Physical Pharmacy M02 (BP403T)

Objectives of the course

Understand various physicochemical properties of drug molecules in the designing the dosage forms

Learning outcomes

1) Students learnt about the behavior of liquid and solid their deformation flow of liquids, determination of viscosity of liquids by various viscometers.

2) Students learnt about the knowledge about terms thixotropy, antithixotropy in various substances which follow non Newtonian systems

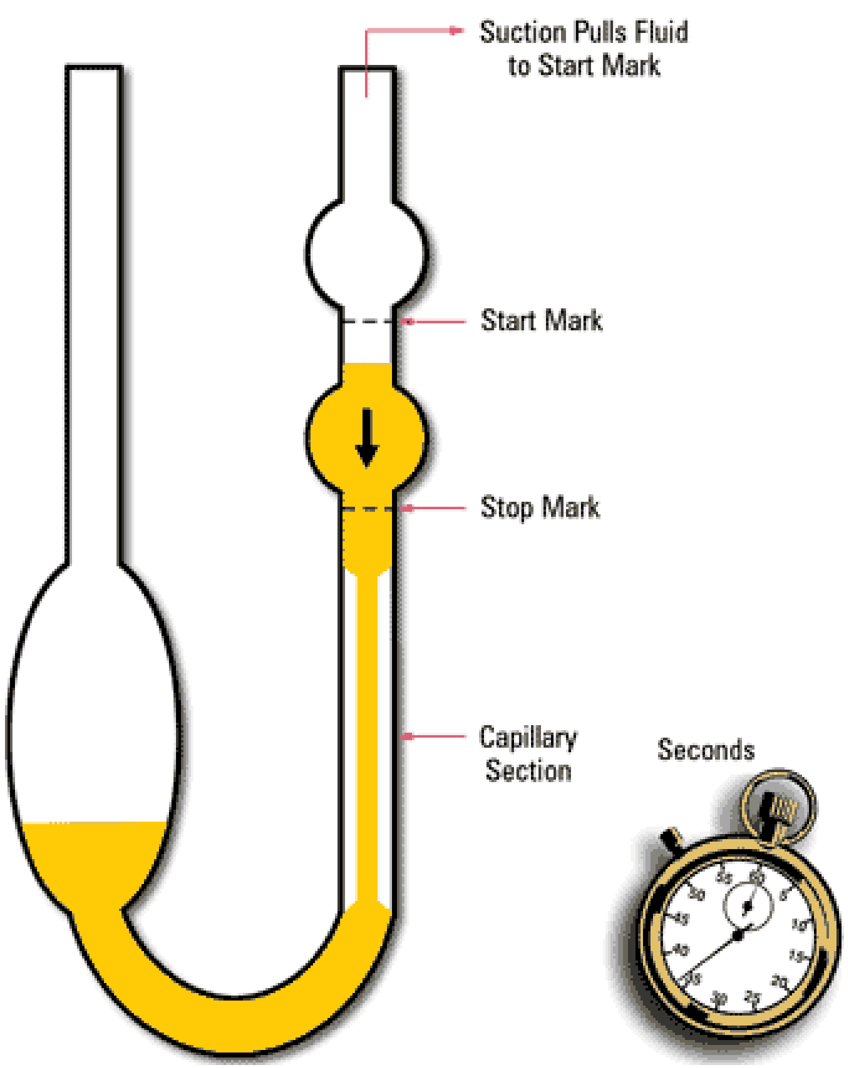
Structure of Module -2 Learning Material

Rheology

- Newtonian systems, law of flow, kinematic viscosity, effect of temperature
- Non- Newtonian systems, pseudoplastic, dilatant, plastic
- Thixotropy, thixotropy in formulation,
- Determination of viscosity, capillary, falling Sphere, rotational viscometers.

Deformation of Solids

- Plastic and elastic deformation
- Heckel equation, Stress, Strain
- Elastic Modulus.


Suction Pulls Fluid
to Start Mark
Start Mark
Stop Mark
Capillary
Section
Seconds

RHEOLOGY

Content

- Introduction to Rheology
- Newtonian Flow
- NonNewtonian Flow
  - Plastic(Bingham Bodies)
  - Pseudoplastic
  - Dialatant
- Thixotrophy/ Antithixotrophy
- Measurement of Viscosity

Viscous Fluid

Viscosity

Viscosity η is the resistance of liquid to flow under stress

Types

- Absolute (Dynamic) Viscosity
- Kinematic Viscosity

Viscosity

- Viscosity is the measure of the internal friction of a fluid.
- This friction becomes apparent when a layer of fluid is made to move in relation to another layer.
- The greater the friction, the greater the amount of force required to cause this movement, which is called sheer.
- Shearing occurs whenever the fluid is physically moved or distributed, as in pouring, spreading, spraying, mixing, etc.
- Highly viscous fluids, therefore, require more force to move than less viscous materials.

RHEOLOGY

- Science describing the flow and deformation of matter under stress.
- Rheo = the flow

Importance of Rheology

- Formulation of medicinal preparations
- Fluidity (syringebility) of solutions for injection.
- Mixing
- Packaging into containers,
- Their removal prior to use, whether by pouring from a bottle, extrusion from a tube
- Patient acceptability (compliance),
- Physical stability, and even bio-availability.

RHEOLOGY

- Rheology describes the deformation of a body under the influence of stresses.
- Ideal fluids such as liquids and gases deform irreversibly -- they flow
- Ideal solids deform elastically.
- The energy required for the deformation is fully recovered when the stresses are removed.

Block of material subjected to shear stresses

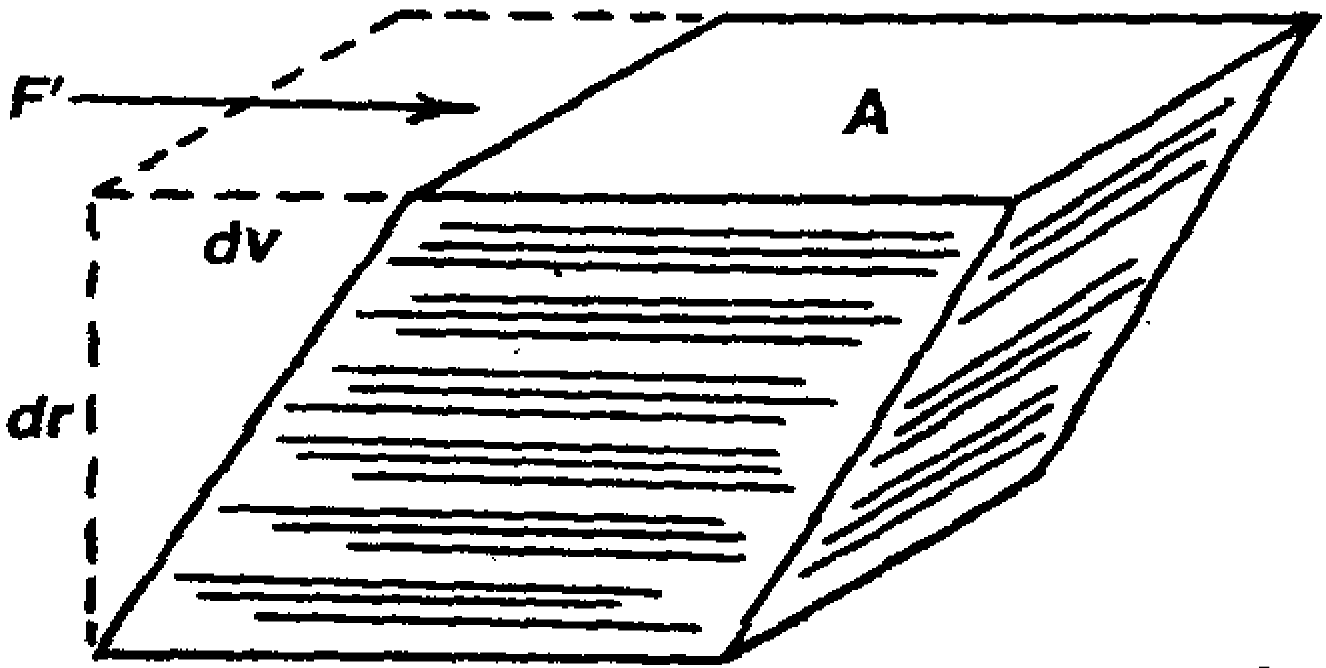


Fig. 1

Terminologies

- *Shear: is the movement of material relative to parallel layer.*
- *Shear stress (F) is the force applied per unit* Area to make liquid flow (Force/Area)
- *Shear rate (G) difference in velocity dv,* between two planes of liquids separated by distance dr (i.e. dv/dr)

