

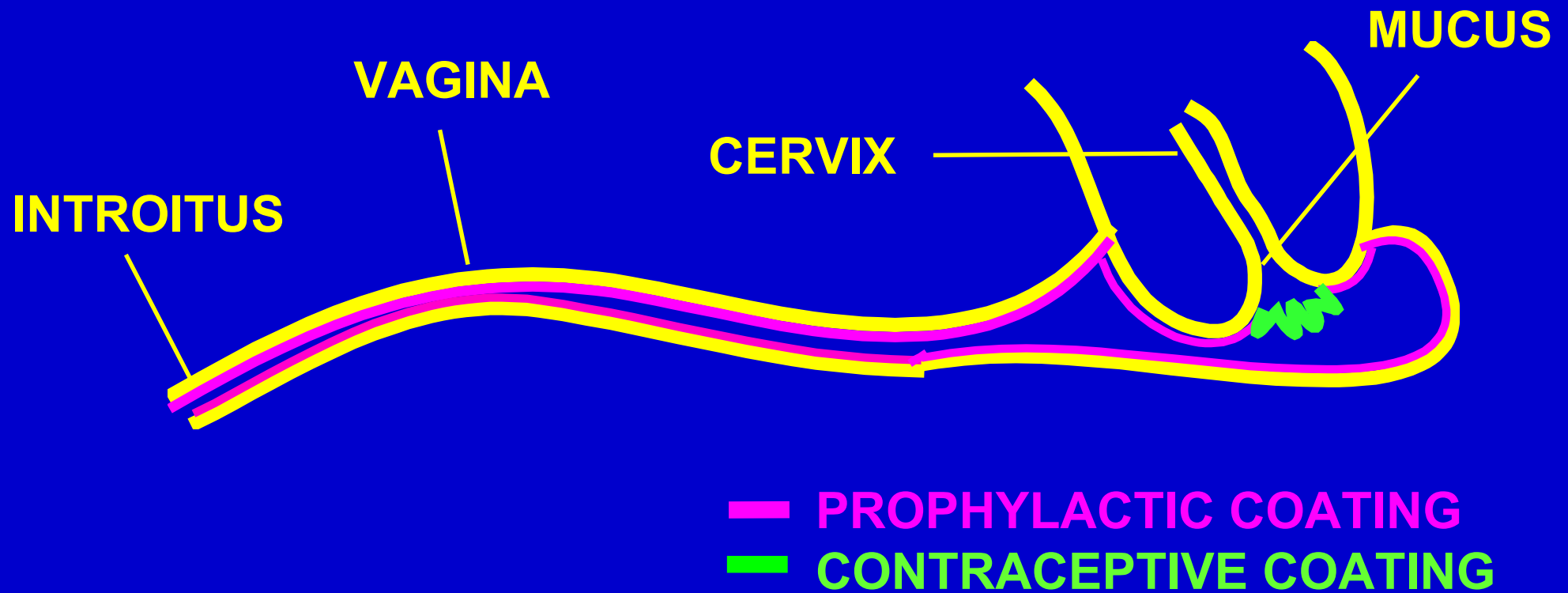
# **Rheological Properties of Microbicidal Formulations Governing Spreading and Retention in the Vagina and Rectum**

**Derek H. Owen<sup>1</sup>, Jennifer J. Peters<sup>1</sup>, Sarah Kieweg<sup>1</sup> (presenting) and David F. Katz<sup>1,2</sup>**

**<sup>1</sup>Department of Biomedical Engineering, Duke University**

**<sup>2</sup>Department of Obstetrics and Gynecology, Duke University**

# Distribution of Intravaginal Formulation



# FORCES ACTING ON BOLUS OF GEL IN VAGINA

## “SQUEEZING”

visceral contractions  
pressure  
tissue elasticity

rugae

mucus,  
transudate

GEL

## “SEEPING”

surface energies  
interfacial tensions

## “SLIDING”

gravity



# Formulation flow and distribution depend upon:

forces on formulation

formulation properties ← rheological, other

vaginal anatomy

vaginal properties

## *What is rheology?*

the study of the flow and deformation  
of materials

# Physiological Environment

Range of *dilutions* with vaginal fluid and semen.

