Lipids

- **Molecules of Mr =150 - ≈ 2000 composed of saturated, unsaturated and/or aromatic or aliphatic hydrocarbon moieties - *Non-polar lipids***
- **When water-binding functional groups (-OH, -COOH, -NH, -C=O, etc.) are covalently linked - *Polar Lipids***
- **Biologically-relevant lipids are molecules with aliphatic chains of at least 12C atoms and/or aromatic/aliphatic structures with at least 3 rings which may be fused**
- **Old system of classification based on solubility in organic solvents is neither strictly true nor useful (e.g., bile salts)**

OCTADECANOL

Graphic representations of a Polar Lipid

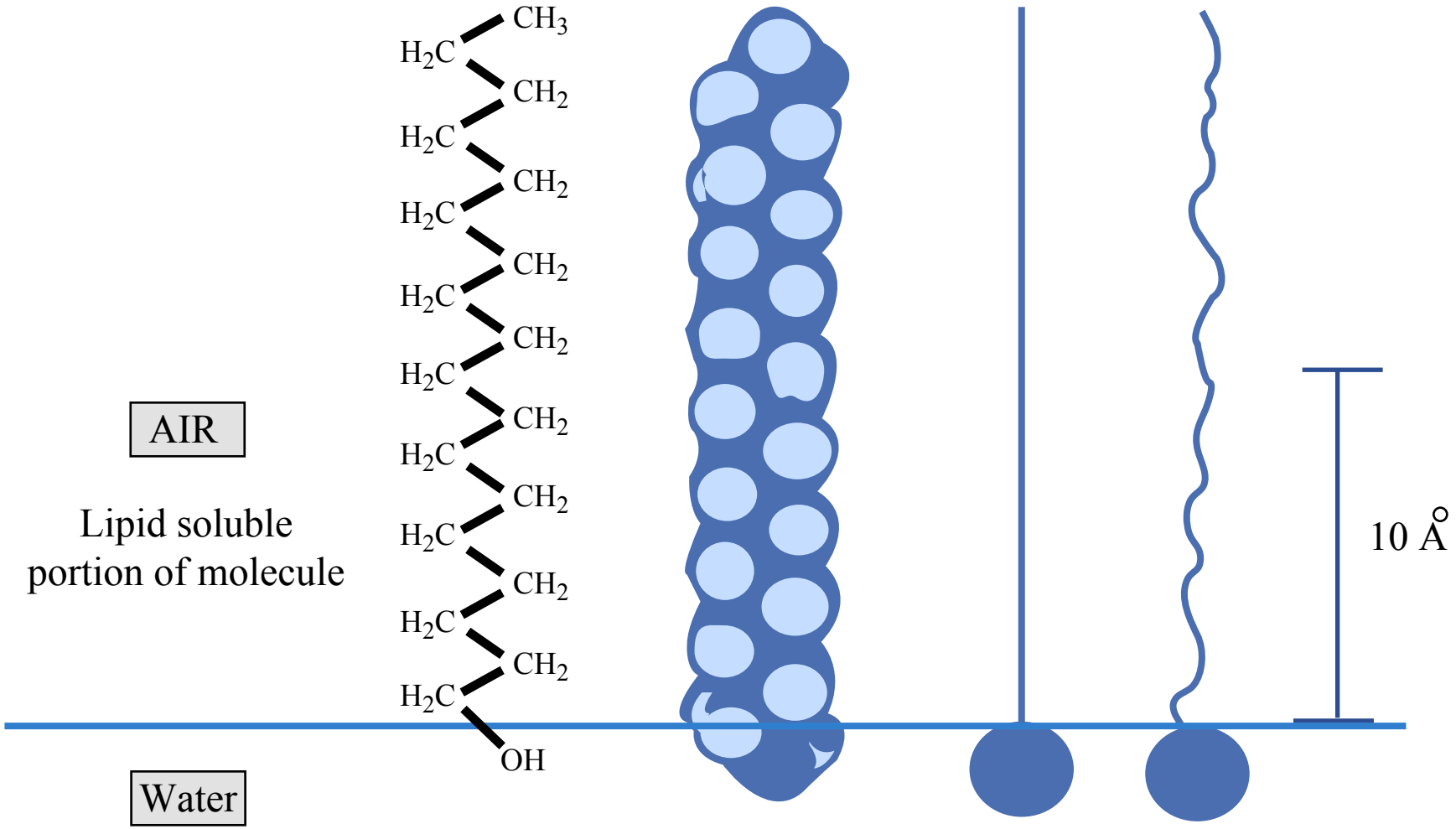

Figure by MIT OCW.