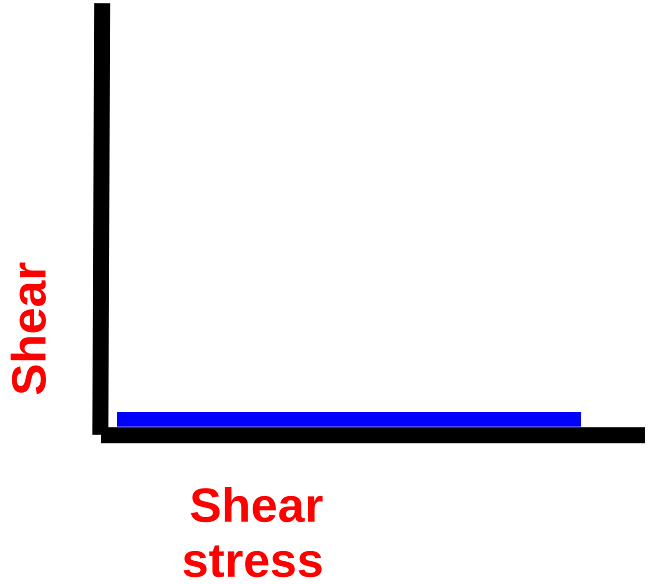
$$G = \frac{dv}{dr}$$

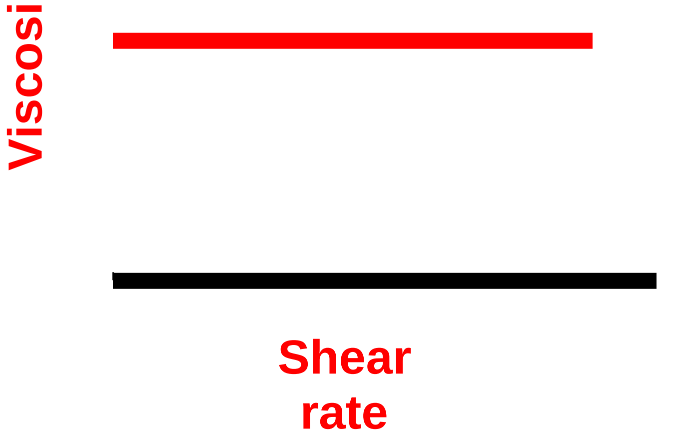
Newton’s law offlow

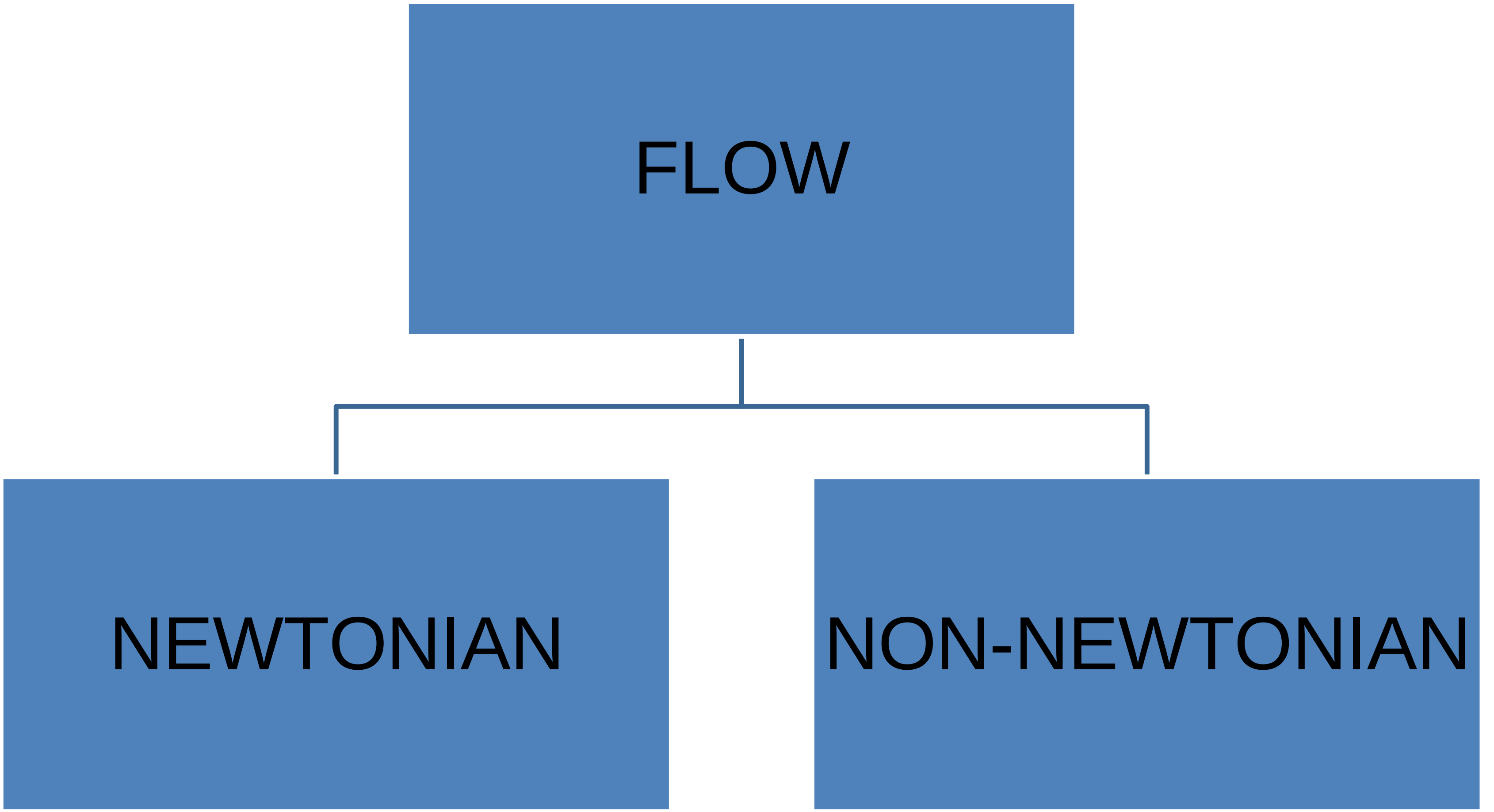
- Rate of shear is directly proportional to shear stress.
- In other words, twice the force would move the fluid twice as fast.

Example- Castor oil

Newtonian






FLOW
NEWTONIAN
NON-NEWTONIAN

Newton's law offlow

- Isaac Newton was the first to express the basic law of viscometry describing the flow behavior of an ideal liquid:

$$F = \eta \times G$$

shear stress = viscosity × shear rate

Absolute (dynamic) viscosity

$$Viscosity(\eta) = \frac{F}{G}$$

- The fundamental unit of viscosity measurement is the *poise*.
- *Shear force required to produce a velocity of 1 cm/sec between two parallel planes of liquid each 1cm^2 in area and separated by 1cm*

- Fluidity; it is the reciprocal of viscosity Ø = 1/

η

its unit *is* inverse poise.

Kinematic Viscosity

It is the absolute viscosity divided by the density of liquid at a specified temperature

$$Kinematic\ Viscosity = \frac{\eta}{\rho}$$

Where ρ is the density of the liquid The unit is Stock (s) or centistock (cs)

Temperature Dependence

When temperature increases viscositydecreases

$$\eta = Ae^{E_v/RT}$$

$\boldsymbol{E_v}$	Is Activation energy to initiate flow between molecules
A	Constant Depending on mol. Wt. and molar volume of

NON-NEWTONIAN SYSTEMS

- A non-Newtonian fluids are those fluids for which the relationship between F and G is not a constant for there flow.
- The viscosity of such fluids will therefore change as the shear rate is varied.
- Examples; colloids, emulsions, liquid suspensions and ointments.

NON-NEWTONIAN SYSTEMS

THREE CLASSES:

– Dilatant flow

– Pseudoplastic flow

– Plastic flow

Rheogram

Rheogram is a plot of shear rate,G, as a function of shear stress, F

Rheogram is also known as consistency curve of flow curve.

Rheograms

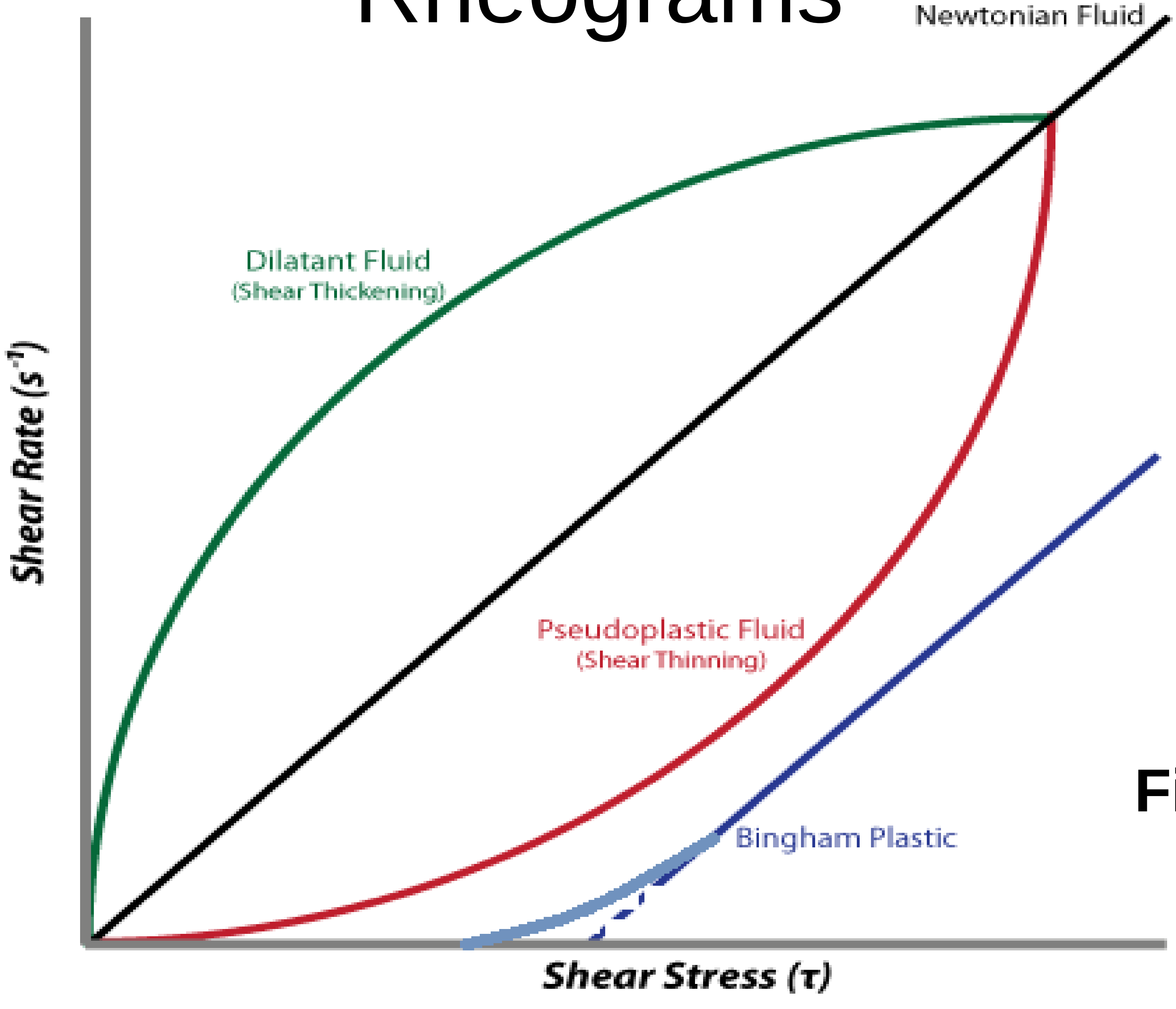
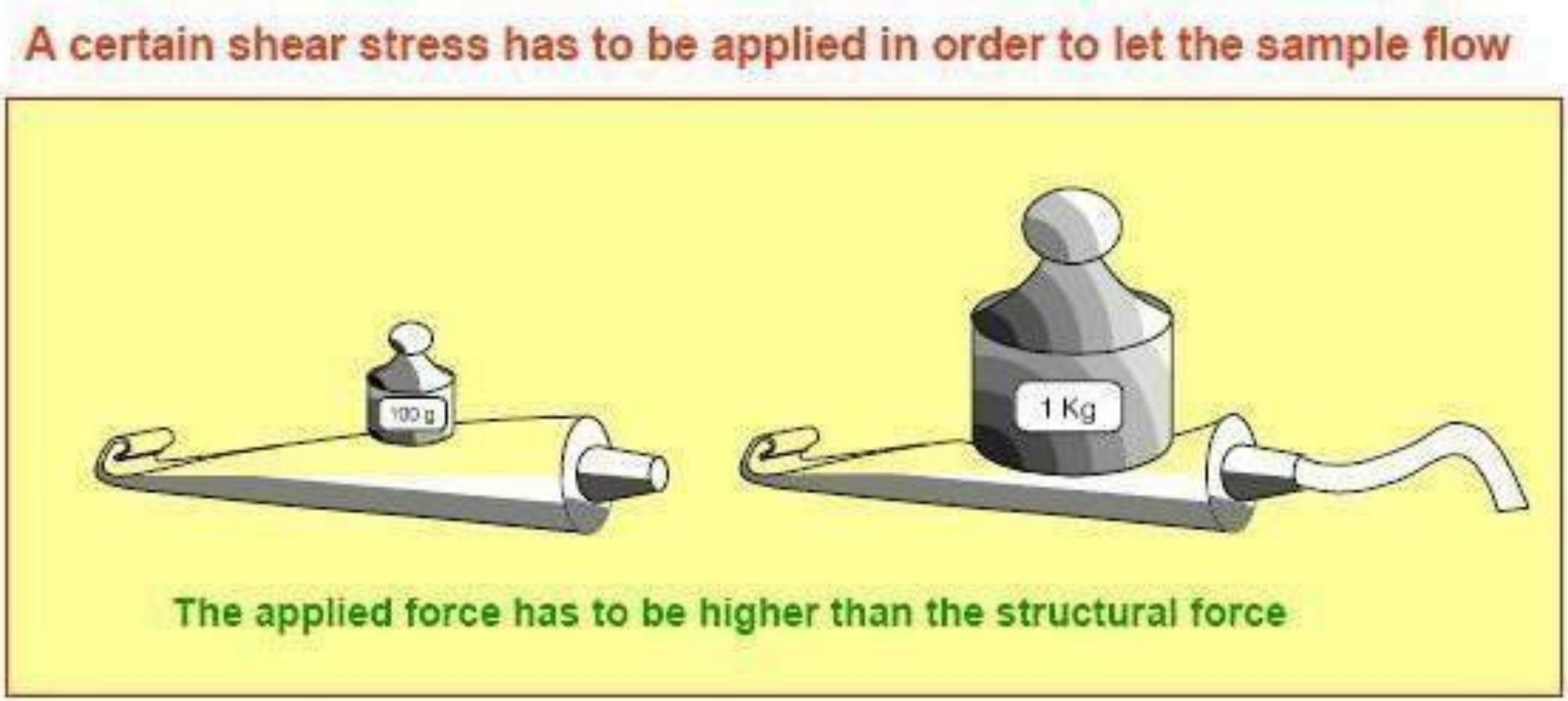


Fig. 2

PLASTIC FLOW

- Associated with flocculated particles or concentrated suspension.
- A Bingham body does not begin to flow until a shearing stress corresponding to the yield value is exceeded.
- Yield value (f); is an indication of the force that must be applied to a system to convert it to a Newtonian System.
- Examples; suspension of ZnO in mineral oil, certain paints, ointments

Plastic flow Contd…



Plastic Flow

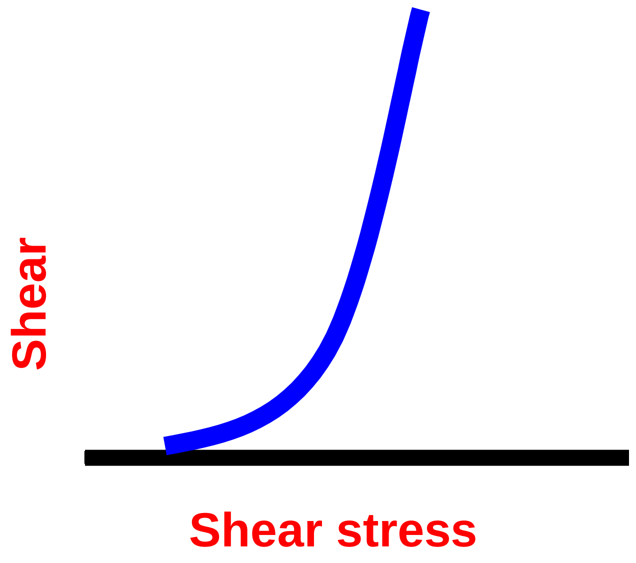


Fig. 3

Contd….

