Plasma (Cell) Membrane

- Composition:
  a. **Phospholipids** (1° component)
  b. **Proteins**: Cellular channels, receptors, anchors & motors
  c. **Cholesterol**: Fluidity regulator
  d. **Glycoproteins & Glycolipids**: Cellular anchors & signals
1. Phospholipids:
   - Amphipathic Phospholipid Property produces:
     a. Phospholipid Bilayer
     b. Membrane semipermeability

   *Phospholipid Bilayer*
   - Hydrophilic surface: Phosphate group
   - Hydrophobic "Core": Hydrocarbon chains
Membrane semipermeability

- Membrane *innately restricts movement* across of MOST substances

1. Permeable substances:
   - A. Small, uncharged molecules (O₂, CO₂, urea)

- B. Lipid soluble molecules: “lipid-like”
  - Steroids, Cholesterol, fatty acids

  Mechanism of action of steroid hormones
  - Hormone enters cell by diffusion across plasma membrane
  - Binds to specific cytoplasmic receptor
  - Translocation to nucleus
  - Alteration in gene transcription
  - Alteration in level of active mediator of effect
2. Impermeable substances:
   - A. Large Non-polar molecules
     - Carbohydrates (glucose), proteins
   - B. Charged substances: Ions & Ionic Molecules
     - Na⁺, K⁺, Cl⁻, Ca²⁺, HCO₃⁻
   - C. Significant Polar Molecules:
     - H₂O

Membrane restricts MOST movement

2. Membrane proteins:
   - A. Integral membrane proteins: Permanently associated with the membrane
     - Anchors: Allowing stabilization of the cell
• **Channels**: Allowing *exchange* through the cell of impermeable substances
• **Receptors**: Allowing *communication* with the cell

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**G Protein Coupled Receptors**

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• **B. Peripheral Membrane proteins**: Temporarily associated with the membrane
  • **Messaging proteins**: Regulate cell signaling
Essential fatty acids: not produced by the body

Eicosanoids: Signaling molecules made by modifying Arachidonic acid (20:4C)

Omega 3 vs Omega 6 health affect

<table>
<thead>
<tr>
<th>Omega-3</th>
<th>Omega-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Good&quot; Eicosanoids</td>
<td>&quot;Bad&quot; Eicosanoids</td>
</tr>
<tr>
<td>Prevents blood clots caused by platelet aggregation</td>
<td>Promotes blood clots caused by platelet aggregation</td>
</tr>
<tr>
<td>Causes dilation (opening) of blood vessels</td>
<td>Causes constriction (closing) of blood vessels</td>
</tr>
<tr>
<td>Reduces pain</td>
<td>Increases pain</td>
</tr>
<tr>
<td>Decreases cell division</td>
<td>Increases cell division</td>
</tr>
<tr>
<td>Enhances the immune system</td>
<td>Depresses the immune system</td>
</tr>
<tr>
<td>Improves brain function</td>
<td>Depresses brain function</td>
</tr>
</tbody>
</table>

Immune cell membrane composition

Omega-6 and omega-3 fatty acid contents of human mononuclear cell phospholipids

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>% of total fatty acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic acid (18:2ω-6)</td>
<td>10</td>
</tr>
<tr>
<td>DGLA (20:3ω-6)</td>
<td>2</td>
</tr>
<tr>
<td>Arachidonic acid (20:4ω-6)</td>
<td>20</td>
</tr>
<tr>
<td>α-Linolenic acid (18:3ω-3)</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>EPA (20:5ω-3)</td>
<td>0.5</td>
</tr>
<tr>
<td>DHA (22:6ω-3)</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Decrease inflammatory molecules
LOW pro-inflammatory potential
Increase Anti inflammatory agents
Summary

- Human inflammatory cells typically contain a relatively high amount of arachidonic acid → precursor of inflammatory eicosanoids
- Omega-3 fatty acids are readily incorporated into inflammatory cells
- Fatty acid composition of inflammatory cells affects membrane fluidity, membrane raft formation, signal transduction processes leading to gene expression, and the pattern of lipid and peptide mediators produced
- Through these effects fatty acids can affect inflammatory cell responses and inflammatory processes
- Fish oil (rich source of ω-3 PUFAs) exerts anti-inflammatory actions in vivo → the findings are clinically relevant

Fish oil (FO) supplementation in humans results in the incorporation of omega-3 fatty acids (FAs) eicosapentaenoic acid (EPA; C20:5) and docosahexaenoic acid (DHA; C22:6) into skeletal muscle membranes. However, despite the importance of membrane composition in structure–function relationships, a paucity of information exists regarding how different muscle membranes/regions respond to FO supplementation. Therefore, the purpose of the present study was to determine the effects 12 weeks of FO supplementation (3g EPA/2g DHA daily) on the phospholipid composition of sarcoplasmic and mitochondrial fractions, as well as whole muscle responses, in healthy young males. FO supplement increased the total phospholipid content in whole muscle (57%; p < 0.05) and the sarclemma (38%; p < 0.05), but did not alter the content in mitochondria. The content of omega-3 FAs, EPA and DHA, were increased (–3–4 fold) in whole muscle, and mitochondrial membranes, and as a result the omega-6/omega-3 ratio were dramatically decreased (–3–6 fold), while conversely the unsaturation index was increased. Intriguingly, before supplementation the unsaturation index (UI) of sarcoplasmic membranes was ~3 times lower (p < 0.001) than either whole muscle or mitochondrial membranes. While supplementation also increased DHA within sarcrolemnal membranes, EPA was not altered, and as a result the omega-6/omega-3 ratio and UI of these membranes were not altered. All together, these data revealed that mitochondria and sarcrolemal membranes display unique phospholipid compositions and responses to FO supplementation.