Classification of Polar Lipids Based on Interactions with H_2O*

*D. M. Small (1968)

Class	Surface and Bulk Interactions with Water
Non-Polar Lipids	Will Not Spread To Form A Monolayer Insoluble In Bulk
Polar Lipids	
A. Insoluble Non-Swelling Amphiphiles	Forms A Stable Monolayer Insoluble In Bulk
B. Insoluble Swelling Amphiphiles	Forms A Stable Monolayer Bulk Phase-pure liquid crystals in pure water
C. Soluble Amphiphiles	
1. with lyotropic mesomorphism → L.C. → Micelle	Forms An Unstable Monolayer Bulk Phase-a micellar solution
2. without lyotropic mesomorphism → Micelle	Forms An Unstable Monolayer Bulk Phase-a micellar solution

Refer to: Small, D. M. "A Classification of Biological Lipids Based Upon Their Interactions in Aqueous Systems." *J Amer Oil Chem Soc* 45 (1968): 108-119.

Self-Aggregated States

i) LIQUID CRYSTALS (L.C.)

- Intermediate Physical States (mesophases) with properties of both liquids and solid crystals.
- Long rage order in at least 1 dimension
  - Lyotropic L.C.
  - Thermotropic L.C.
- Have distinct optical textures by polarizing microscopy