- The slope of the rheogram is termed *Mobility, analogous to fluidity in Newtonian* system, and its reciprocal is known as

  Plastic viscosity, U

$$U = \frac{\mathrm{F} - \mathrm{f}}{G}$$

- *Where f is the yield value*

Pseudoplastic Flow (shear-thinning)

- The curve begins at the origin (or approach it) and there is no yield value.
- Occurs in for polymers in solution (e.g. syenthetic or natural gum, cellulose derivatives)
- As the shearing molecules orient themselves to the direction of flow.
- This orientation reduces internal friction and

Pseudoplastic Flow Behaviour

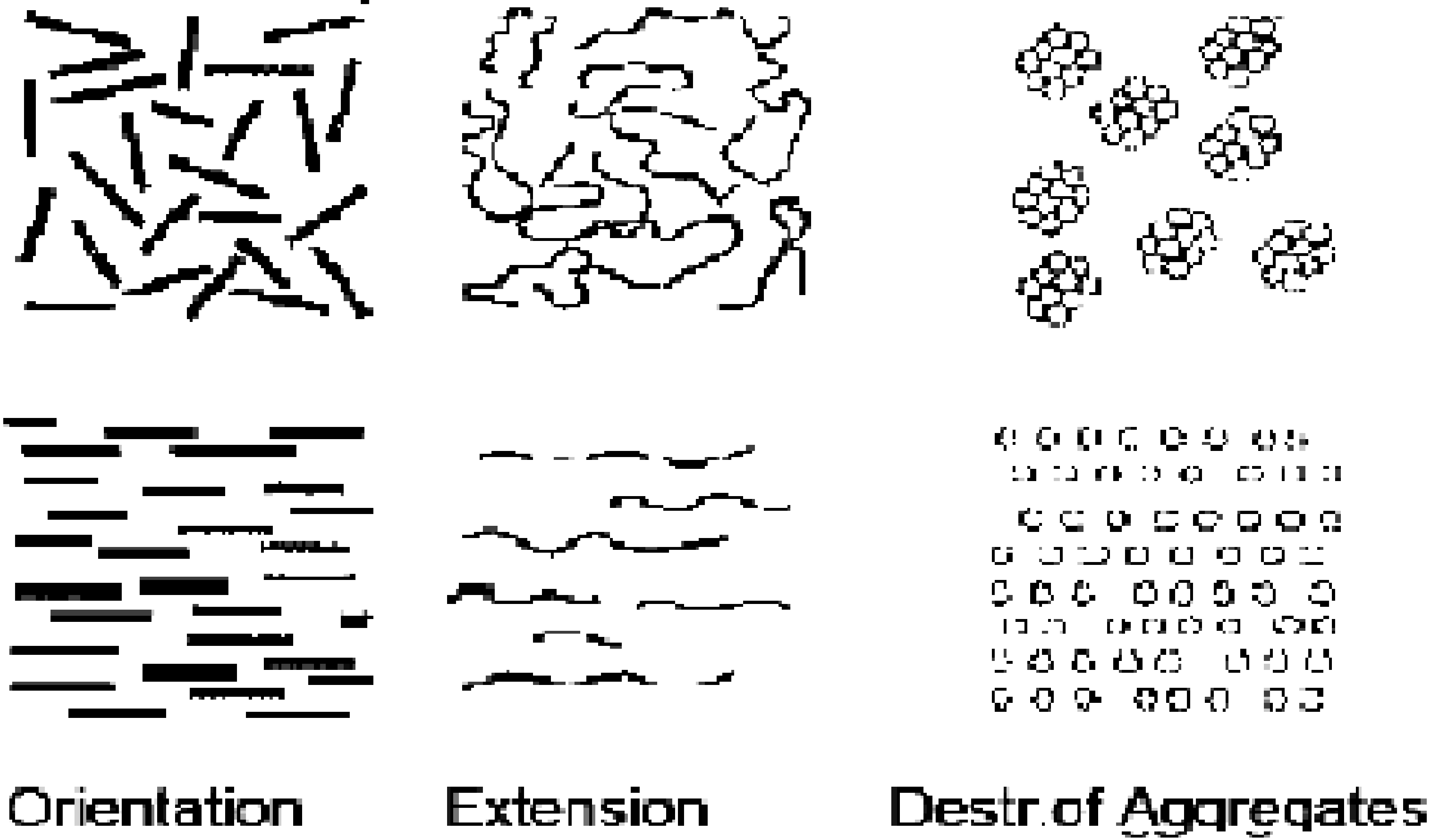
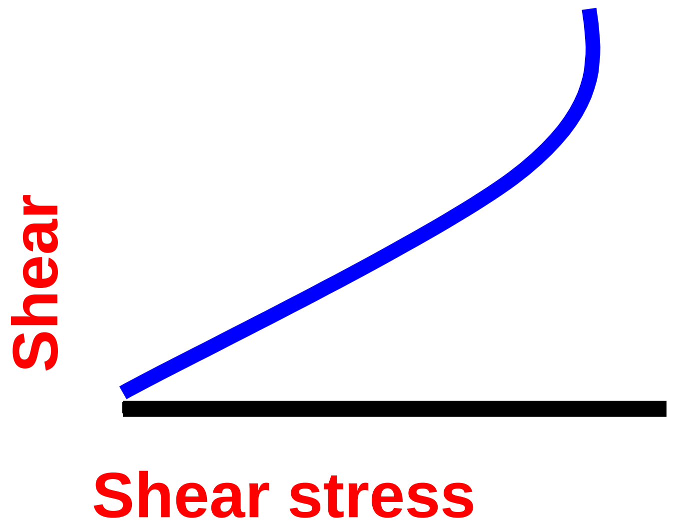


Fig. 4

Pseudo plastic systems (shear-thinning)



$$F^N = \eta' G$$

Fig. 5

DIALATANT Flow
(shear-thickening)

- Certain suspensions with a high percentage (upto 50%) of deflocculated solids exhibit an increase in resistance to flow with increasing rate of shear.
- Such systems actually increase in volume when sheared and hence termed *dilatant* and phenomenon as **rheopexy**
- When stress is removed, a dilatent system returns to its original state of fluidity.
- E.g. corn starch in water.

Dilatant Flow Behaviour

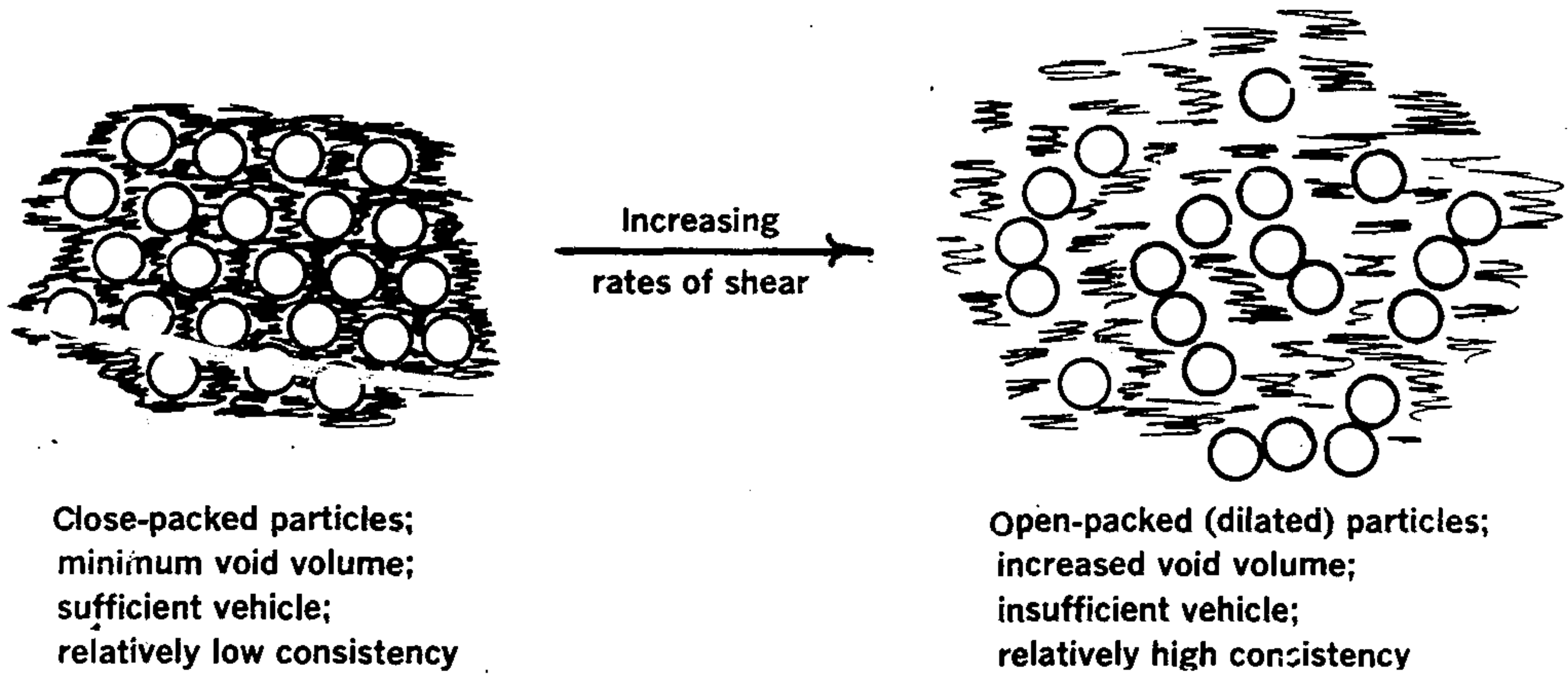


Fig. 20–3. Explanation of dilatant flow behavior.

Fig. 6

Reasons for Dilatency

- Particles are closely packed with amount of vehicle is enough.
- Increase shear stress, the bulk of the system expand (dilate), and the particles take an open form of packing.
- The vehicle becomes insufficient
- Particles are no longer completely lubricated by the vehicle.
- Finally, the suspension will set up as a firm paste.

Dilatant Systems

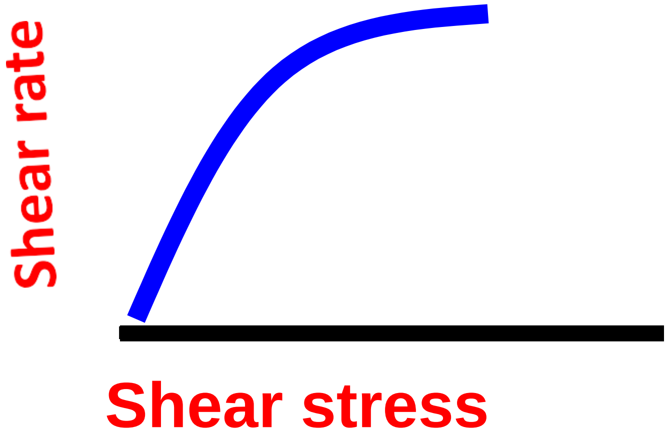


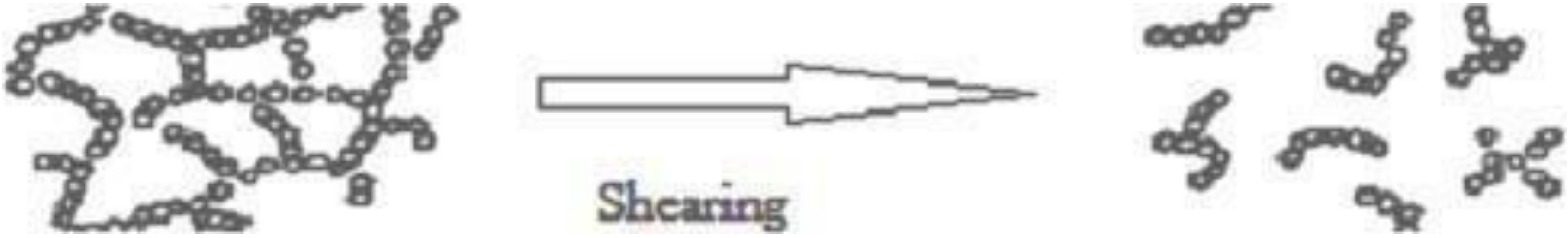
Fig. 7

Significance of dilatency

- Such behaviour suggests that appropriate precautions should be used during processing of dilatent materials.
- Mixing (powder+granulating liquid) is usually conducted in high speed mixers, dilatent materials may solidify under these conditions thereby damage the equipments.

