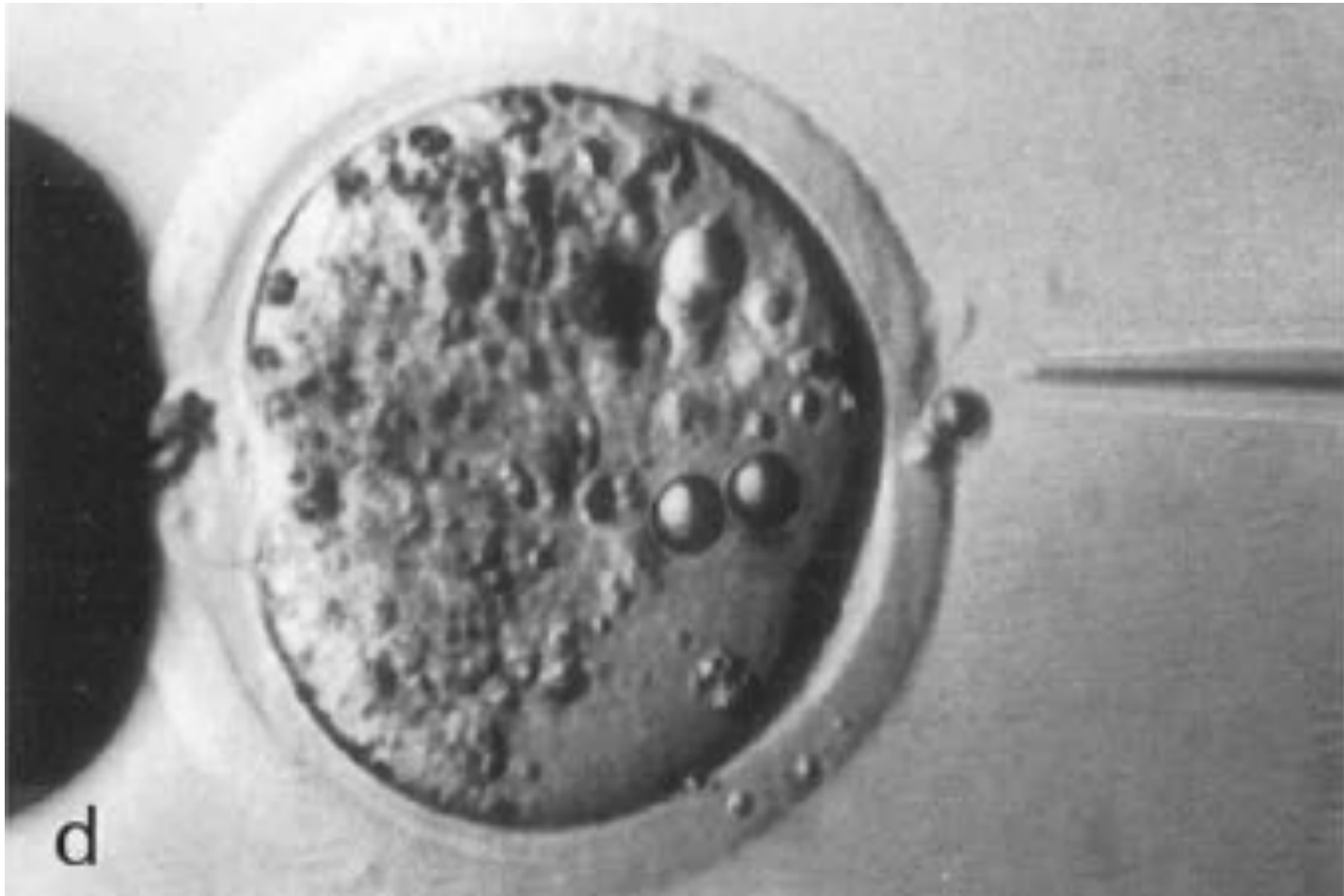
Scrambling



More Scrambling (20 seconds)