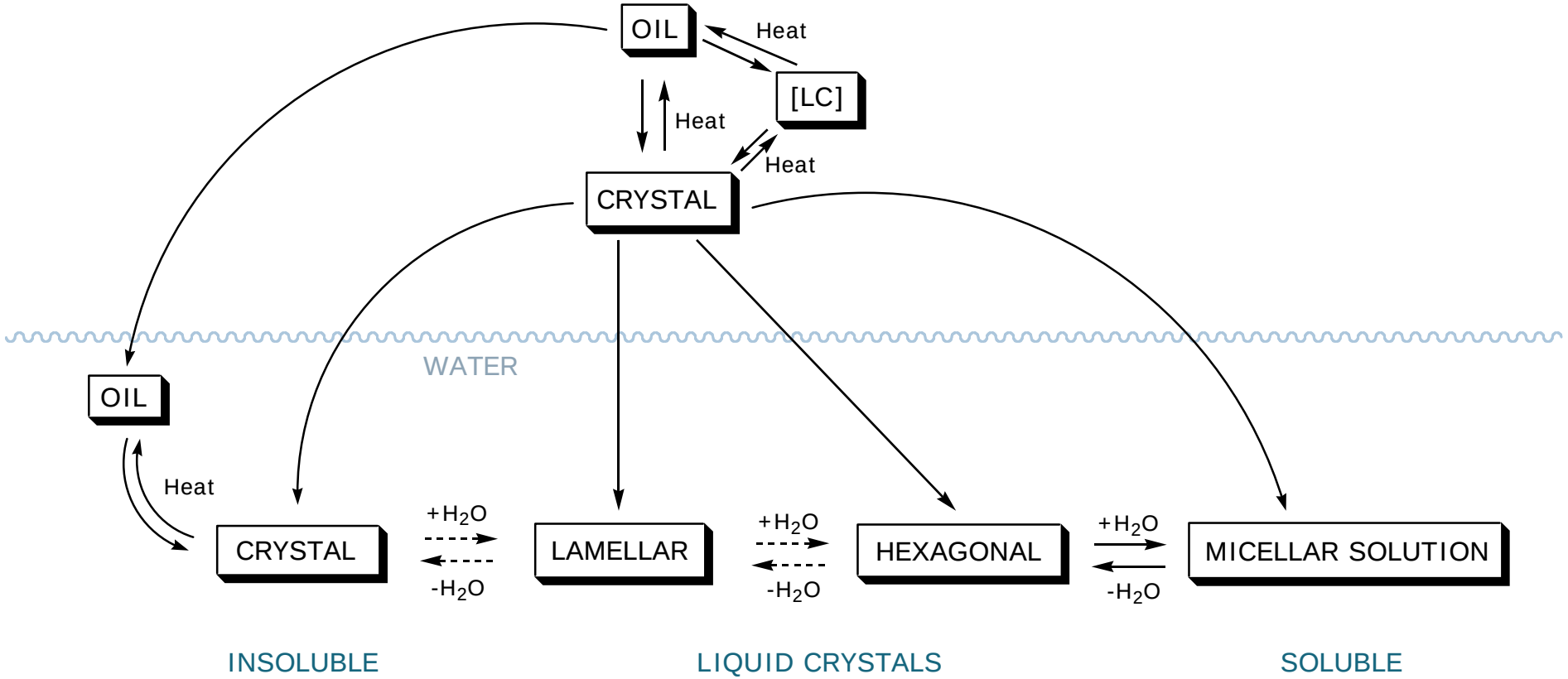

Figure by MIT OCW.

Self Aggregated States

ii) MICELLES

Thermodynamically stable aggregates of soluble amphiphilic lipids that form spontaneously above a critical micellar concentration (CMC) and critical micellar temperature (CMT)

- **in aqueous systems: regular micelles**
  "The hydrophobic effect"
- **in organic solvents: reverse micelles**