THIXOTROPY

- Non-Newtonian
- Time Dependent behaviour
- Downcurve displace left to upcurve for shear thinning system
- It is the decrease in viscosity as a function of time upon shearing, then recovery of original viscosity as a function of time without shearing.



THIXOTROPY

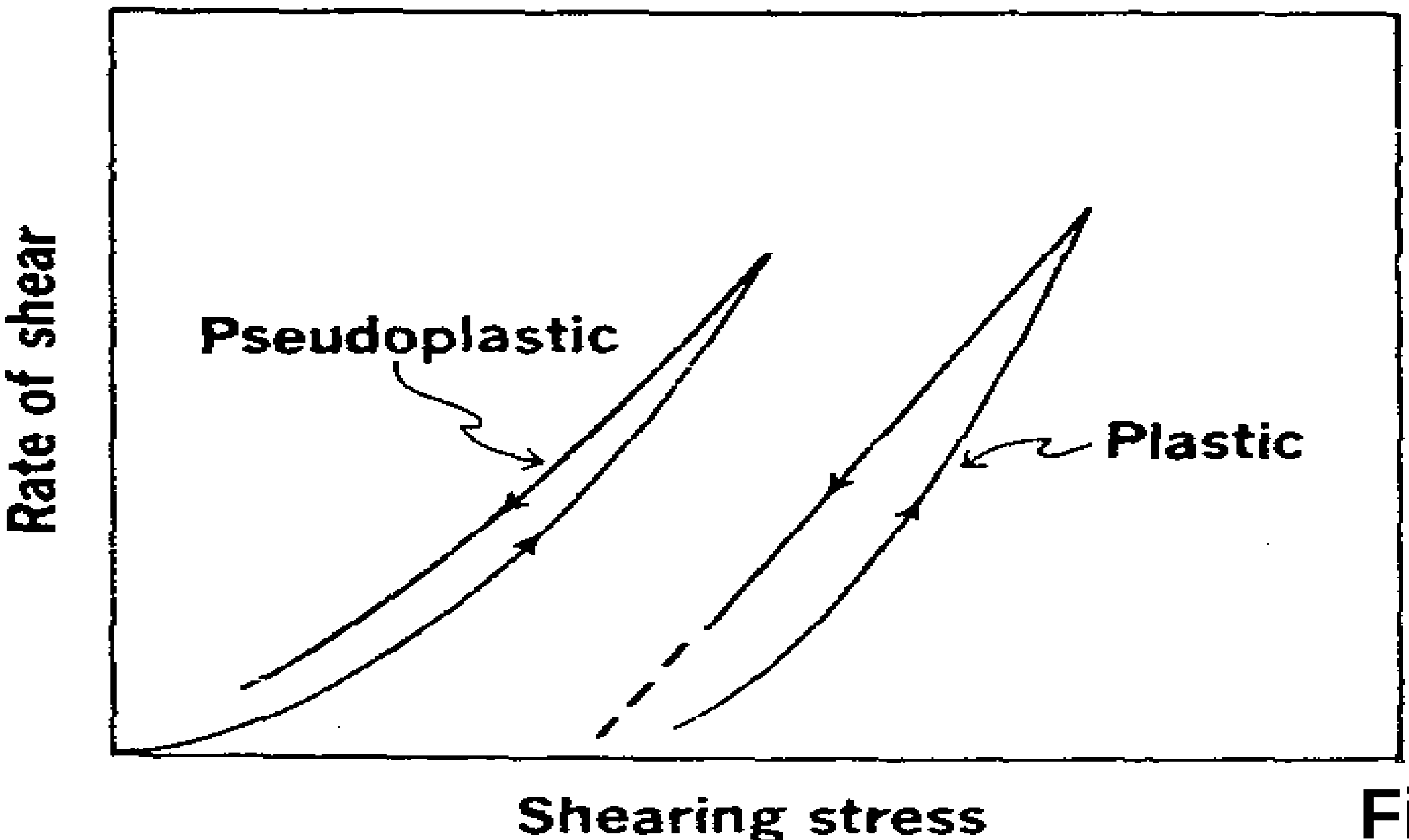


Fig. 8

Thixotropy in plastic and pseudoplastic flow systems.

THIXOTROPY

- Loose network through sample.
- At rest, its Rigidity is like Gel
- As shear applied, the structure begin to break and the material undergo Gel-to-Sol transformation.
- Finally, at rest the structure is restored again (Sol-to Gel)
- e.g. Procaine penicilline G (40-70% w/v in water)

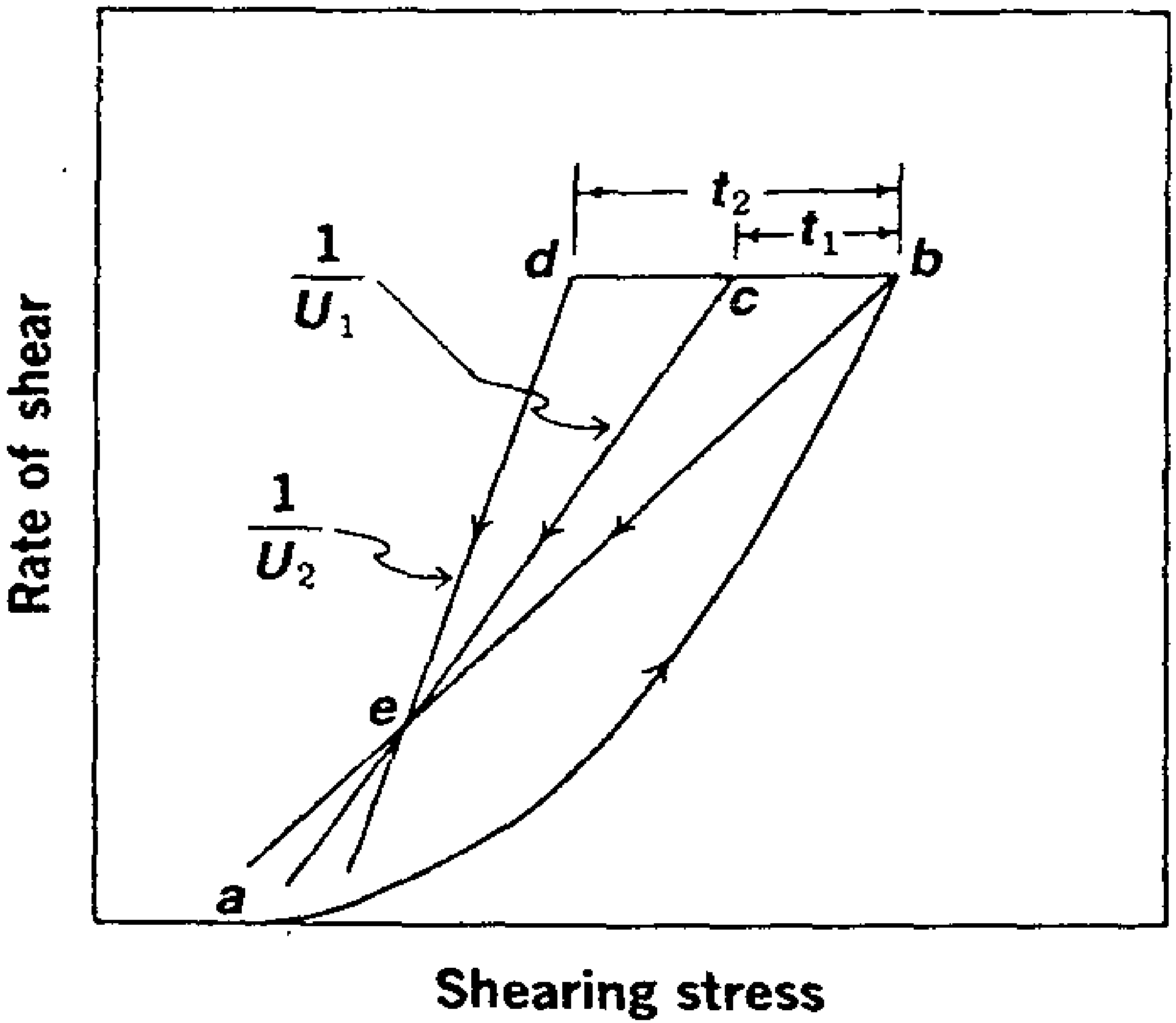
Measurement of thixotropy

- **Hysteresis loop** formed by upcurve and down curve… Measurement of area of hysteresis loop
- For Bingham plastic two approaches are used to estimate degree of thixotropy

Approach 1

- Structural breakdown with time at constant 'shear rate' (Fig 9).
- B= thixotropic coefficient (rate of breakdown at with time at constant rate of shear)

Constant Rate of shear



$$B = \frac{U_1 - U_2}{\ln \frac{t_2}{t_1}}$$

U_1 & U_2=

PlasticViscosities abe =

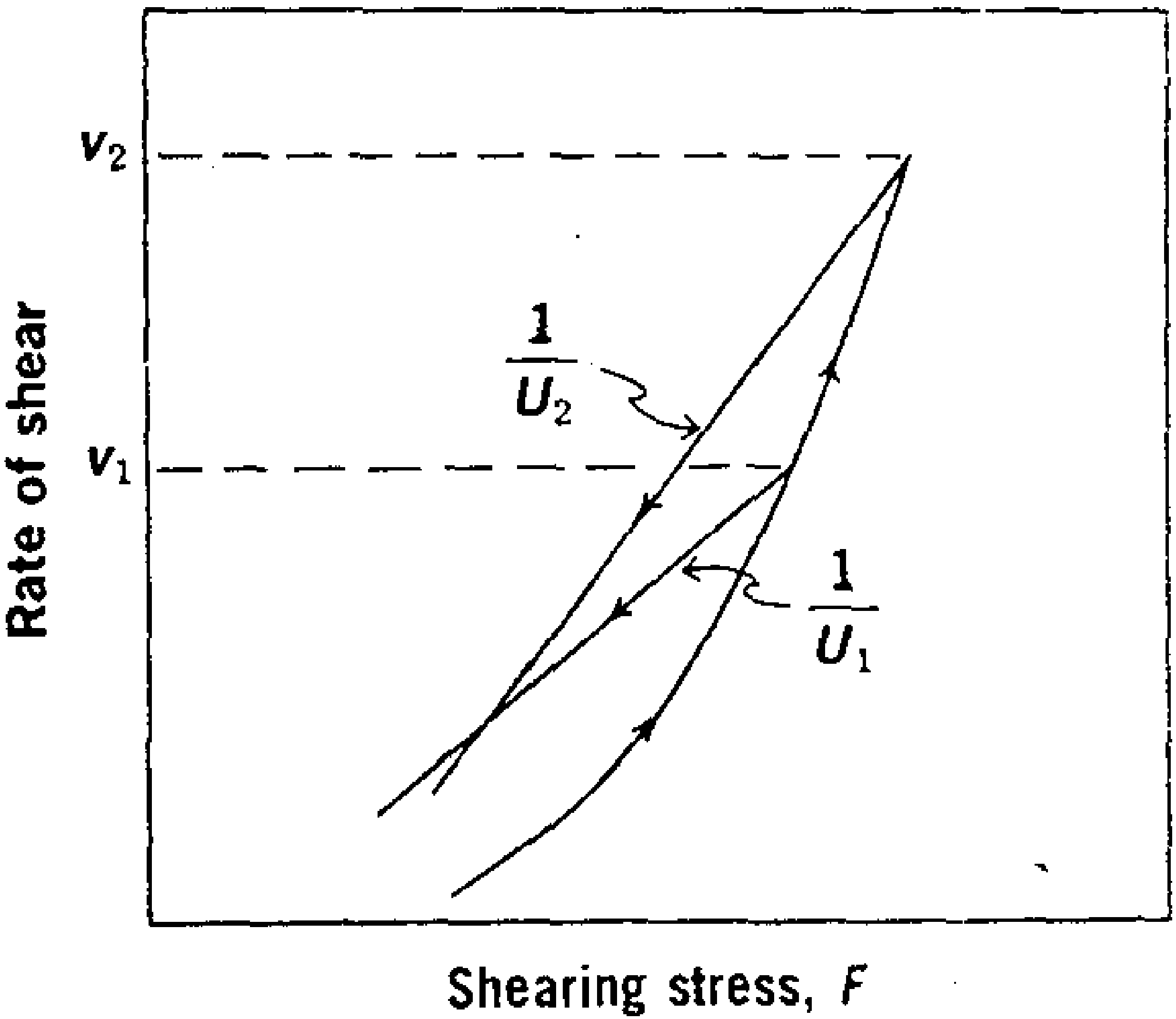
hysteresis loop

Fig. 9

Approach 2

- Determine structural breakdown due to increasing shear rate (Fig. 10). Two hysteresis loop are obtaind having different maximum
  ‘shear rate’
- M= loss in shearing stress per unit increase in
  ‘shear rate’