Scrambling stopped



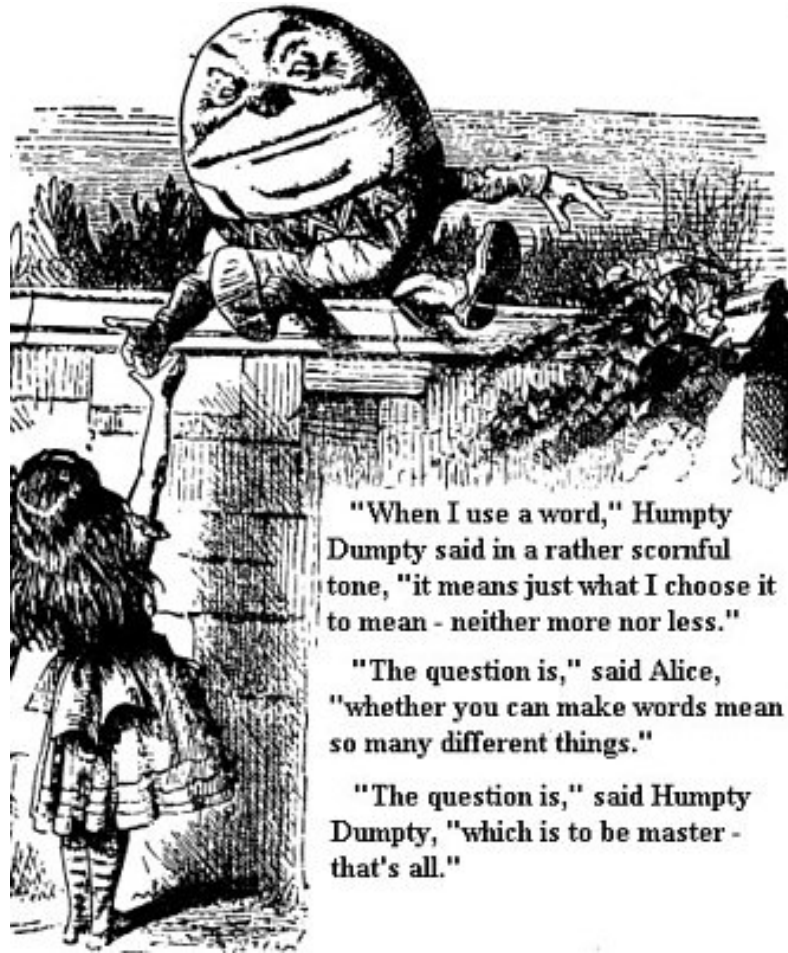
Results of Scrambling

- 119 out of 136 zygotes (88%) developed in vitro to the morula and blastocyst stages
- Twelve embryos, developed after cytoplasm scrambling, were transferred to a pseudopregnant female, and 3 normal, fertile males were born

Continuing December 16, 2009:
Critique of Evsikov's Work
that was presented so far

- Are the scrambled images smooth because of motion blurring during the exposure?
- Did the cytoplasm mostly rotate, rather than actually get stirred?
- What is the scale of scrambling?
- Could the phenomenon of unstirring account for the results?

Humpty Dumpty



"When I use a word," Humpty Dumpty said in a rather scornful tone, "it means just what I choose it to mean - neither more nor less."

"The question is," said Alice, "whether you can make words mean so many different things."

"The question is," said Humpty Dumpty, "which is to be master - that's all."



Humpty Dumpty

Humpty Dumpty sat on a wall.
Humpty Dumpty had a great fall.
All the king's horses and all the king's men
Couldn't put Humpty together again!

Unscrambling, or Putting Humpty Dumpty Together Again

[http://
nurseryrhymes.allinfoabout.com/
humpty-dumpty](http://nurseryrhymes.allinfoabout.com/humpty-dumpty)