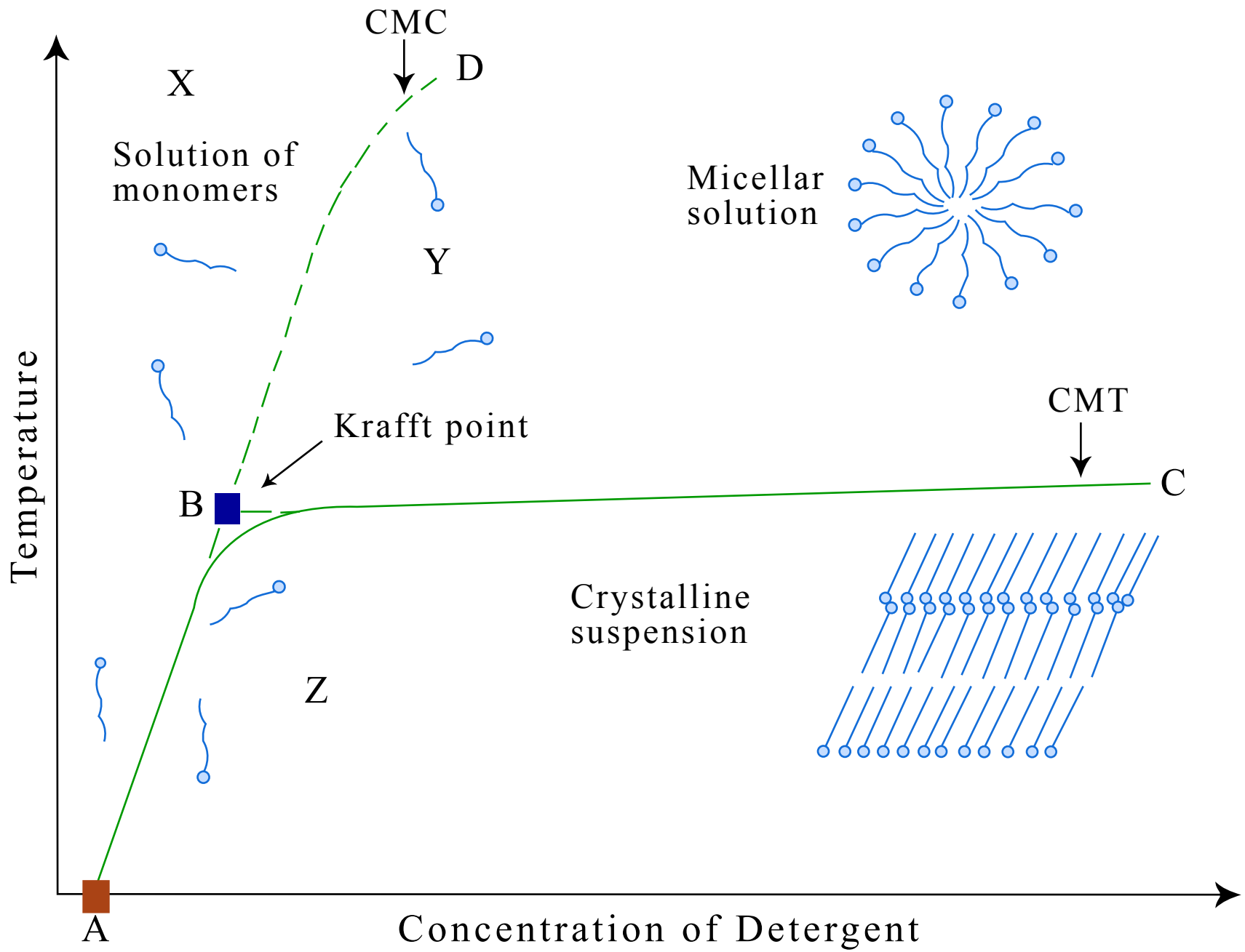

Figure by MIT OCW.

Self-Aggregated States

iii) EMULSIONS

Dispersions of one liquid in a continuous phase of another liquid: O/W, W/O systems

The dispersed (discontinuous) phase consists of microscopic droplets, usually 0.1-100 μm in diameters

Self-Aggregated States

iv) SOLID CRYSTALS

Classically lipids such as Cholesterol (Gallstones, Atheroma), fatty acids + bile acids (Enteroliths), glycolipids (neural storage diseases) – all are pathologic

Anhydrous Cholesterol and Cholesterol Monohydrate

Figures removed due to copyright reasons. Please see:

Shieh, H. S., et al. "Crystal structure of anhydrous cholesterol." *Nature* 267 (1977): 287-9.

Craven, B. M. "Crystal structure of cholesterol monohydrate." *Nature* 260 (1976): 727-9.

Figure 1 in Loomis, C. R., et al. "The phase behavior of hydrated cholesterol." *J Lipid Res* 20 (1979): 525-535.

Principal Mixed Lipid Systems in Living Organisms

- Stable Emulsions (dietary fat, plasma lipoproteins, intracellular fat droplets, gut luminal lipids pre-digestion, etc.)
- Mixed Micelles (bile, gut lumen, certain brain lipid storage diseases)
- Mixed Liquid Crystals (biologic membranes, serum lipoprotein X in cholestasis, myelin sheet, mixed vesicles in gut lumen, etc.)

BEHAVIOR OF LECITHIN IN WATER

Figure removed due to copyright reasons.

ADDITION OF BILE SALT TO LECITHIN - CHOLESTEROL LIQUID CRYSTAL

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The 3 “P” Rules

- Predictability Rule
- Predominance Rule
- Phase Rule (F=C-P+2)

How Lipids Traverse Biological Membranes

- As single molecules (molecule need not be water soluble)
- As aggregated particles (i.e., stable emulsions)
- Transporter control: Genomic (slow), nongenomic (fast)