Variable Rate of shear



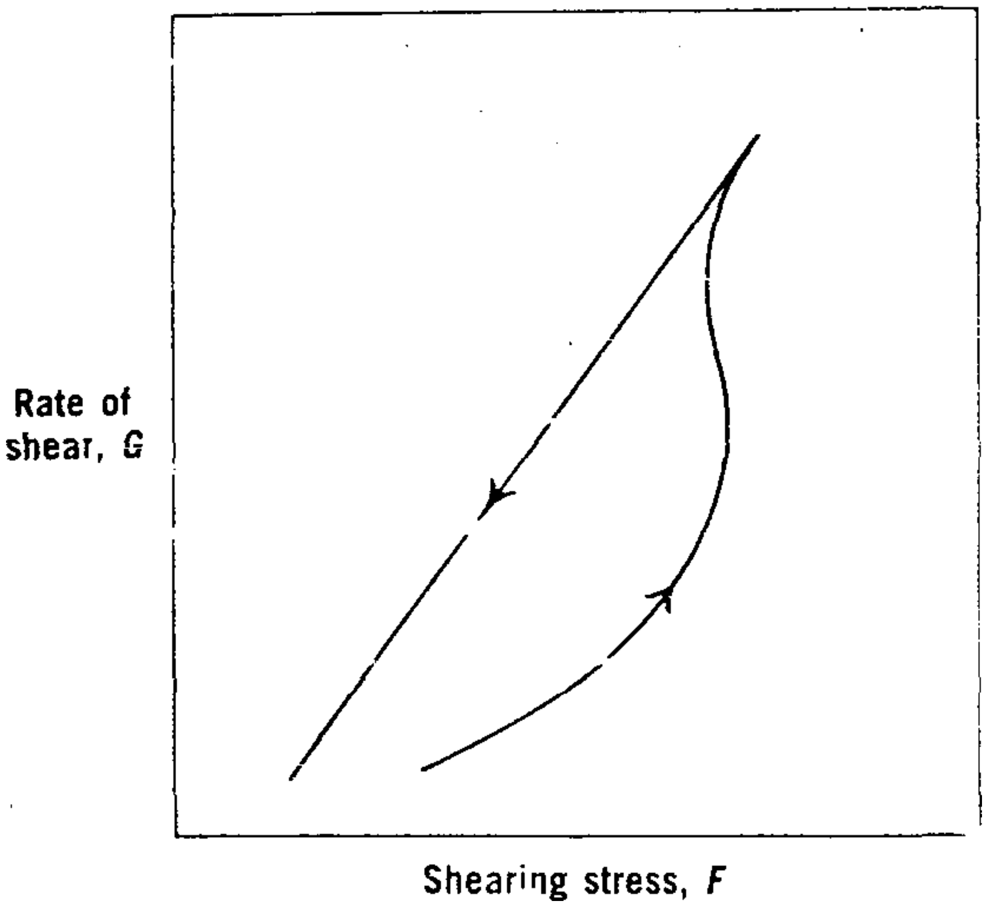
$$M = \frac{U_1 - U_2}{\ln(v_2/v_1)}$$

U_1 & U_2= Plastic Viscosities

v_1 & v_2= Shearing rates

Fig. 10

Bulge

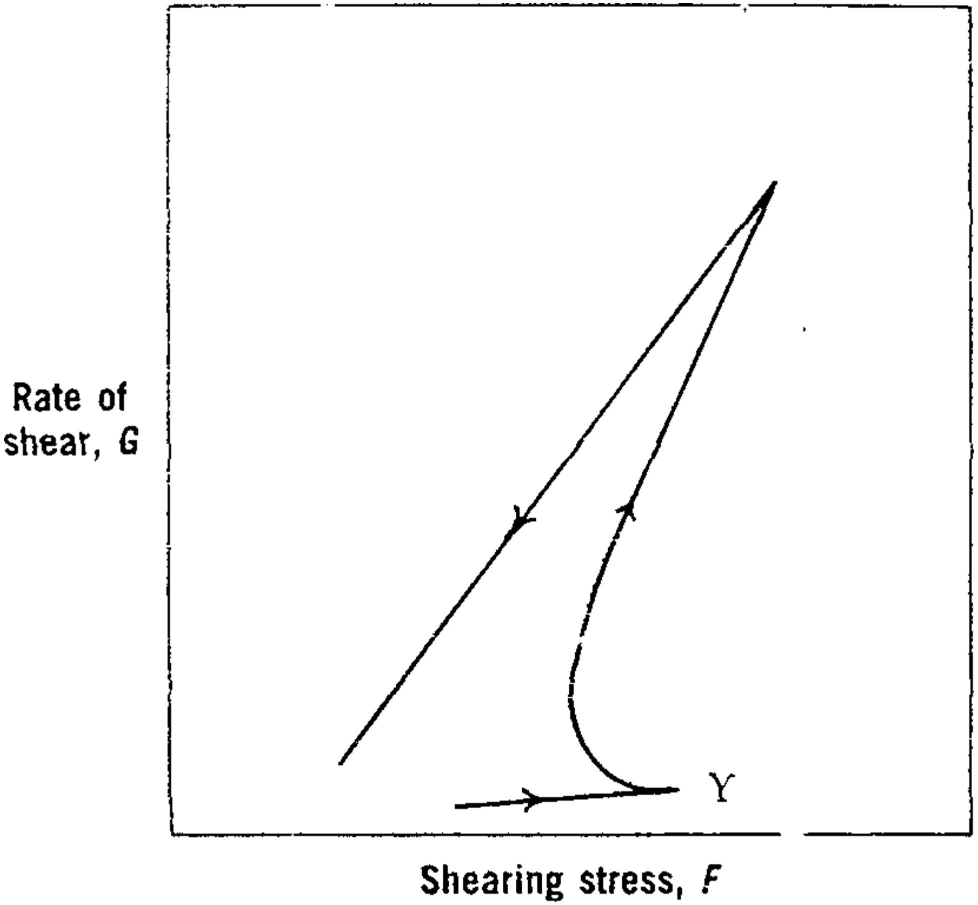


3-Dimentional structure result bulge formation.
Crystalline plates of bentonite ‘house of card’structure

E.g. 10-15% bentonite magma.

Crystalline plate → **`House of Cards`**

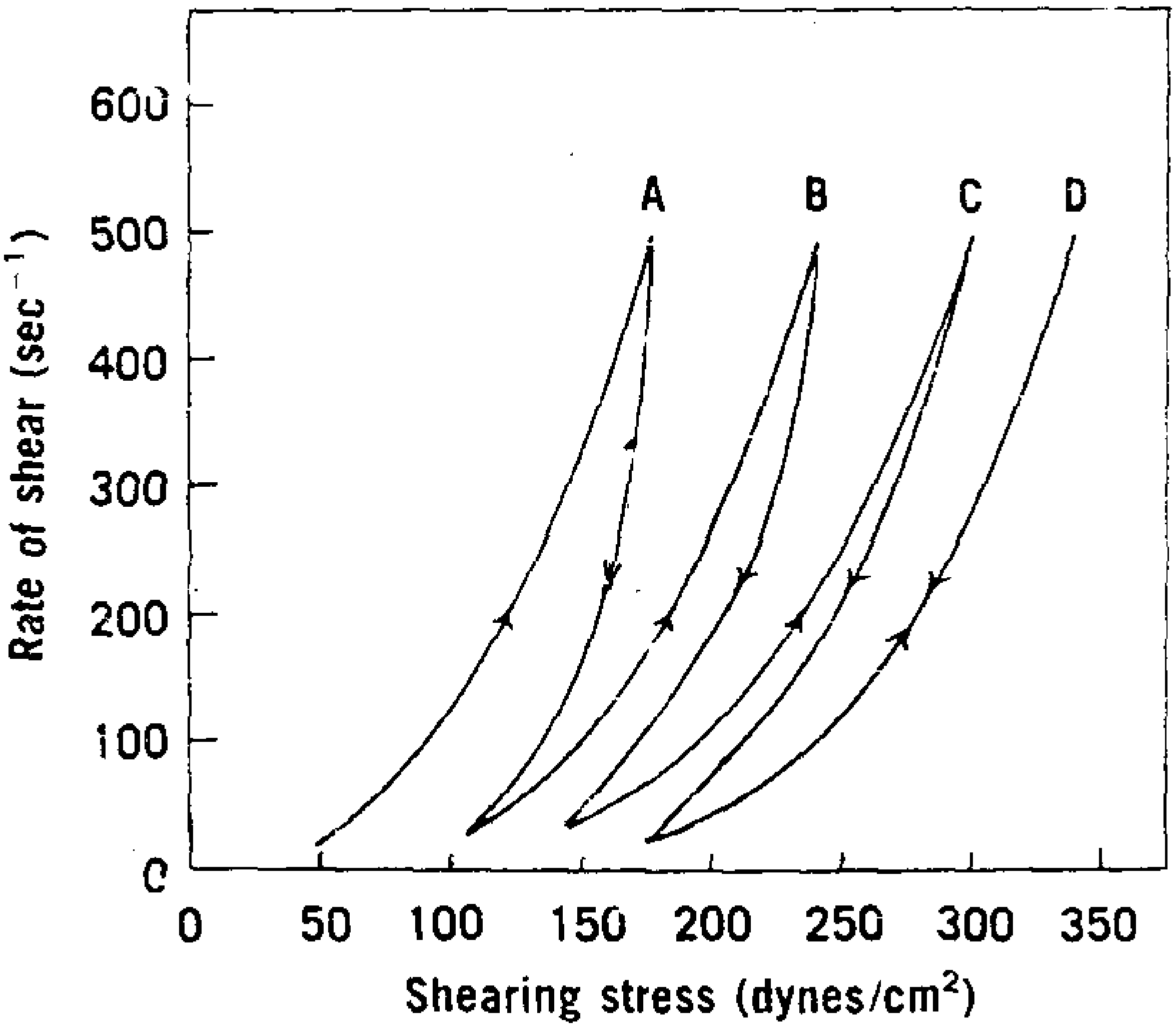
Spur



Sharp point of Structural breakdown at low shear

E.g. Procain Penicillin

Antithixotrophy



Increase in consistency (resistance to flow) on down curve with increase in time of shear.

Example,
Magnesia Magma

showing
Antithixotrophy

Antithixotrophy

- Increase in consistency (resistance to flow) on down curve with increase in time of shear.
- Reason for antithixotropy is Increased collision frequency of particles and bonding with time.

Example,

Magnesia Magma

Antithixotropy vs Dilatency

Antithixotropy (Negative thixotropy)

- Occur in **flocculated** system with **low** solid content (1-10%)
- *Solid form gel more readily in resting state than sheared state*

- **Sol** is equilibrium form

Dilatency (Rheopexy)

- Occur in **deflocculated** system with **high** solid content (50% by volume)
- *Solid form gel more readily when sheared rather than resting condition*
- **Gel** is equilibrium form

Thixotropy vs Antithixotropy

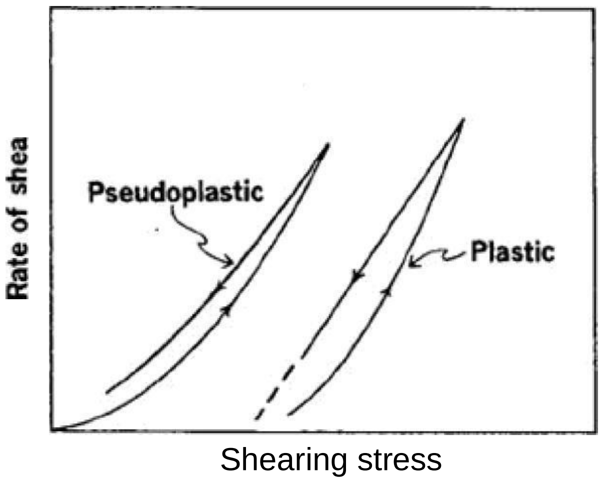
THIXOTROPY

decrease in viscosity as a function of **time** upon shearing
then recovery of original viscosity as a function of time without shearing
e.g. Procaine penicilline G
(40-70% w/v in water)

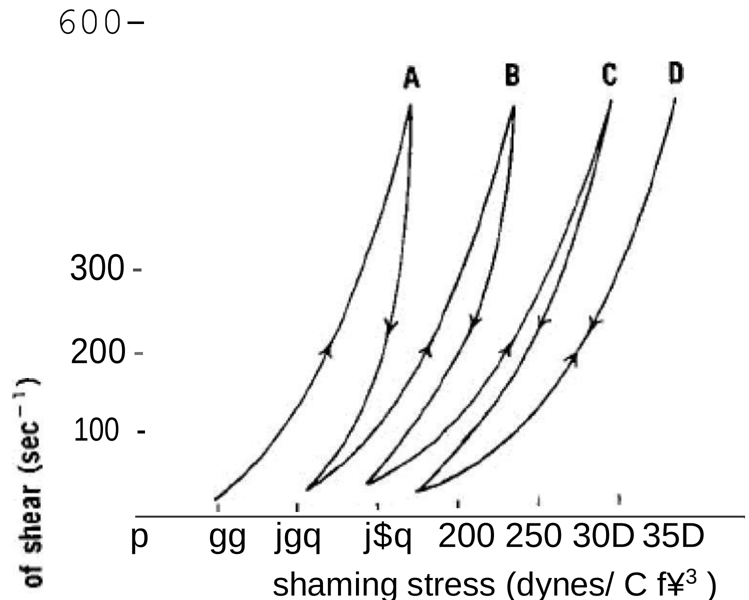
ANTITHIXOTROPY

Increase in consistency (resistance to flow) on down curve with increase in time of shear Increased collision frequency of particles
E.g. Magnesia magma

Thixothropy andanti-thixc›tr»py



fig,20-4. Thixovopy in plastic and pseudoplsstic flow systems.