Change in *temperature* upon formulation insertion

Wide range of *shear rates* (application -> coitus)

## ◆ Shear Rates

- squeezing, 0.1-10 s<sup>-1</sup>
- coitus, 100 s<sup>-1</sup>
- seeping, 0.01 s<sup>-1</sup>

## ◆ Dilutions

- gel volume, 1.5 - 5.0 ml, pH low
- semen volume, 1.5 - 5 ml, pH physiologic
- vaginal fluid volume, 0.5 - 1.0 ml, pH low

# STUDY DESIGN

- **Four gels:** 2 *polyacrylic acid (PAA)* derivatives and 2 *carboxymethylcellulose* based.
- **Two diluents:** *vaginal fluid simulant* (pH 4.2), and *semen simulant* (pH 7.7) in 1:1 dilutions.
- **Two temperatures:** 25° C and 37° C.
- Biologically relevant **range of shear rates.**
- Rotational viscometry.

# Gel and Diluent Properties

	<u>Undiluted Gels</u>	<u>pH</u>	<u>Osmolarity</u>
<i>PAA</i>	<b>Advantage-S</b>	4.1	1990
	<b>KY Plus</b>	4.6	1380
<i>cellulose</i>	<b>Gynol II</b>	4.7	920
	<b>Conceptrol</b>	4.7	945