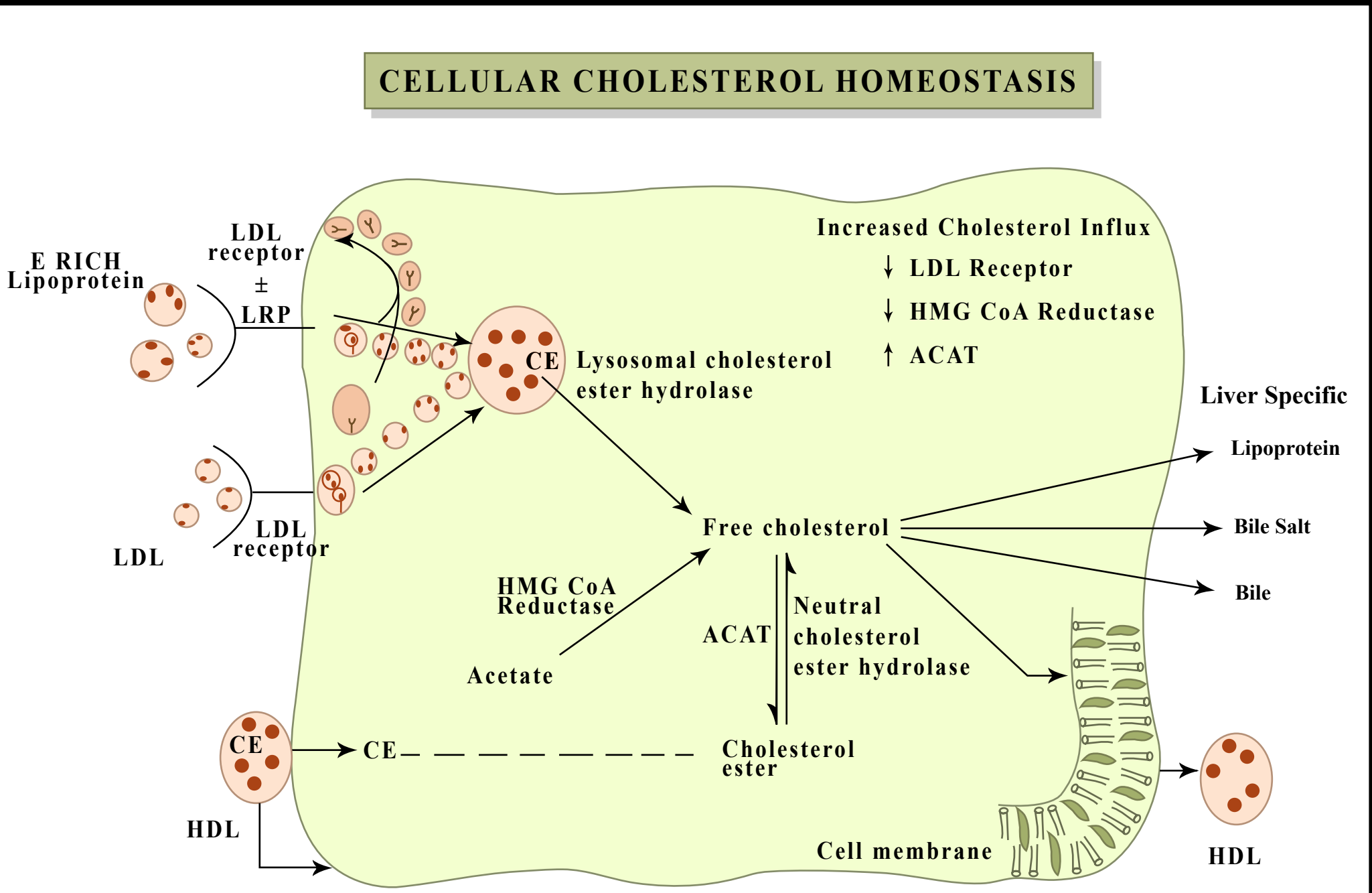

Figure by MIT OCW.