Sir Geoffrey Taylor



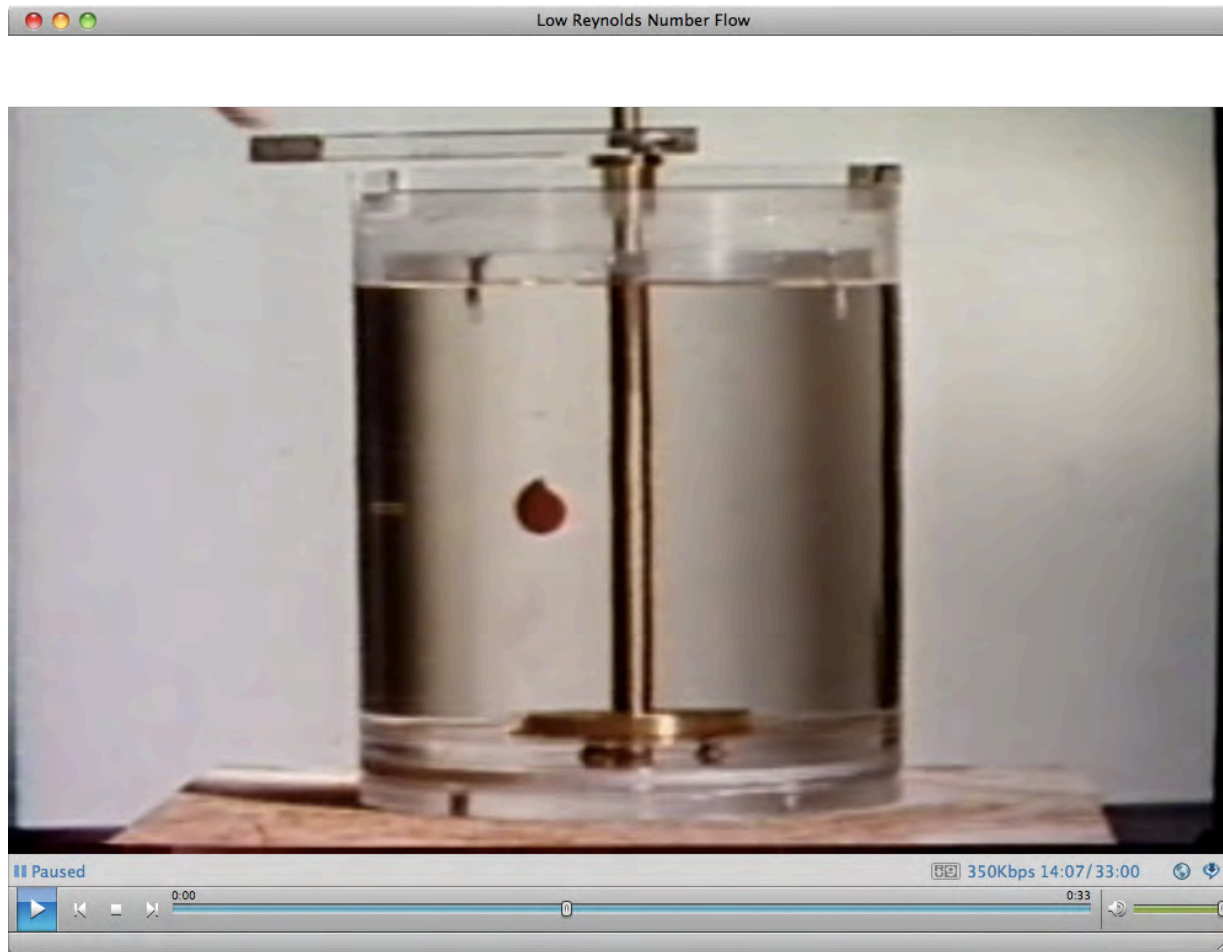
Two concentric cylinders



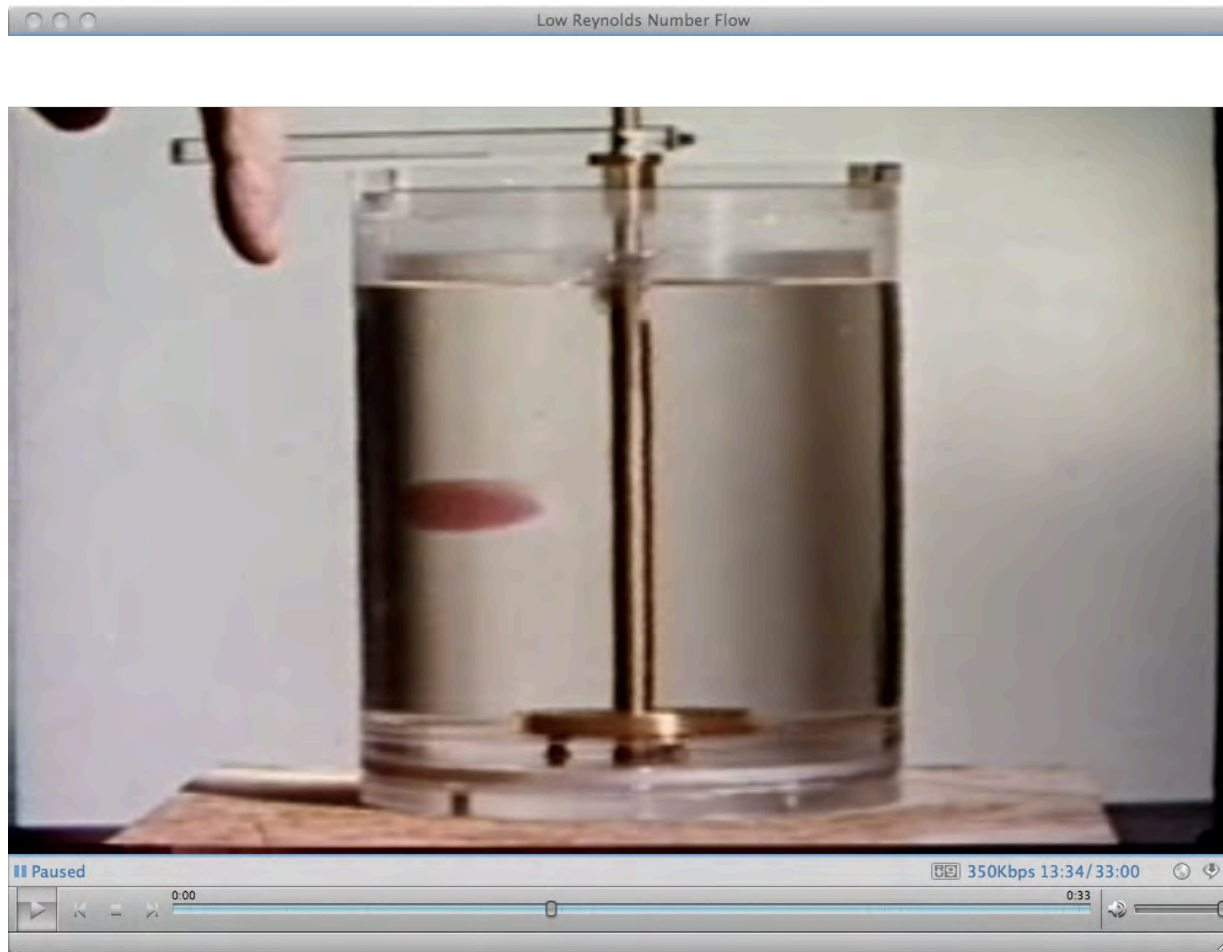
Introducing dye



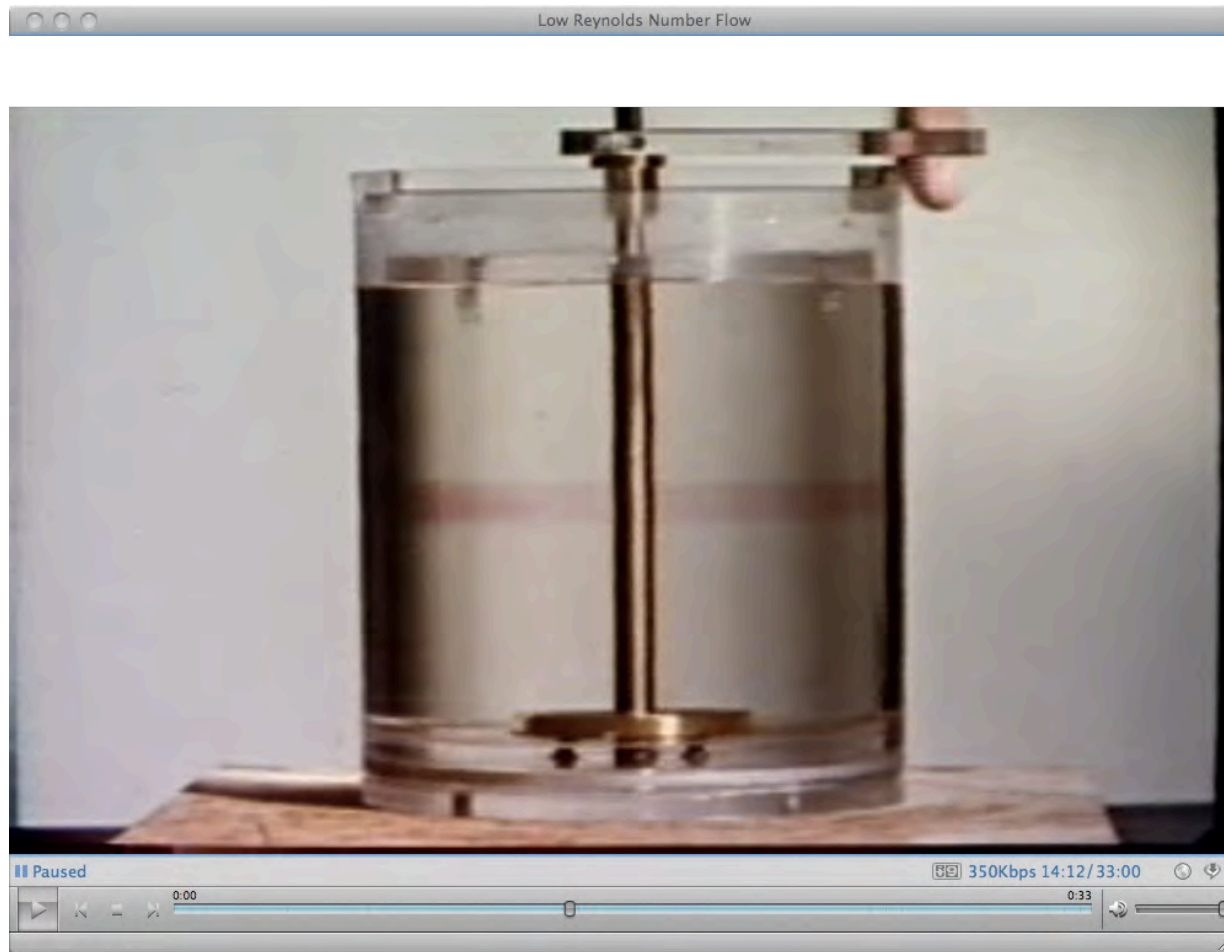
Initial position of blob



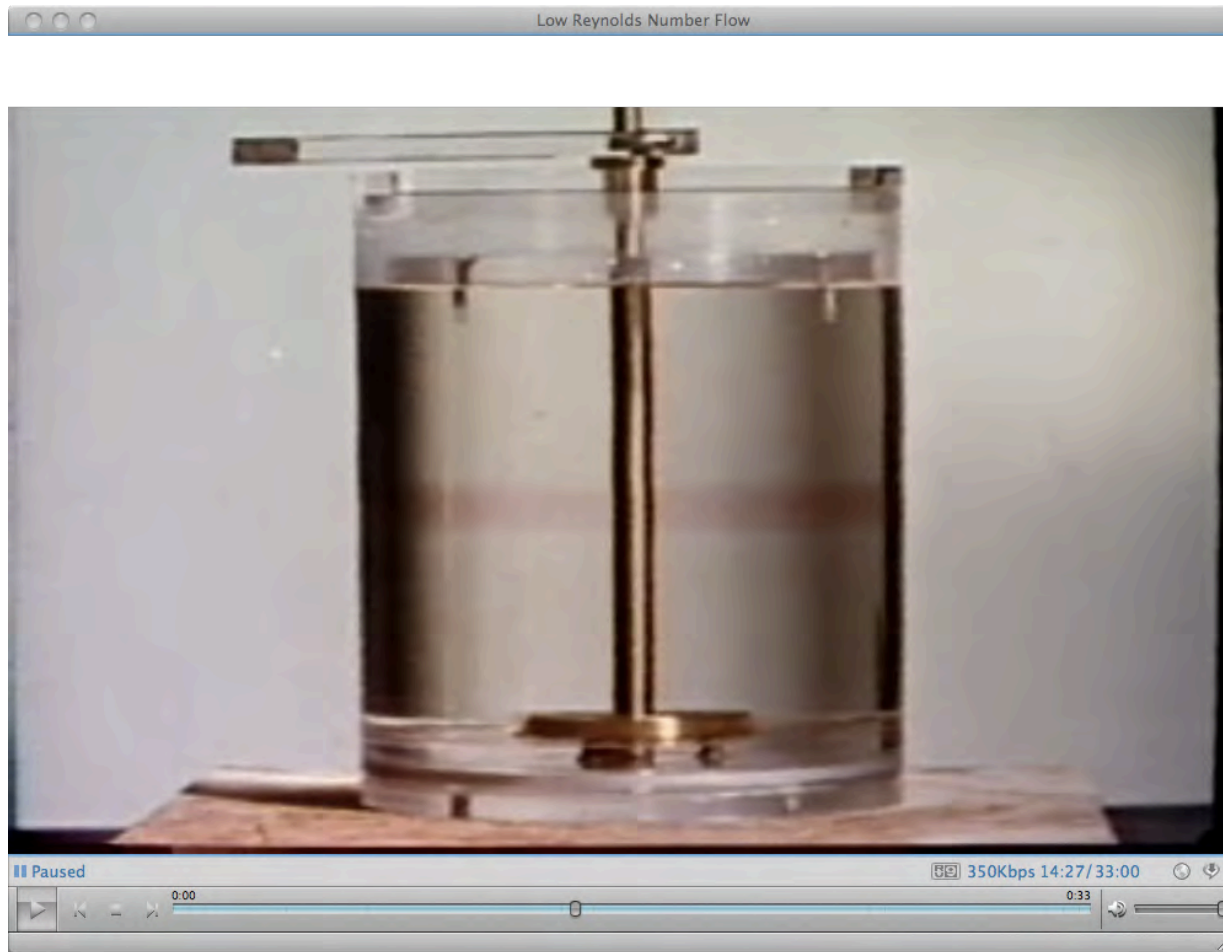
Rotation started



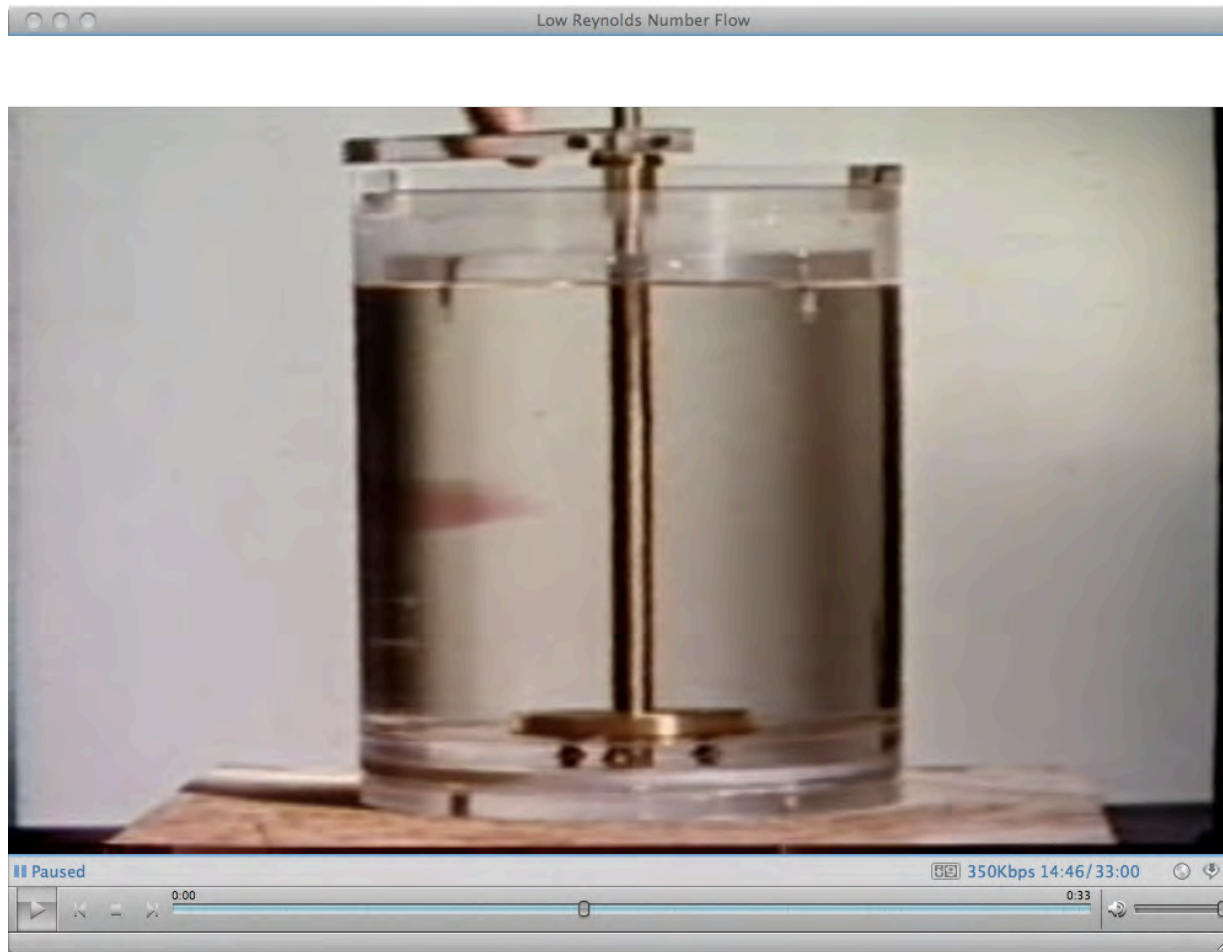
Half turn



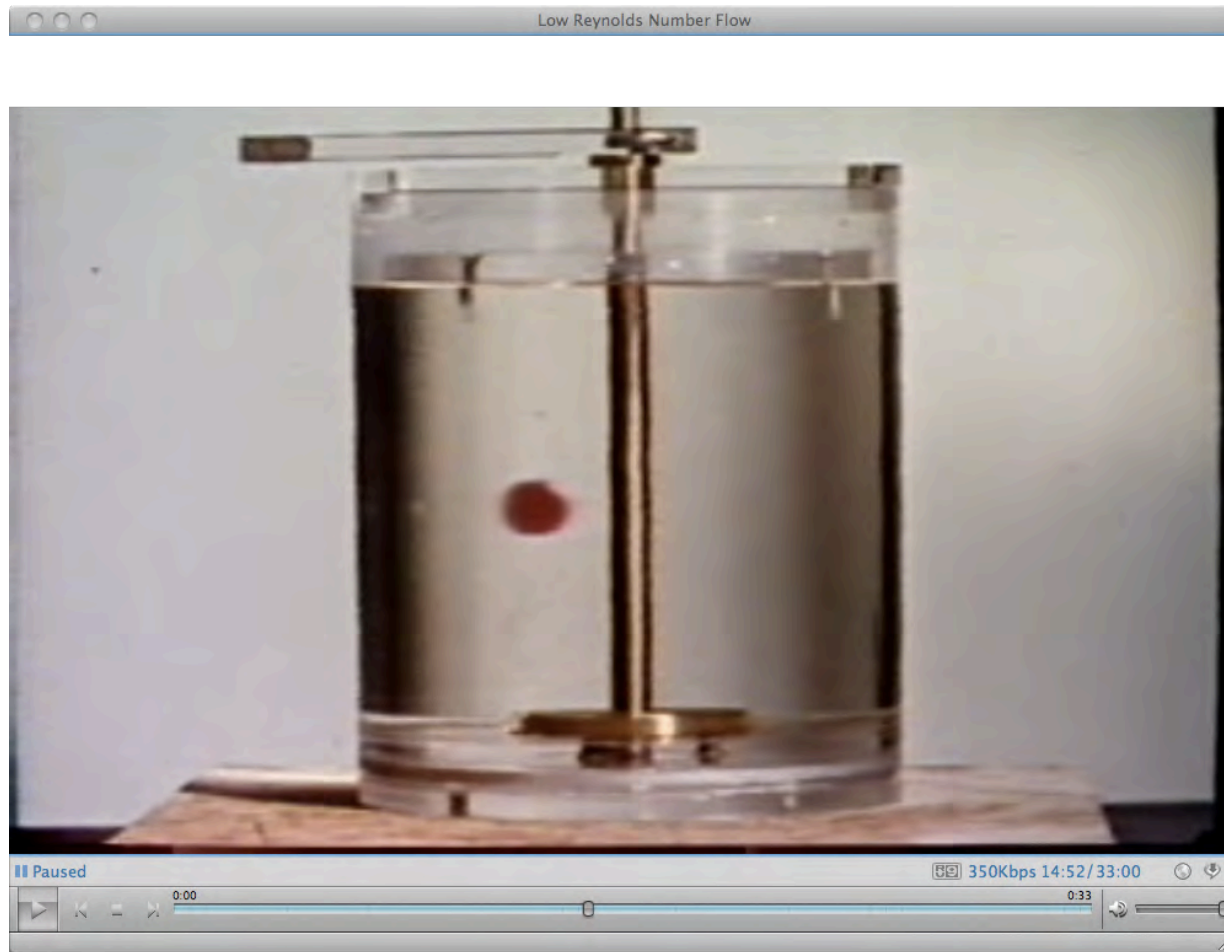
Four turns



Three & half turns back