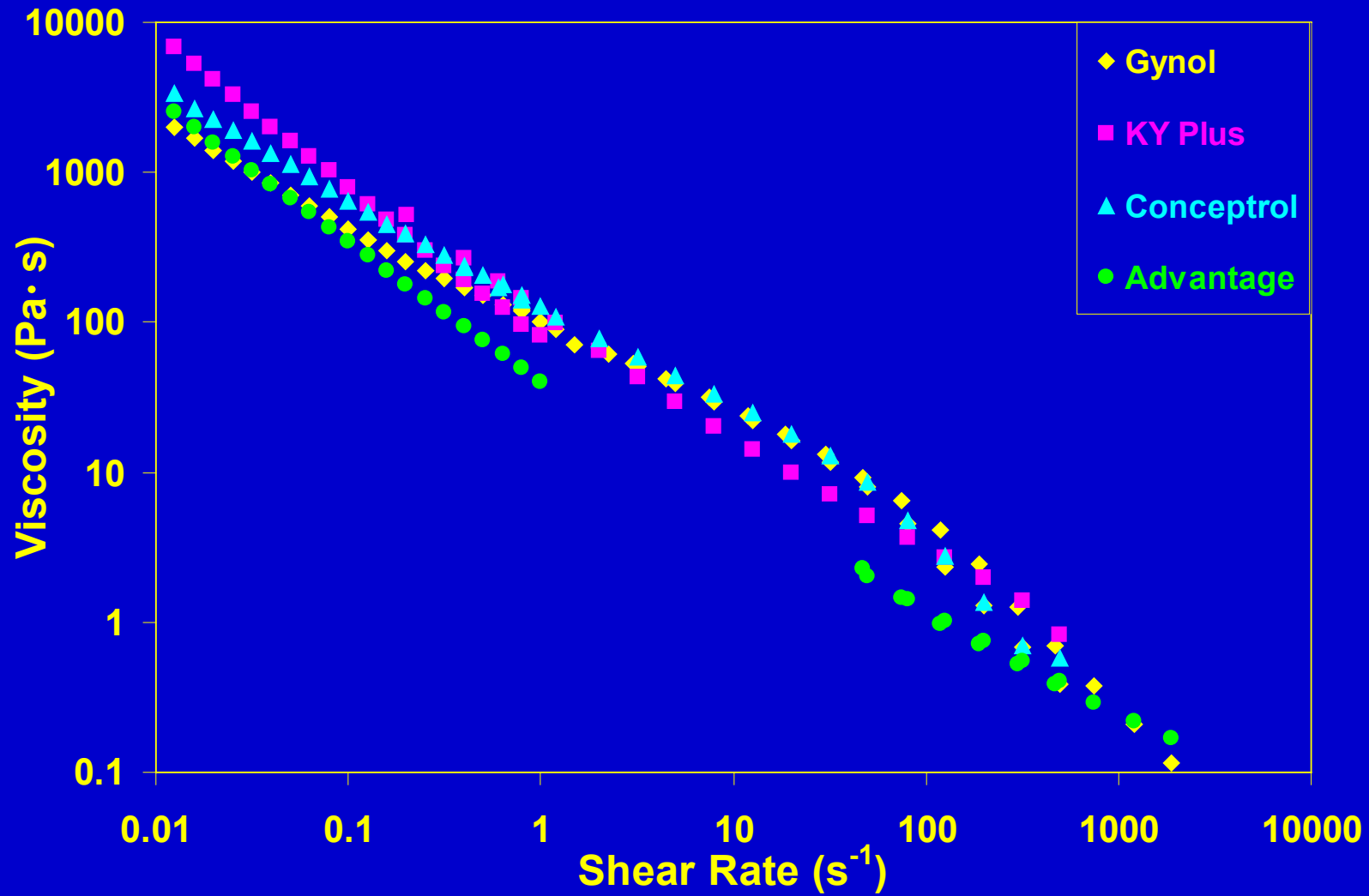
## Diluents

<b><i>Vaginal fluid</i></b> simulant*	4.2	210
<b><i>Semen</i></b> simulant**	7.7	370

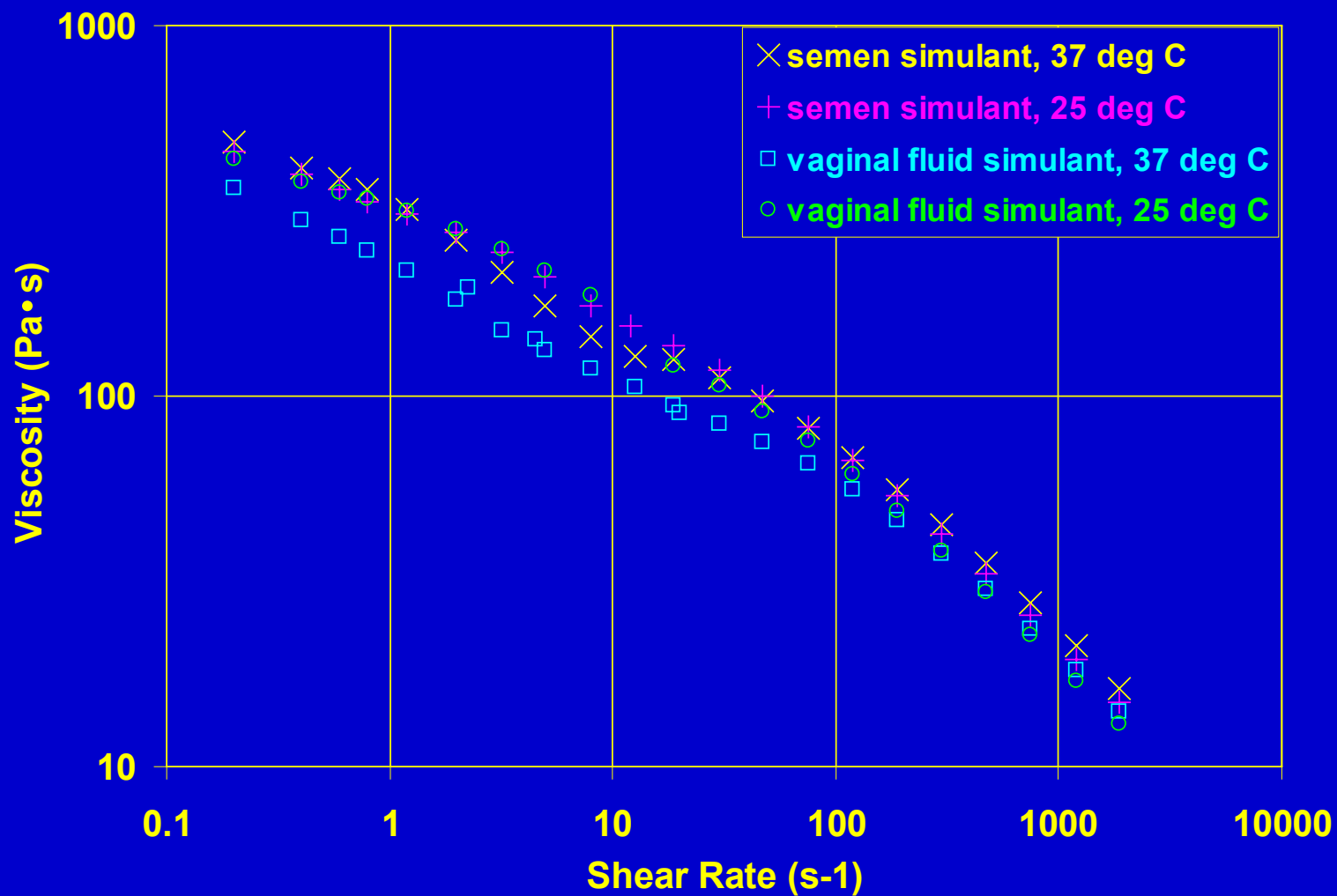
\* Contraception 59: 91 - 96 (1999); citrate buffer