The Liver And Plasma Lipid Homeostasis

1. All VLDL made in liver.
2. ~ 80% of LDL removed by liver.

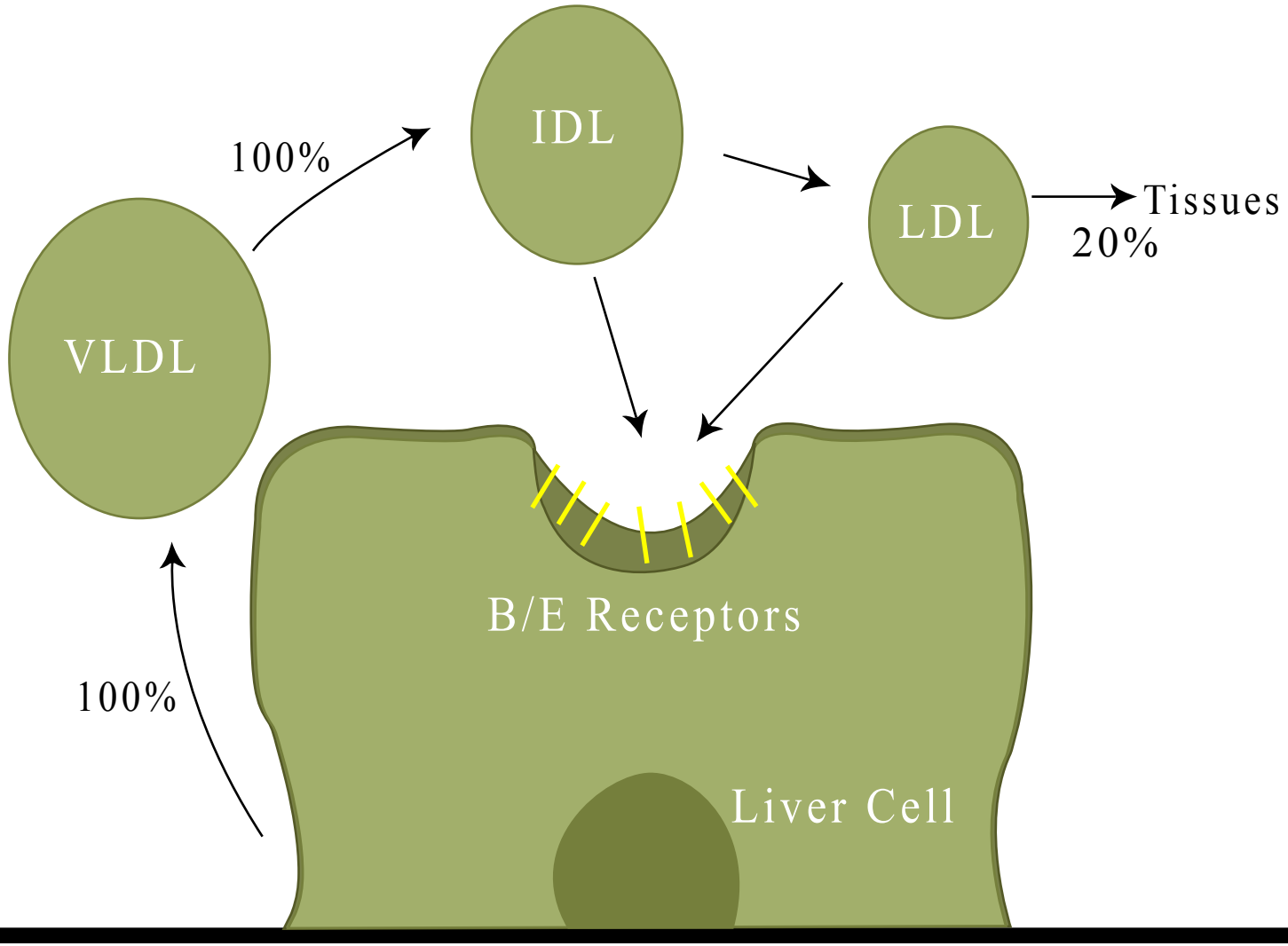

Figure by MIT OCW.

