



**FIGURE 1.1** Schematic drawing of the skin and its lipid structure. Section I: Organ-scale drawing of the skin. Section II: Tissue-scale drawing of the epidermis. Section III: Molecular-scale drawing of the skin's barrier lipid structure.

The characteristic features of the stratum corneum lipid composition (Wertz and Norlén, 2003) are (1) extensive compositional heterogeneity with broad, but invariable, chain length distributions (20 to 32C; peaking at 24C) in the ceramide fatty acid and free fatty acid fractions; (2) almost complete dominance of saturated very long hydrocarbon chains (C20:0 to C32:0); and (3) large relative amounts of cholesterol (about 35 mol%).

These features are the same as those typically stabilizing lipid gel phases. It has therefore been proposed that the skin's lipid structure exists as a single and coherent gel phase (Norlén, 2001b). The viscous gel-like behavior of the lipid structure has been demonstrated *in situ* by its remarkable malleability (Iwai et al., 2012) and *in silico* by its gel-like molecular dynamics (Lundborg et al., 2018a).

### 1.3 SKIN BARRIER STRUCTURE

Using cryo-electron microscopy of near-native skin sections (skin CEMOVIS) combined with MD simulation and EM simulation, it has been shown that the skin's lipid structure is organized as stacked bilayers of fully splayed ceramides with cholesterol largely associated (about 75 mol%) with