\*\* New; phosphate buffer

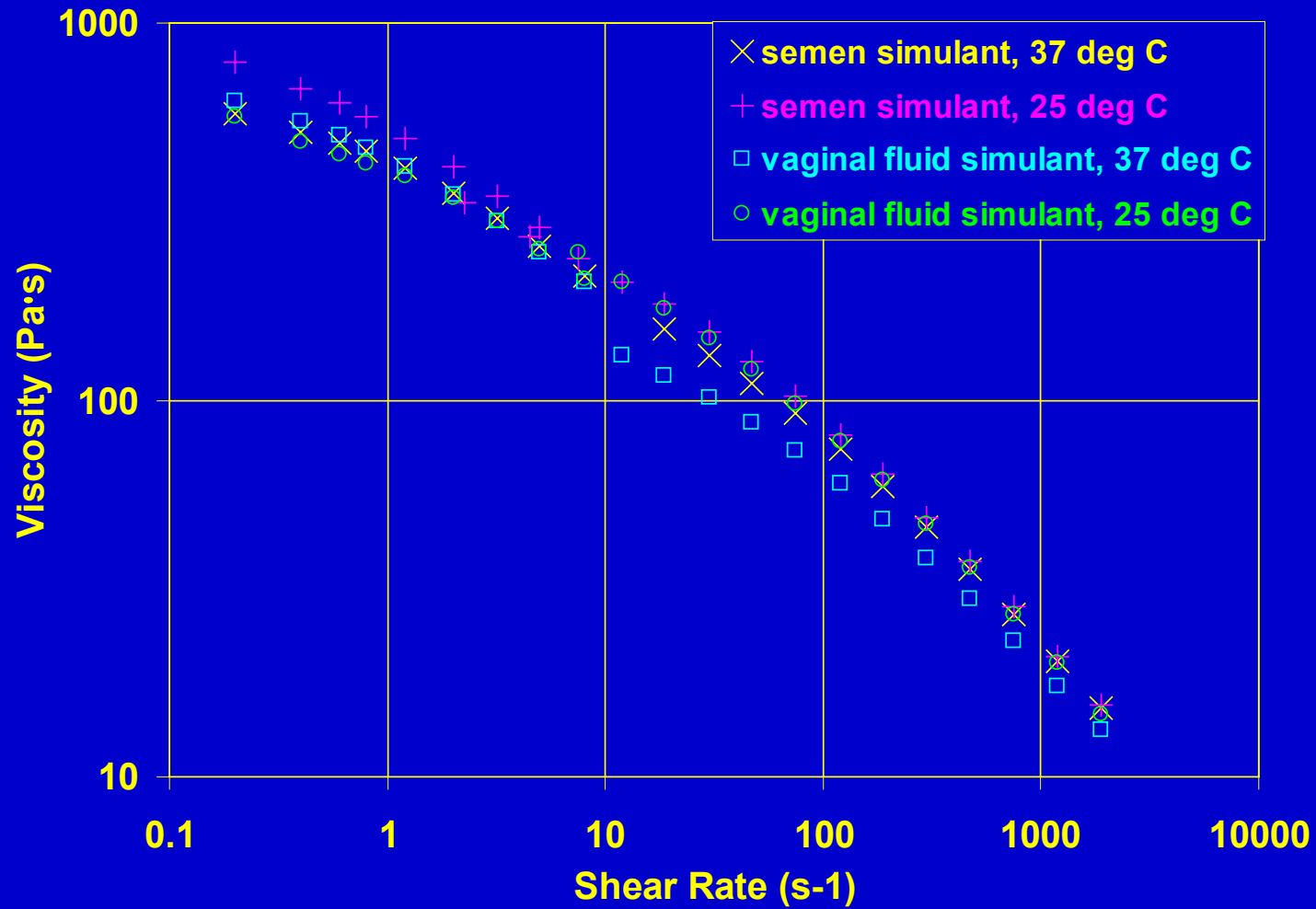
# Viscosity vs. Shear Rate for Undiluted Gels