Fig, 20-é. Rheogram of magnesia jyjggpjg g|j OW]Ij g BnñthiXOtf0 IC behavior. ThB fTl8terial s shesred at rapeeted increasing and thefl decreasing rates of shear. At 5t6ge d , furthef cycling no long6£ increased the consistency, and the upcurves and downcurVBS C0In-cided. lFrom C.W.thong, S.P, Eriksen, and J.W. tflt0Sl0/, J.Am. Pharm. Assoc. SCi. E4,49,54?, 1960, With permission.)

CHOICE OF VISCOMETER

Instruments used for measurement of viscosity are known as viscometers

- Newtonian fluids: (Because shear rate is directly proportional to shear stress) instruments that operate **at single rate of shear** can be used.
- Non- Newtonian fluids: Instrument which could operate at (multiple) **variable rate of shears** are required.

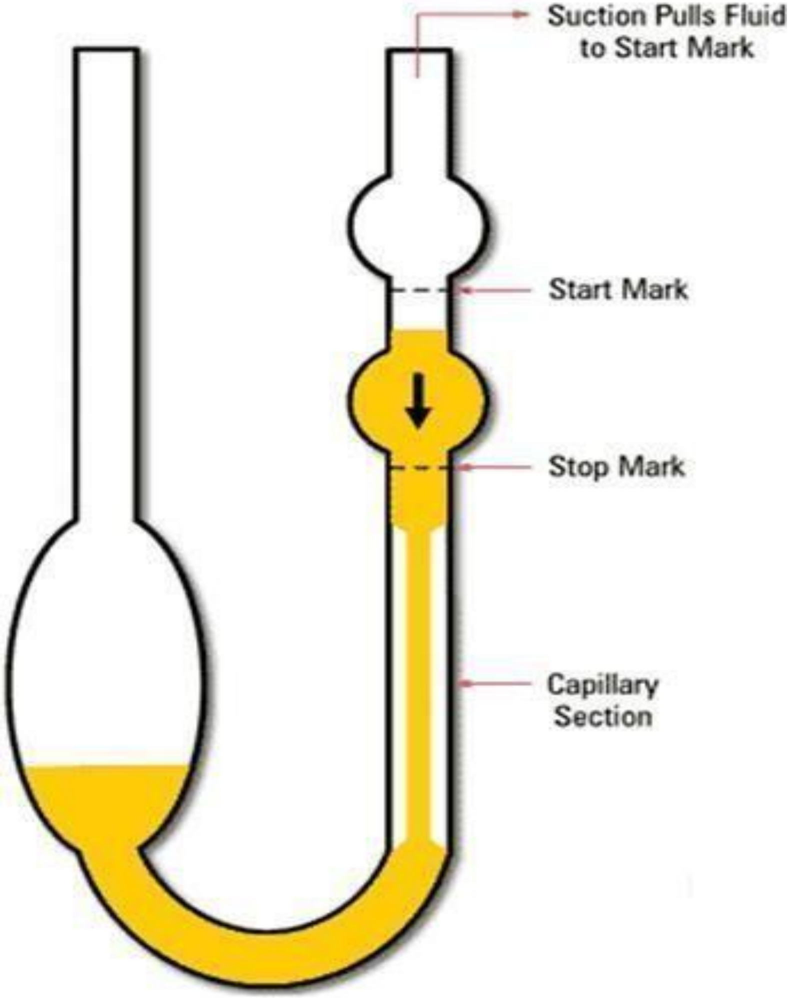
Measurement of Viscosity

- Capillary viscometers (single rate of shear)
- Falling sphere viscometers (single rate of shear)
- Rotation viscometers (**variable** rate of shear)

Oswald Viscometer (Capillary viscometer)

- It follow *Poiseuille's Law* for flow of liquid through capillary
- The apparatus consists of a glass U-tube
- viscometer made of clear borosilicate glass and constructed in accordance with the dimensions given in official books.

Oswald Viscometer



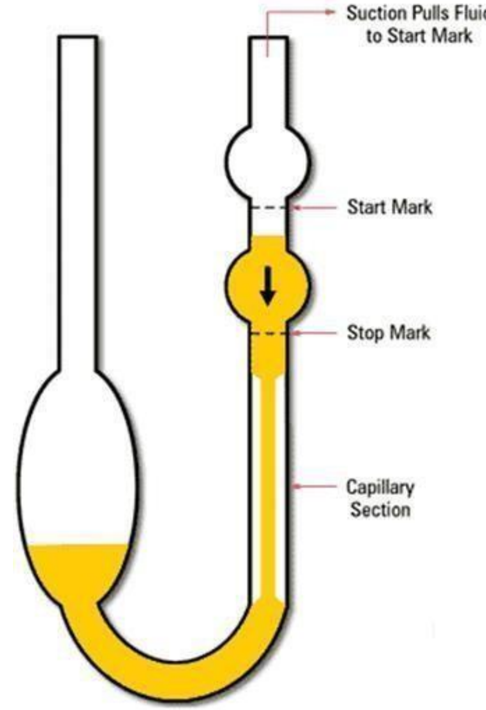
$$\eta = \frac{\pi r^4 t \Delta P}{8 l V}$$

Relative viscosity

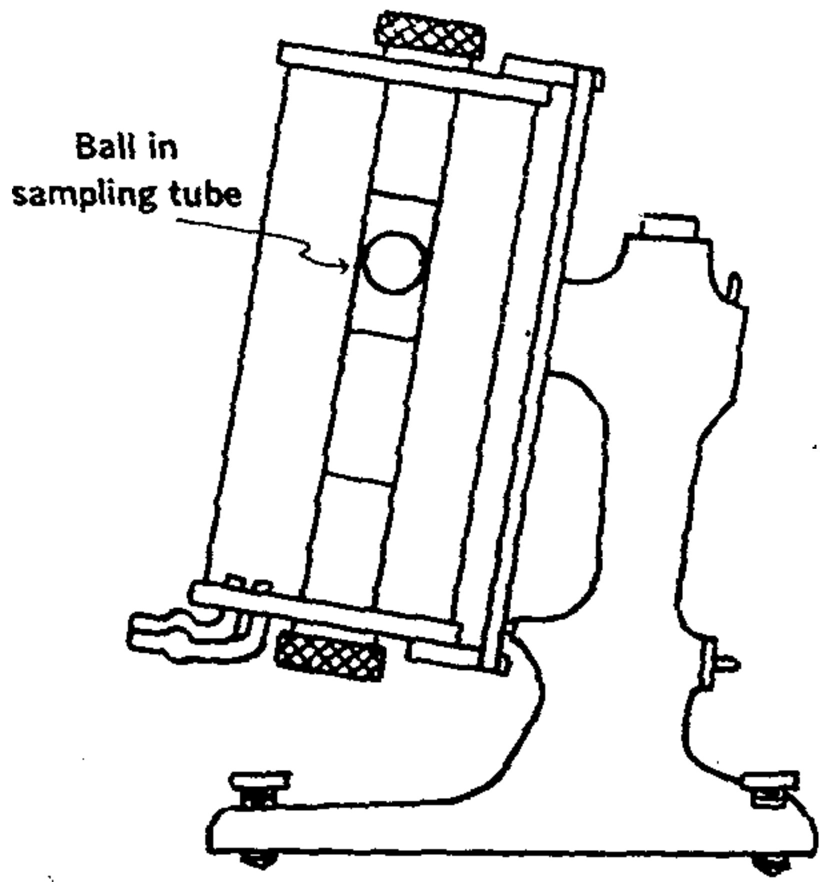
$$\frac{\eta_1}{\eta_2} = \frac{\rho_1 t_1}{\rho_2 t_2}$$

Method

- Clean viscometer using chromic acid
- Fill the viscometer with the liquid being examined through left arm of tube to slightly above the bubble using a pipette
- Suck the liquid till start mark then allow it to flow till stop mark.
- Note the time of flow for liquid from start to stop mark.
- Determine the viscosity using formula where viscosity of water η_1 =0.9 cP
- $\eta_2 = (\varrho_2 t_2 / \varrho_1 t_1)\, \eta_1$



Hoeppler Falling ball Viscometer



$$\eta = t(S_b - S_f)B$$

Hoeppler Falling ball Viscometer

- It follows Stoke's law
- Glass or steel ball roll down almost vertical tube containing the test liquid
- Rate (speed) at which ball with particular density and diameter falls is inversely proportional to viscosity of liquid
- Sample and ball are placed in inner tube and allowed to equilibrate at temperature (jacket)
- Tube and jacket inverted and time required for ball to fall between two

marks is noted and it is repeated several times.

Hoeppler Falling ball Viscometer

Viscosity is calculated using the formula

$$\eta = t(S_b - S_f)B$$

t = time interval in seconds

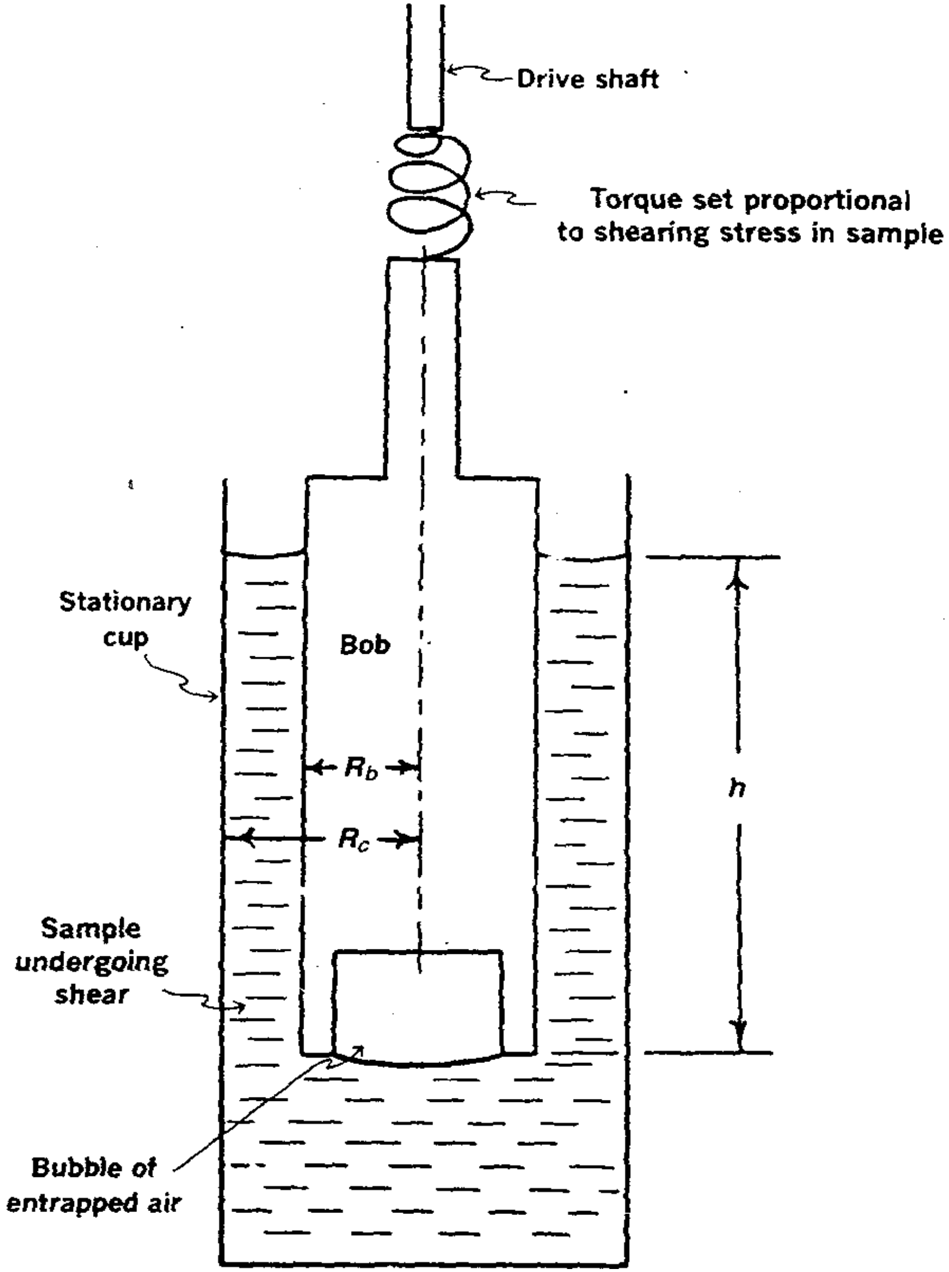
S_b-S_f = specific gravities of ball and fluid