Overall Membrane Functions:

1. Physical isolation & Self identity: Phospholipid bilayer prevents movement across membrane
2. Regulation & Homeostasis: Proteins control movement in & out of cell

3. Sensitivity: Allows outside environment to interact with the cell

4. Structural support: Proteins shape membrane and stabilize cell
Molecular Movement:

- **Brownian Movement**: Innate random movement of matter due to the bombardment by other particles.
  - Degree of motion depends on quantity of energy in system.

Brownian Motion

2nd Law of Thermodynamics:

- “Universe naturally becomes more disorganized”
  - **Entropy**: Degree of randomness
    - All naturally occurring motions function to increase Entropy.
Molecular Movement

- Diffusion: Movement
  - From a high concentration to a low concentration
  - From an organized state to a less organized state
  - Down a concentration gradient

Diffusion results in system \textit{equilibrium}
- All constituents equally distributed
- Randomly distributed
- High entropy
Clinical Basis: Dialysis

Cellular membrane transport:
1. Passive transport: Cell invests NO energy in moving substances across membrane
2. Active Transport: Cell invests energy in moving substance across membrane
Cells expend NO energy in transport of substances

A. Passive diffusion: Substances diffuse directly through the membrane

B. Facilitated diffusion: Substances diffuse through protein channels
Active Transport:

- Cells expend energy in transport of substances
- Concentration gradient is created or increased

A. Primary Active Transport:
- Energy is supplied in the form of ATP

B. Secondary Active Transport: “Co-transport” or “Coupled Transport”
- Energy is supplied by another substance's concentration gradient
1. Passive transport: Movement results in *decreasing* of a concentration gradient
2. Active Transport: Movement results in *increasing* of a concentration gradient
Osmosis: Diffusion of solvent (water)

- Movement from **HIGH solvent** concentration to **LOW solvent** concentration

![Diagram of osmosis]

- Movement from **LOW solute** concentration to a **HIGH solute** concentration
  - *Water moves to DILUTE*
1. EXGERGONIC Reactions: Release Energy
   • “Dismantling” reactions: Breaking Bonds
   • Reactants:
     * Contain more energy than products
     * Greater degree of organization
     * Greater number of bonds

Glucose → 2 Pyruvic Acids + Energy
2. **ENDERGONIC Reactions: Consume Energy**

   - "Building" reactions: Making Bonds
   - **Products:**
     - * Contain more energy than reactants
     - * Greater degree of organization
     - * Greater number of bonds
     - ✔ Construction of bonds requires energy

   ![Endergonic Reaction Diagram]

**Activation Energy:**

- Energy required for a reaction to proceed at **biologically appropriate rates**

![Activation Energy Diagram]

- Only **small numbers** of reactants possess **enough energy** to become products

![Activation Energy Diagram]
Question:
How can cells increase product formation?

or

Increase Reaction Rates

Answers:

1. Increase energy in reaction system
   - Heat

- Not Feasible: Adverse cellular affects
  - Denaturation

- Unable to regulate which reactions proceed
  - Accelerates all reactions
2. **Enzymes**: Specialized **Proteins** + (RNA)

- **Catalysts**: Molecules which:
  a. Increase rate of reactions
  b. Are *not changed* in reaction
  c. Do not change *nature of the reaction*

- **Function**: *Lower Activation Energy*

  ![Decrease Energy Barrier](image)
More reactants have energy to form products.

- Enzymes increase reaction rate without increasing temperature.

- Function as biological ON switches for cellular reactions.

- Enzymes allow cells to regulate biochemical reactions.
Enzyme Mechanism of Action

- Increase the likelihood of a chemical reaction
  - A. Hold substrates in close proximity
  - B. Stress existing bonds and / or
  - C. Encourage “new” bonds (or stabilize transition state)

Enzyme: Specific 3-D shape & Chemical nature

- Active site: Substrate held both physically and chemically

Enzyme Substrate Complex: Enzyme binds substrate
  - Stresses existing bonds and / or
  - Encourages “new” Bonds

Lock and Key Hypothesis:
  - Lock: Enzymes
  - Keys: Substrate
1. Turning **ON & OFF** reactions
2. Assist enzyme function
   - **Cofactors**: Non-protein chemicals required for a protein's biological activity

| A. Ions & inorganic molecules: Ca$^{2+}$, Mg$^{2+}$, Zn$^{2+}$ |
| Function: Bind enzymes & can: |
| * Help form **functional active site** |
| * Help **hold**: stress, encourage substrate bonds |

**DNA polymerase:**
- **Cofactor**: Magnesium ion

Two metal ions bound to DNA polymerase catalyze nucleotide addition.
B. **Coenzymes:** “** Helpers**” Non-protein organic molecules Assisting enzyme function

- Function as **reaction shuttles between enzymatic reactions and locations**

**Vitamins:** Niacin, Riboflavin, Pantothenic acid

**Vit B3**  **Vit B2**  **Vit B5**

**Moves e**

**NAD**: Electron shuttle within cell

**Co–enzymeA**: mitochondrial shuttle