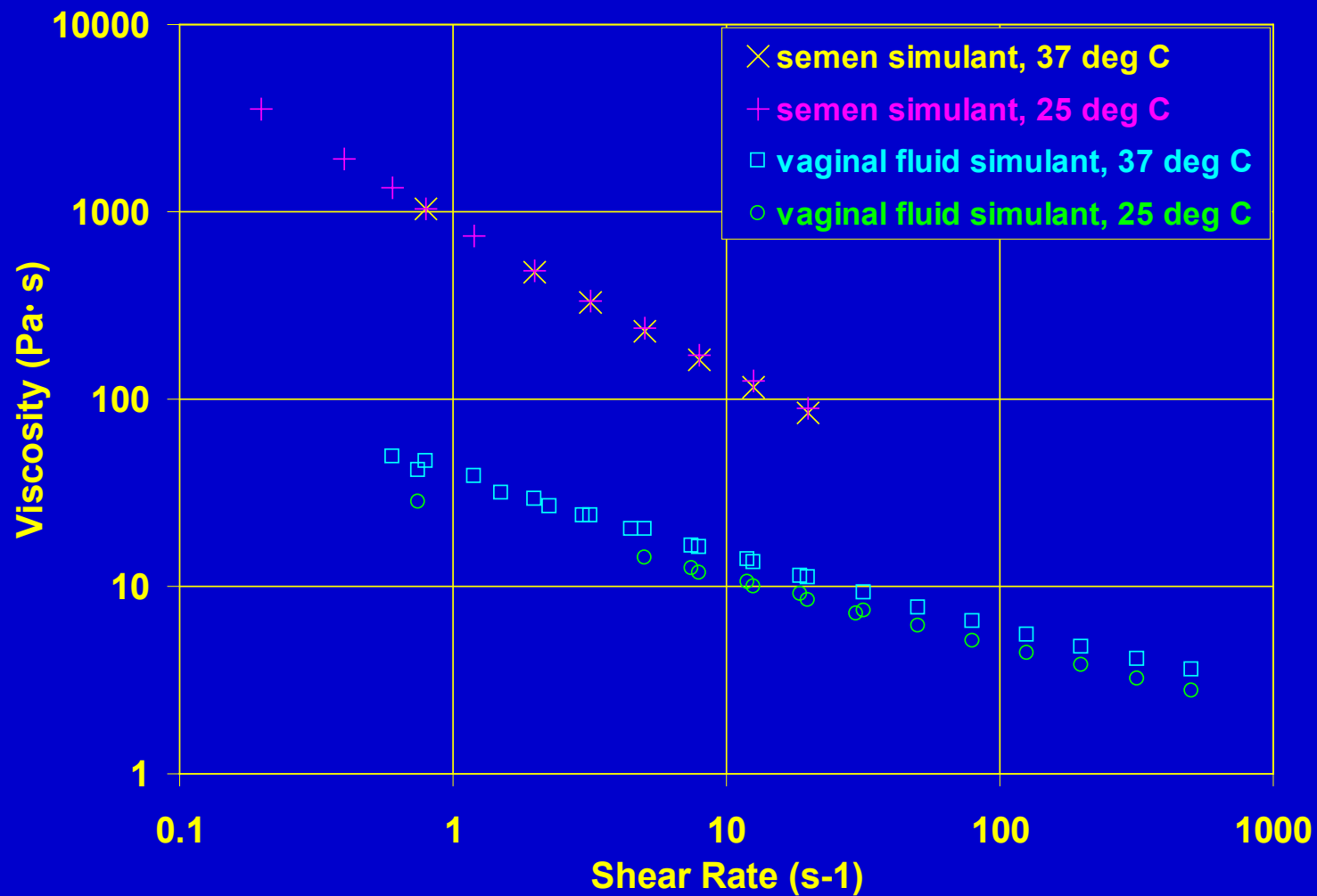
# Viscosity vs. Shear Rate for Diluted Conceptrol