B = constant for ball supplied by instrument manufacturer

Rotational Viscometers

- Cup and Bob (Disadvantage: Plug flow)
  - Couette type ➐ **Cup rotate** ➐ e.g. MacMichael
  - Searle type ➐ **Bob rotate** ➐

    e.g. Stor the (Plug flow can be minimized by reducing gap between bob and cup)
- Cone and Plate (Advantage: No plug flow)
  - Ferranti Shirley
  - Brookfield



Cup and Bob viscometer

- Sample is sheared in space between outer wall of bob and inner wall of cup
- Viscous drag on bob due to sample causes it to turn
- Resultant torque is proportional to viscosity of sample
- *MacMichael viscometer*: **Rotating cup** and stationary bob
- *Searle*

viscometer:
Rotating bob and stationary cup

Cup and Bob viscometer

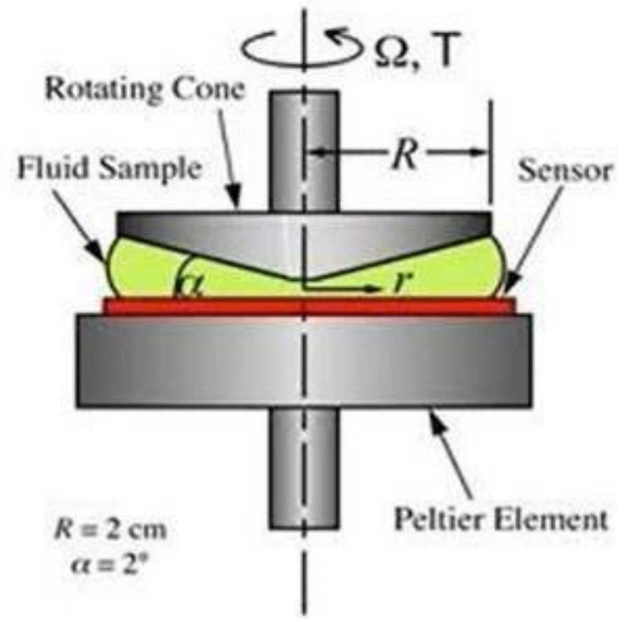
The equation for plastic viscosity when employing the Stormer viscometer is

$$U = K_v \frac{w - w_f}{v}$$

where U is the plastic viscosity in poises, w_f is the yield value intercept in grams, and the other symbols have the meaning given in equation .

Cone and Plate viscometer

- The cone to plate angle is less than 1^0 centigrade
- sample required is small 0.1 to 0.2 ml
- Principle:



pseudo plastic Viscosity estimated by

$$\eta = C.\ T/v$$

plastic viscosity estimated by

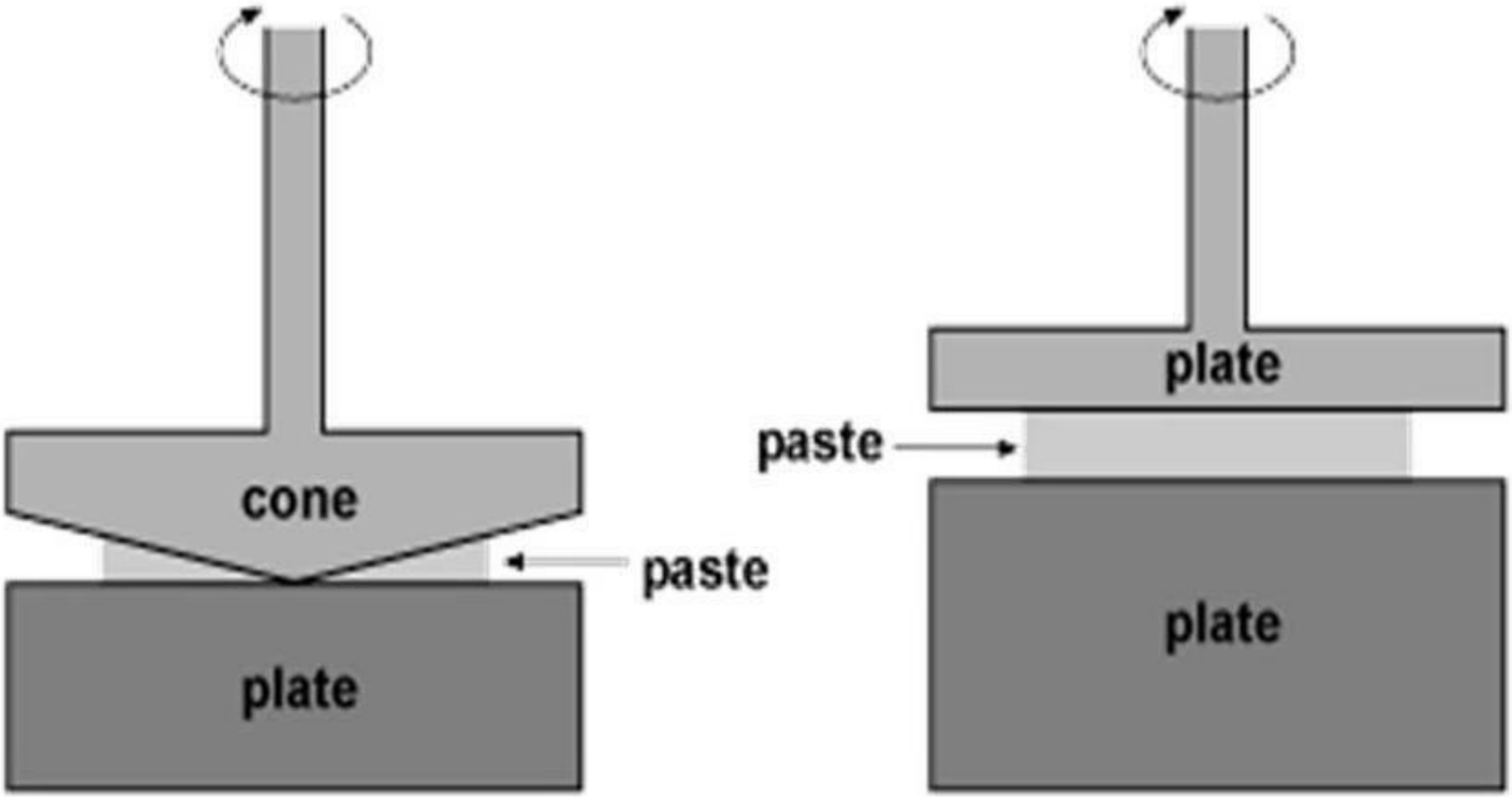
$$U = C\frac{T - T_f}{v}$$

and the yield value is given by

$$f = C_f \times T_f$$

T= torque
V= speed of rotation of cone f= yield value
C_f = instrumental constant

Cone and Plate viscometer



Cone and Plate viscometer

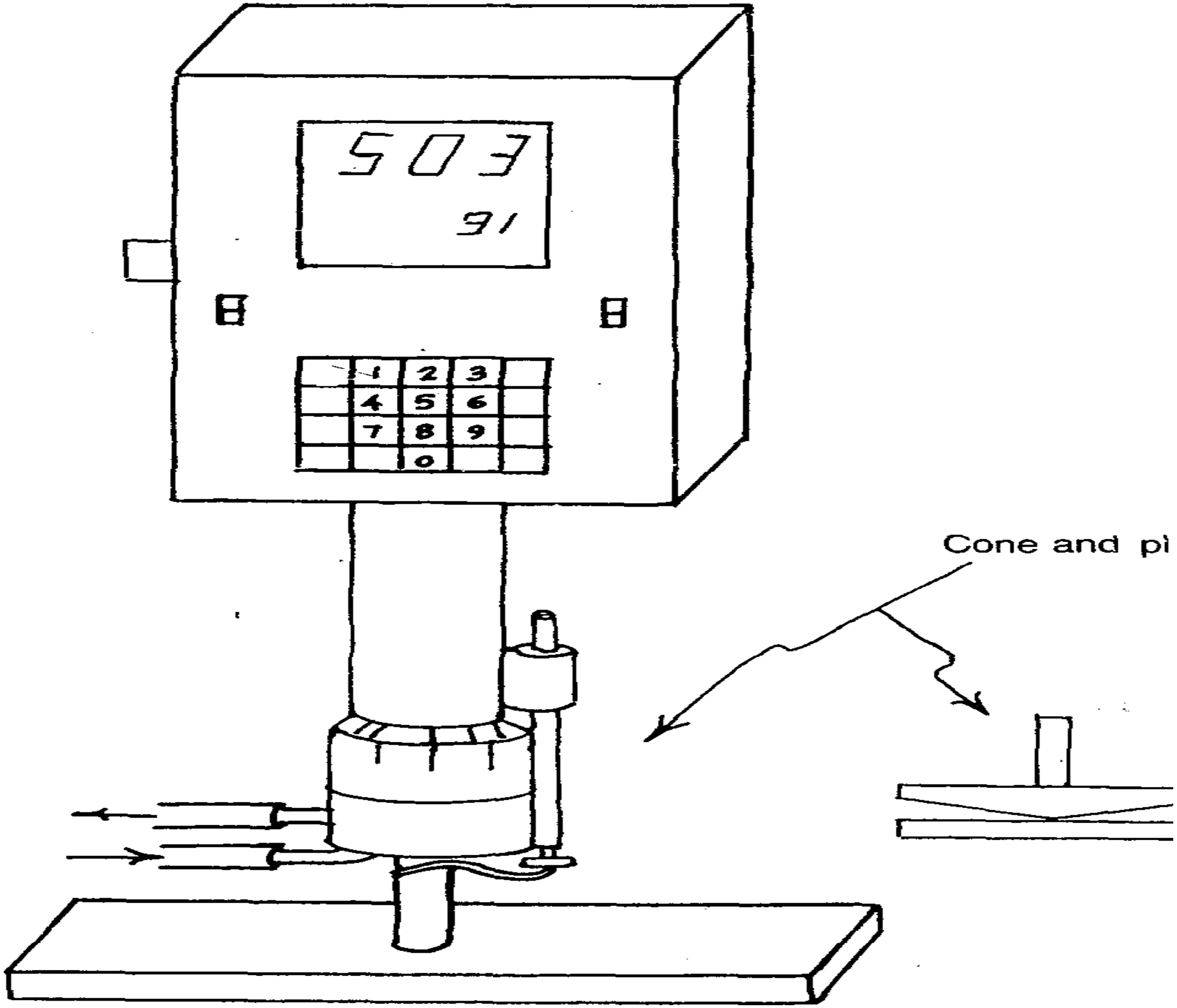
- Rate of shear is constant,no chance for plug flow.
- Temperature stabilization is good.
- It needs to vary little samples for the study sample volume of 0.1 to 0.2 ml
- Valuble aid for det.of hysteresis loops obtained in thixotropic system,and det. The thixotropic coefficient.

Brookfield viscometer

- The rotational viscometer basically consists of two parts - a **head unit** with a motor and **a spindle** that is driven by the motor.

- The viscosity is determined by measuring the **resistance of a spindle rotating** in the sample.