CHEMICAL COMPOSITIONS OF HUMAN PLASMA LIPOPROTEINS

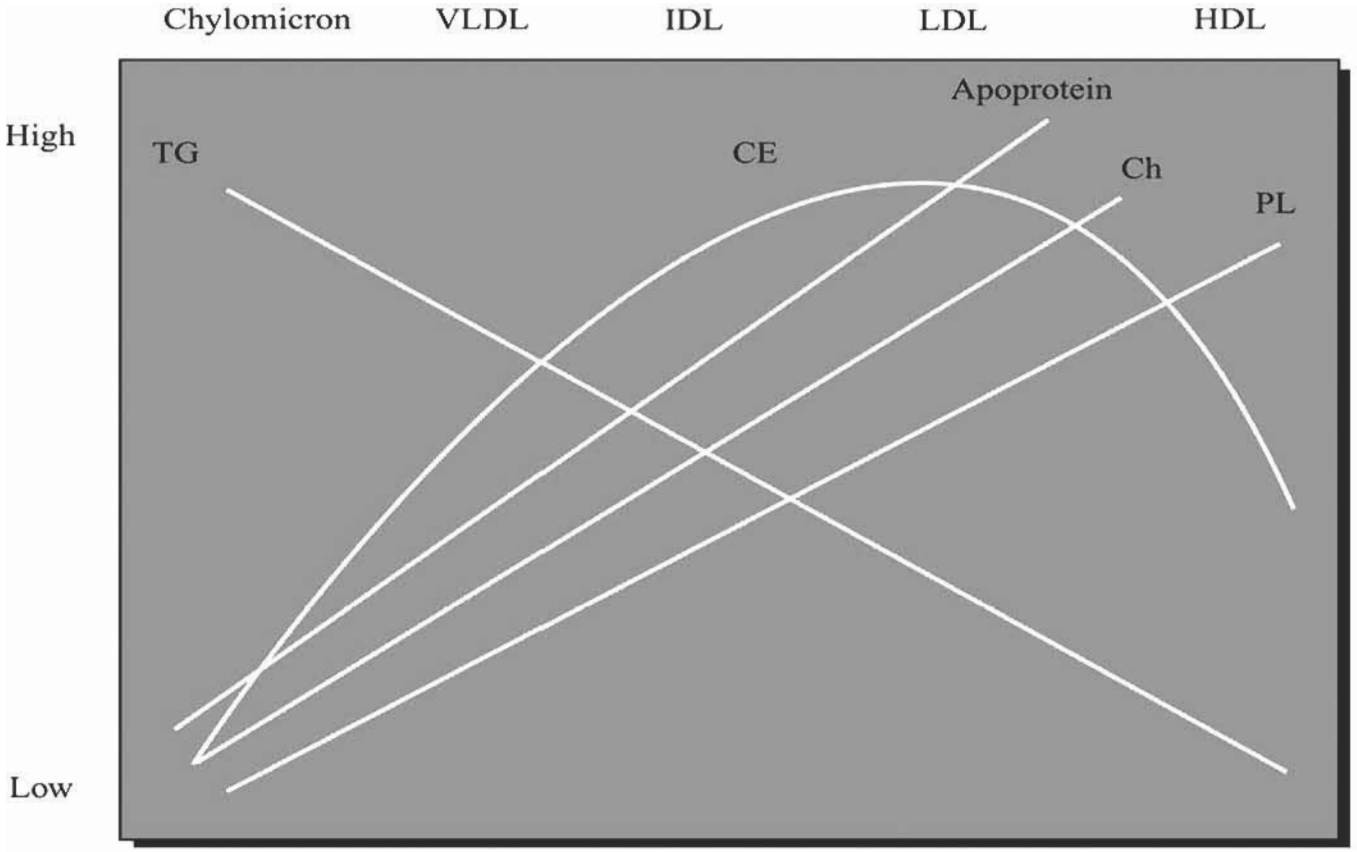

Figure by MIT OCW.

GI Movements of Single Molecules: Examples

	Bile Salts (soluble)	**Cholesterol/Phytosterols** (insoluble)
Enterocytes:	Distal Ileocytes Influx: ASBT, FABP6, OATα/β	Proximal > Distal Influx: NPC1L1 Efflux: ABCG5/ABCG8
Transport:	Portal Blood	Lymphatics
Binding:	Albumen, HDL	ChE and free Ch in chylomicrons and nascent HDL
Hepatic Uptake:	NTCP – 80% OATPs – 20%	ApoB/E receptor LRP receptor
Nuclear Control:	FXR/RXR SHP, LRH1	SREBP's LXR/RXR
Biliary Secretion:	BSEP, MRP2	ABCG5/ABCG8, (others unknown)
Facilitators:	Needs intact FIC1 function	Same + hydrophobic "sink" in bile

That’s All Folks!