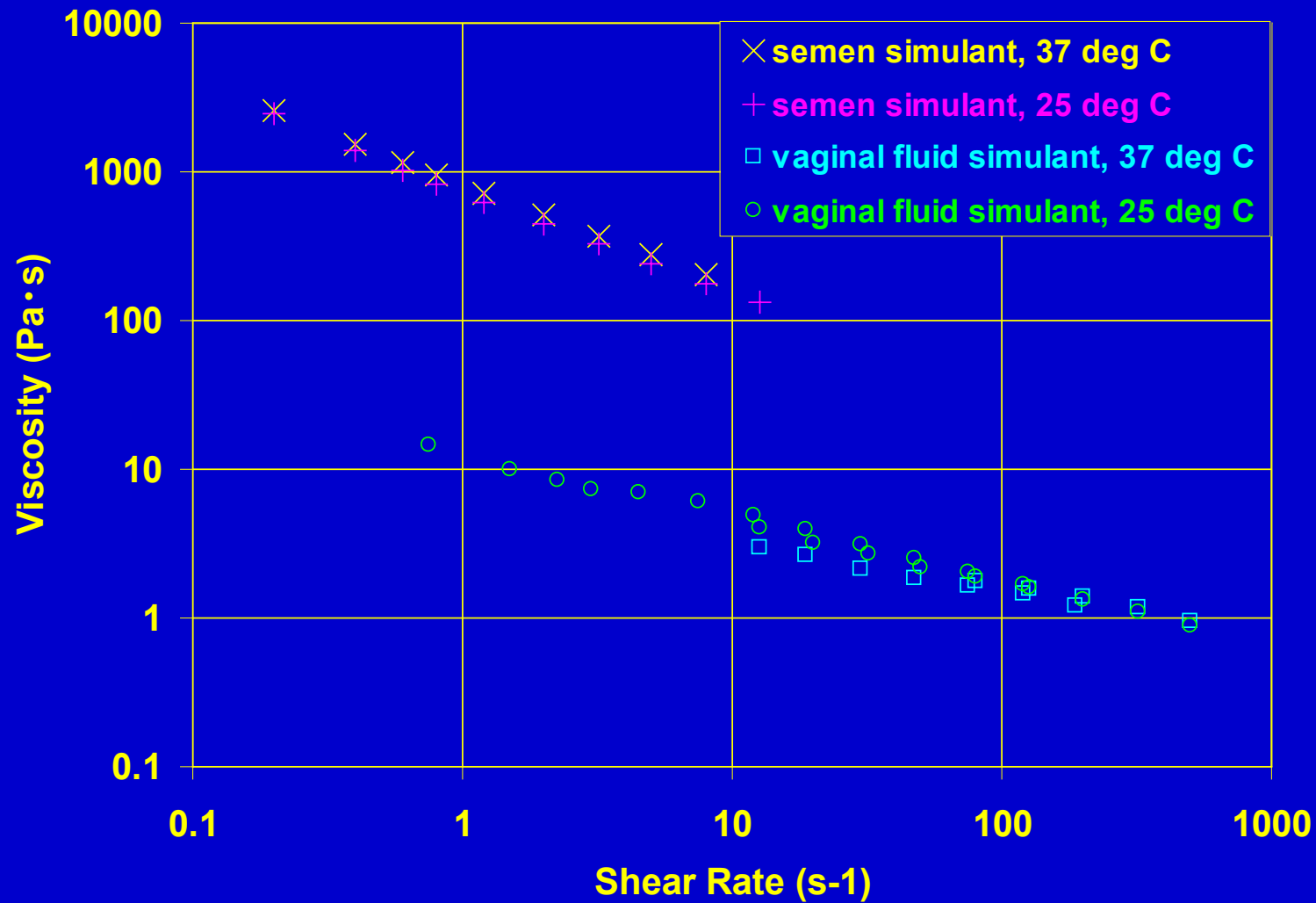
# Viscosity vs. Shear Rate for Diluted Gynol II



# Viscosity vs. Shear Rate for Diluted KY Plus



# Viscosity vs. Shear Rate for Diluted Advantage-S



# Analysis

Viscosity versus shear rate data analyzed to determine significance of temperature and diluent.

- **Analysis of covariance** with log shear rate as covariate.
- **Multivariate non-linear regression** analysis to isolate influence upon viscosity of shear rate, temperature and diluent type.

# Results

- **Temperature effects small.**
- **Dilution reduces viscosity.**
- **Strong effect of diluent type on PAA gels (Advantage, KY Plus) - much greater loss of viscosity due to dilution with vaginal fluid (pH effect).**

# Discussion

- Rheology must be studied under chemical and physical conditions that are biologically relevant.
- Rheological properties change due to interactions with vaginal environment.
- PAA gels different from cellulose gels - different undiluted properties and responses to vaginal environment.
- Rheological data serve as inputs to analyses of specific coating mechanisms (**platform presentation this afternoon**).

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