Brookfield Viscometer




Instrument Setup
Measurement
→ Information
viscolead
one
ON
QUIT
ENTER
TAB
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Viscoelasticity

Continuous shear (rotational viscometer) dose not allow material to be in ‘ground state’ but in deformation state

Analysis of viscoelastic materials (Cream, lotion, suppositories etc.) is designed not to destroy ground state of material

Viscoelastic measurement depend upon mechanical properties of material

Viscoelasticity

- Semisolids exhibit properties of both states…
  elasticity of solid and **viscosity** of fluids.
- Viscosity of Newtonian fluids is expressed by
- $\eta = F/G$
- Elasticity of solids is expressed by Hook's law
- $E = F/\gamma$
  - *E= elastic modulus,* γ *= Strain*

Maxwell unit

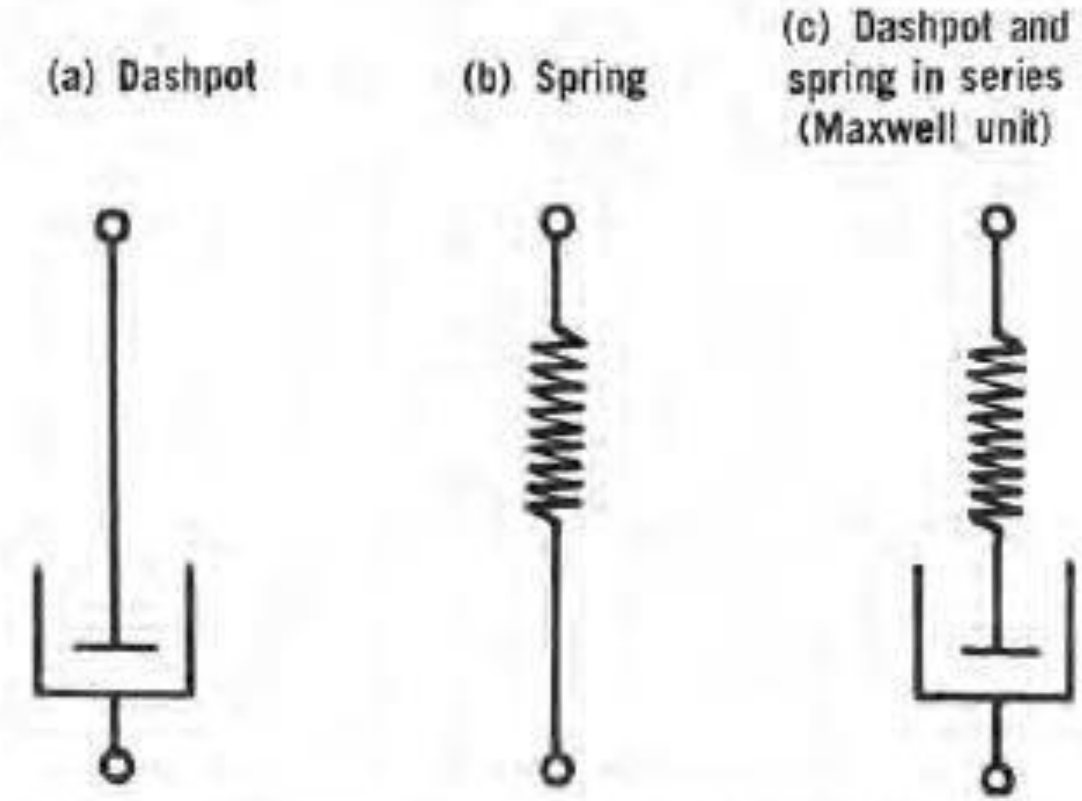


Fig. 19–20. Mechanical representation of a viscoelastic material using a dashpot and spring. The dashpot and spring in series is called a *Maxwell element* or *unit*.

Maxwell unit

- When a constant stress is applied on Maxwell unit there is a strain on material which corresponds to displacement of spring
- Applied stress ❼ displacement of piston in dashpot due to viscous flow
- When stress is removed ❼ spring return to original position but viscous flow show no recovery

Voigt unit

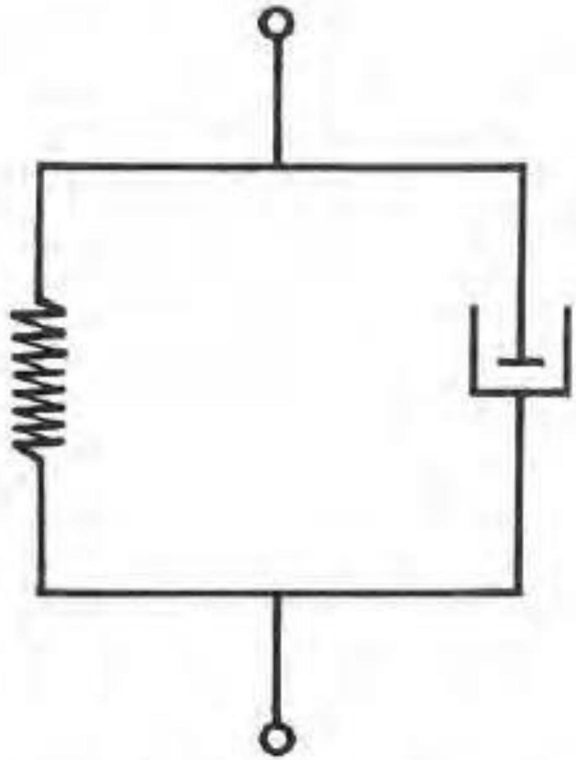


Fig. 19–21. Spring and dashpot combined in parallel as a mechanical model of a viscoelastic material, known as a *Voigt element.*

Voigt Unit

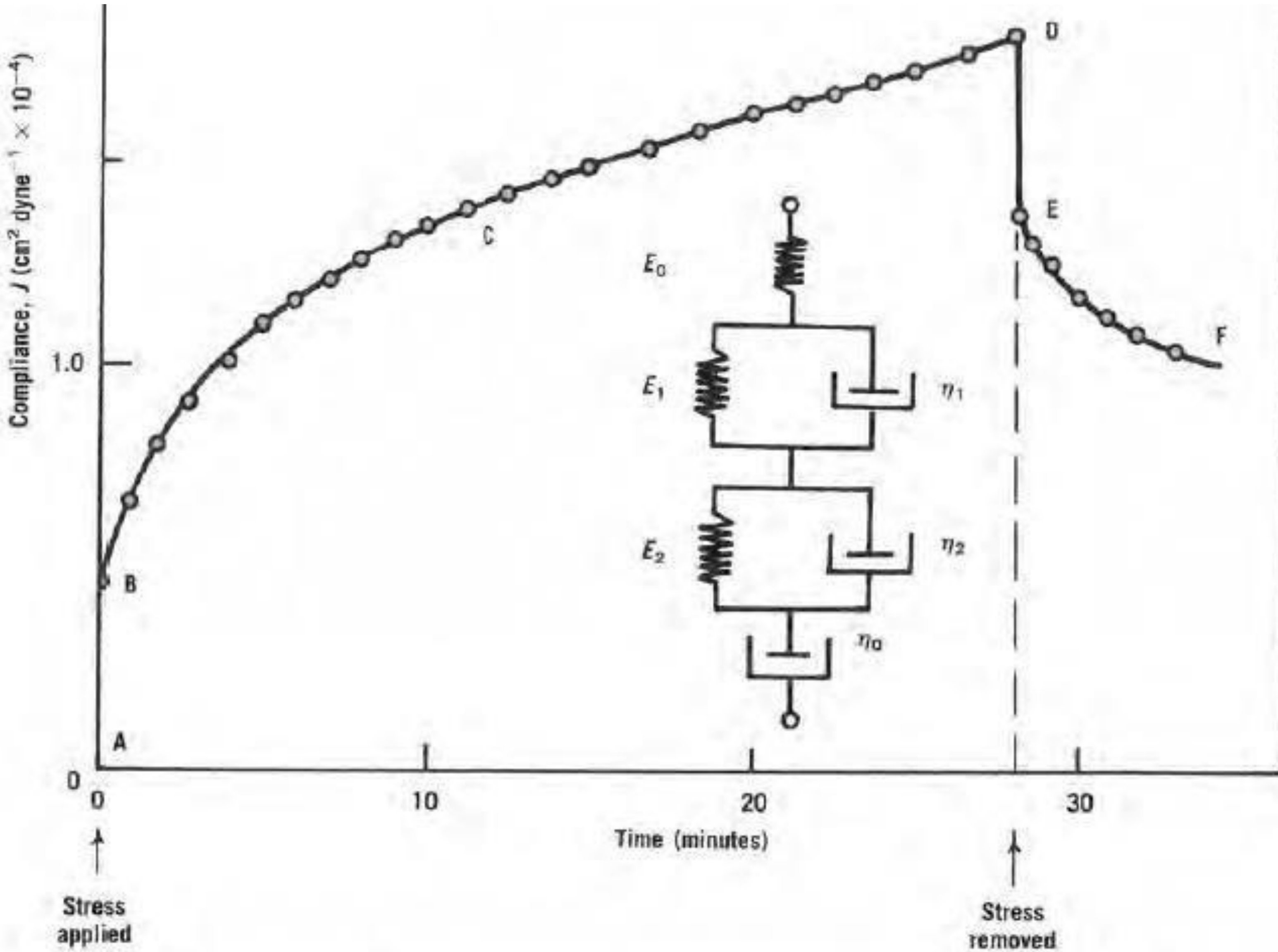
- Drag of viscous fluid in dashpot simultaneously influences extension and compression of spring
- Strain is expressed as deformation or compliance , J (strain per unit stress)
- $J = J_{\infty}(1-e^{-t/\tau})$
- $\tau =$ viscosity per unit modulus
- J_{∞} = compliance at infinite time

Creep viscometer (creep curve)

Maxwell element can be combined with Vogit unit to make creep viscometer

Creep curve is used to measure viscoelasticity of non-Newtonian pharmaceutical systems

Creep Curve for viscoelastic materials

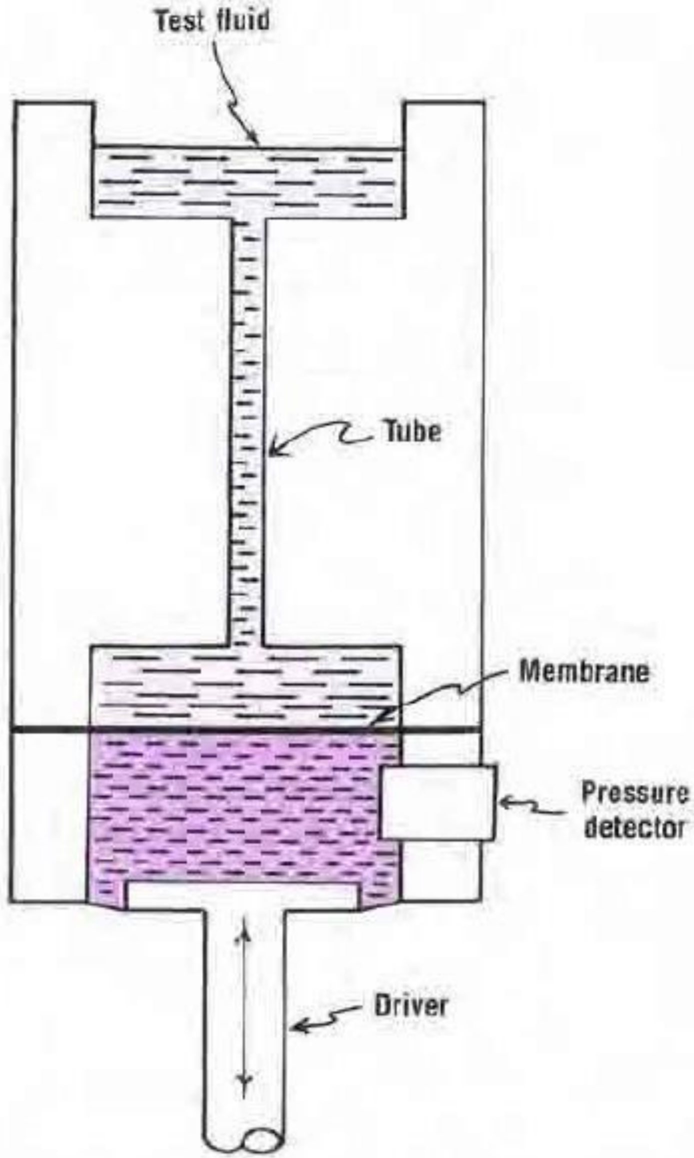


Creep Curve for viscoelastic materials

AB= Elastic movement .. Top spring
BC= viscoelastic flow …. Two Voigt unit
CD= Viscous flow… Movement of piston at bottom of Maxwell unit

When stress is removed there is instant elastic recovery **DE** (equivalent to AB) followed by EF (figure on previous slide)

Rheogoniometer



Oscillatory viscometer which combine Maxwell and Vogit unit Oscillatory shear (in membrane of apparatus) measure viscoelasticity

Reference

- ‘Martin’s Physical Pharmacy and Pharmaceutical Sciences’ Fifth edition, Lippincott Williams and Wilkins, Indian Edition distributed by B.I.Publications Pvt Ltd, 2006.


Thank You!