Turned back, some diffusion



Syrup experiment



Top view



Stretching as turned



Stretched



Turning back



Turned back



$$R \ll 1$$



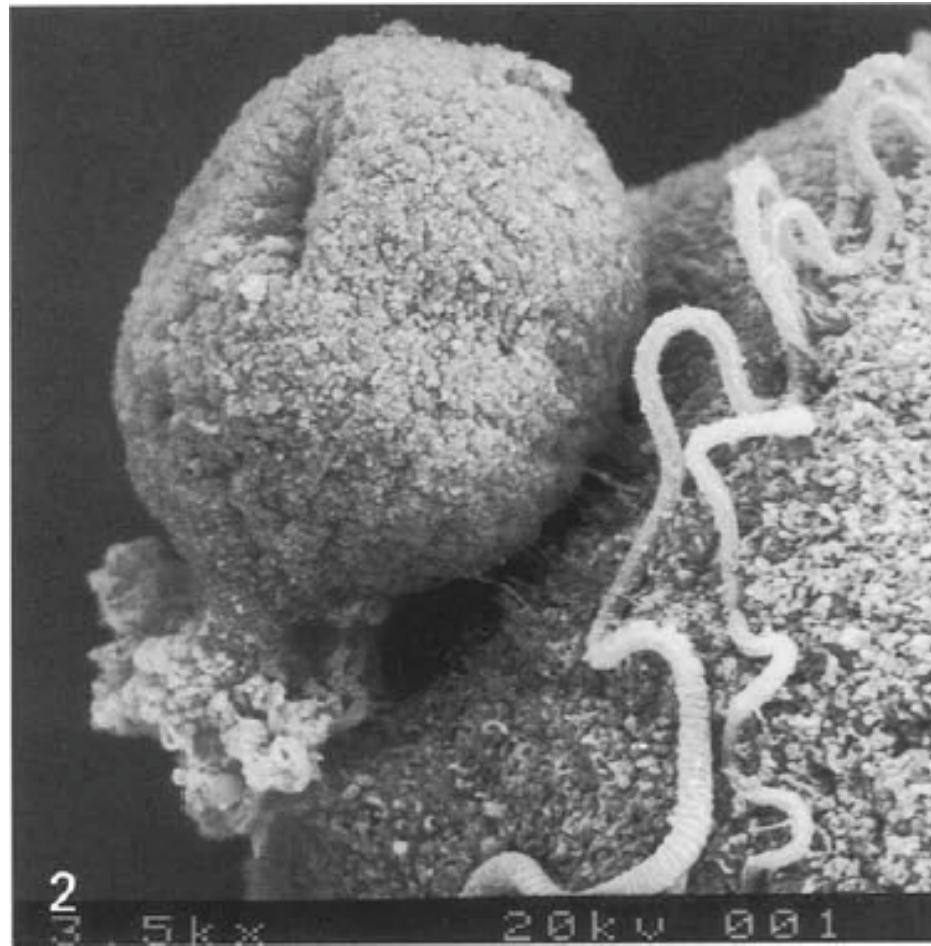
$R \ll 1$ stretched



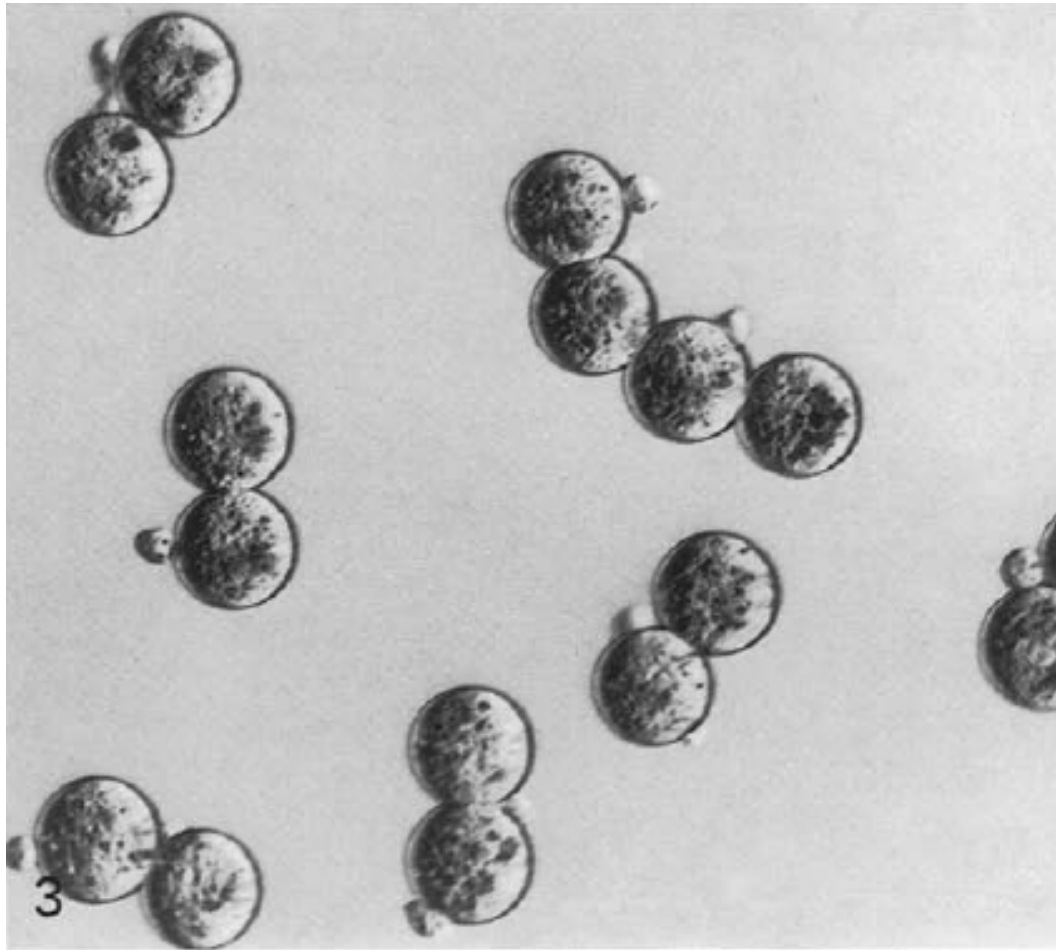
$R \ll 1$ returned



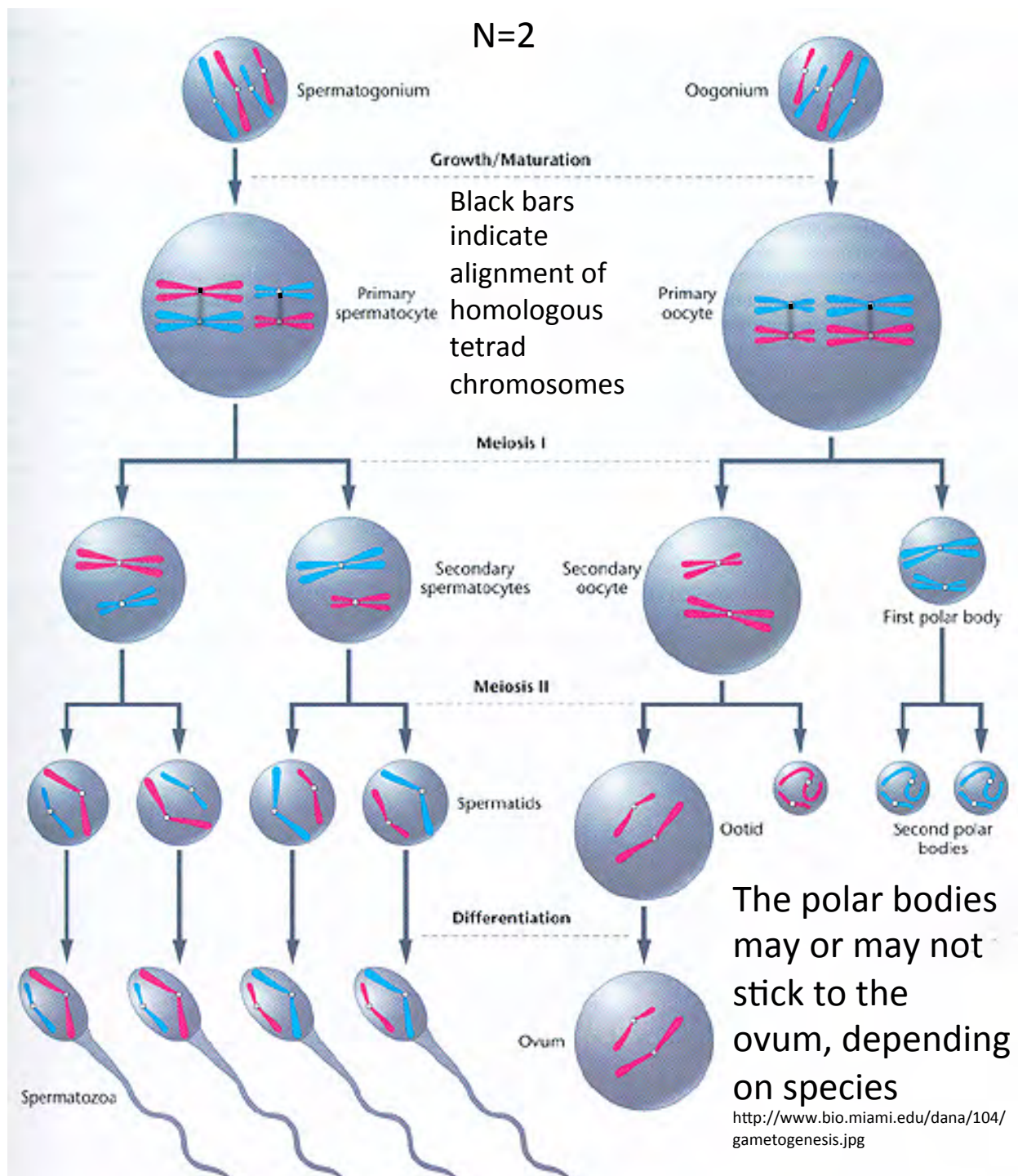
Polar Bodies and Axial Symmetry



Result: 1st Cell Division at Random Angles



