Coupled in vitro and computational model of the skin

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Skin

Cells are dead; represented only by flat membranous sacs filled with keratin. Glycolipids in extracellular space.

Cells are flattened; organelles deteriorating; cytoplasm full of lamellated granules (release lipids) and keratoxyline granules.

Cells contain thick bundles of intermediate filaments made of pre-keratin.

Cells are actively mitotic stem cells; some newly formed cells become part of the more superficial layers.

(Diagram of skin layers and cellular components)

(A adapted from http://www.imperial.edu/~thomas.morrell/cha_5_marieb_integumentary.htm on 21 June 2011)
Skin disease

- Atopic dermatitis (eczema)
  - 15%-20% children in developed countries
- Psoriasis
- Ichthyosis vulgaris
- Epidermises blistering disorders
How to study the skin

http://thereconditequetzal.wordpress.com/2010/10/

http://www.pgbeautygroomingscience.com/innovations-in-technology-clinical-testing.html

http://www.ecademy.com/node.php?id=157022
Agent-based model

• Each cell = single entity (sphere)

• Rules define cell behaviour and interaction with neighbours, governed by environment (nutrients)

• Effect of physical forces

• FLAME
<table>
<thead>
<tr>
<th>Keratinocyte agent</th>
<th>Agent type</th>
<th>Colour code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 0: Stem Cell</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1: Progenitor Cell</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2: Stratum Spinosum Cell</td>
<td></td>
<td></td>
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<tr>
<td>Type 3: Stratum Granulosum Cell</td>
<td></td>
<td></td>
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<tr>
<td>Type 4: Stratum Corneum Cell</td>
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<td></td>
</tr>
<tr>
<td>Type 5: Skin flake (dead cell)</td>
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<td></td>
</tr>
<tr>
<td>Basement membrane agent</td>
<td>Type 10: Surface tile / basement membrane</td>
<td></td>
</tr>
</tbody>
</table>

(Bullock, A., experiment, 2011)

10um (Koehler et al. 2011)

200um
Biological rules – cell cycle

- Only basal cells (stem cell and progenitor cell) can divide

http://cyberbridge.mcb.harvard.edu/mitosis_3.html
Biological rules - differentiation

If (cell leave basal layer) {
    basal -> spinosum
} else if (t==T1) {
    spinosum -> granulosum
} else if (t==T2) {
    granulosum -> corneum
}
Physical forces

• Newton’s Second Law

\[ m \frac{d^2 \mathbf{u}_i}{dt^2} + c_i \frac{d \mathbf{u}_i}{dt} = \sum_{j=1}^{n} F_{ij} \]

• The RHS force term

\[ F_{ij} = F_{ij}^r + F_{ij}^a \]
Physical rules

Cell-cell repulsive force

Cell-cell adhesive force within 5um apart (Walker, et al. 2010)

Cell-substrate

Cell-cell repulsive force
Results
Homeostasis with H&E

Day 3

Day 5

Day 7

Day 14

Day 21
Acknowledgements

- Prof. Sheila MacNeil
- Prof. Rod Smallwook
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