Stages for Oogenesis	#centromeres	#copies of DNA = #chromatids	#chromosomes
Oogonium	2N	2N	2N
Maturation:	DNA x2	+Crossing over	+alignment
Primary oocyte	2N	4N	2N
Meiosis I:	Random assortment		
1 st polar body & Secondary Oocyte	N	2N	N
Meiosis II			
2 nd polar bodies & Ootid & Ovum	N	N	N
Zygote	2N	2N	2N



Evsikov's Conclusions

- Position of the second polar body on the surface of the 2-cell embryos demonstrates that the cleavage furrow passes irrespectively of the (presumed) axis of zygote symmetry
- The possibility exists that the subplasmalemmal regions of the cytoplasm have not been disturbed, or that asymmetric distribution of some membrane proteins will play a role in differentiation

Evsikov's Conclusions

- any gradients set during oogenesis or by fertilization have been destroyed by the scrambling procedure
- Normal preimplantation development of scrambled zygotes proves that the first steps of cell differentiation do not involve any factors of autonomous cell specification

Evsikov's Conclusions

- These results present an experimental proof for the idea that the pattern of embryo body is set up exclusively by cell interactions rather than by segregation of cytoplasmic determinants
- the loss of ooplasmic morphogenetic determinants during evolution was initiated in mammals by the transition to intrauterine development

Topics for manuscript on whether or not zygotes are “biologically spherically symmetric”

- Evidence that all eggs are initially spherically symmetric
- ...and contrary opinions
- Volunteers needed to find pros & cons of sphericity in fertilized eggs of:
 - *Xenopus*
 - *Drosophila*
 - Nematode
 - Zebrafish
 - Polyembryonic Wasps
 - *Fucus*