

# 皮膚バリア機能と製剤開発

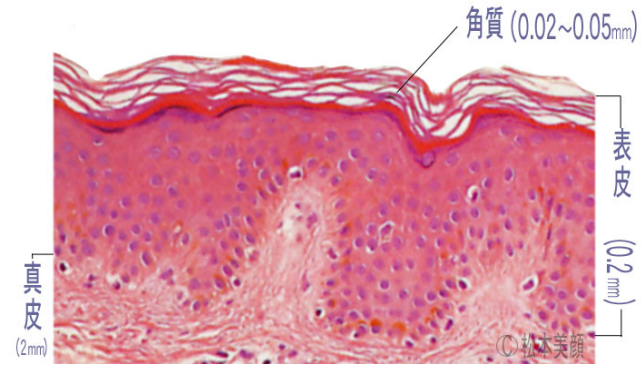
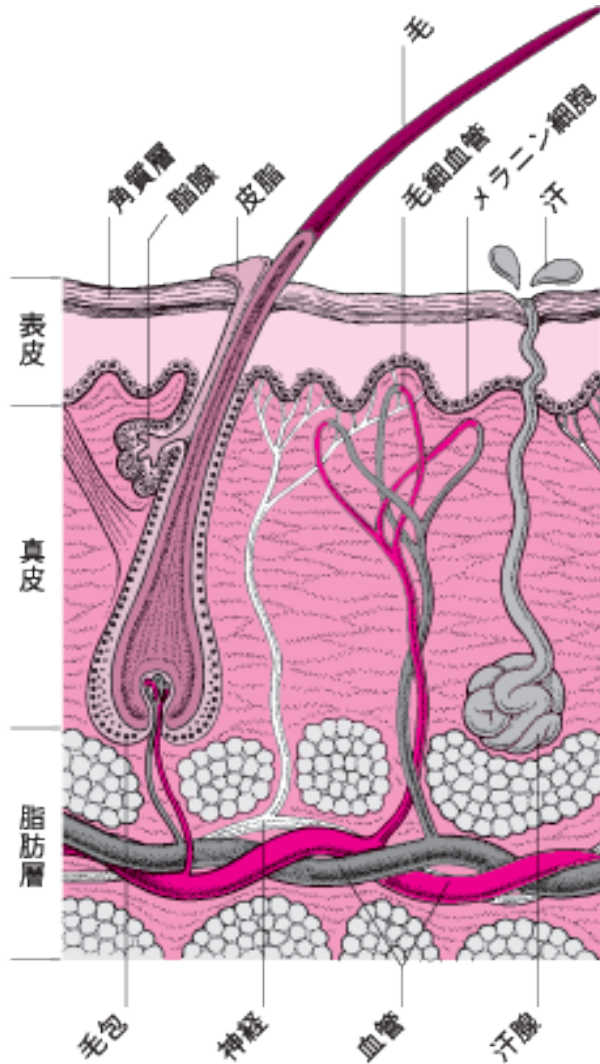


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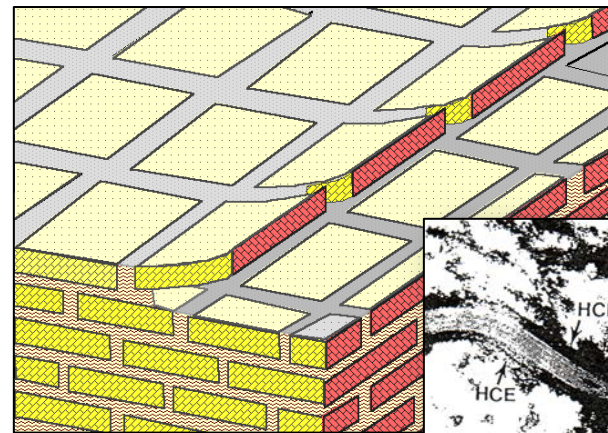
# 内 容

1. はじめに
2. 角層細胞間脂質の構造解析
3. 細胞間脂質の熱特性と製剤成分の適用による変化
4. まとめと将来展望

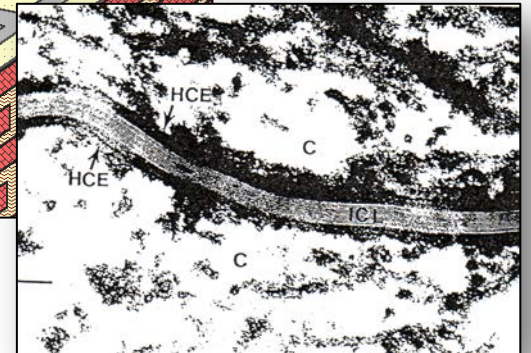
# 皮膚の構造と機能



[http://matsumotobigan.com/nagoya/seiyo/seiyo\\_p/seiyou-kakusitusou.html](http://matsumotobigan.com/nagoya/seiyo/seiyo_p/seiyou-kakusitusou.html)



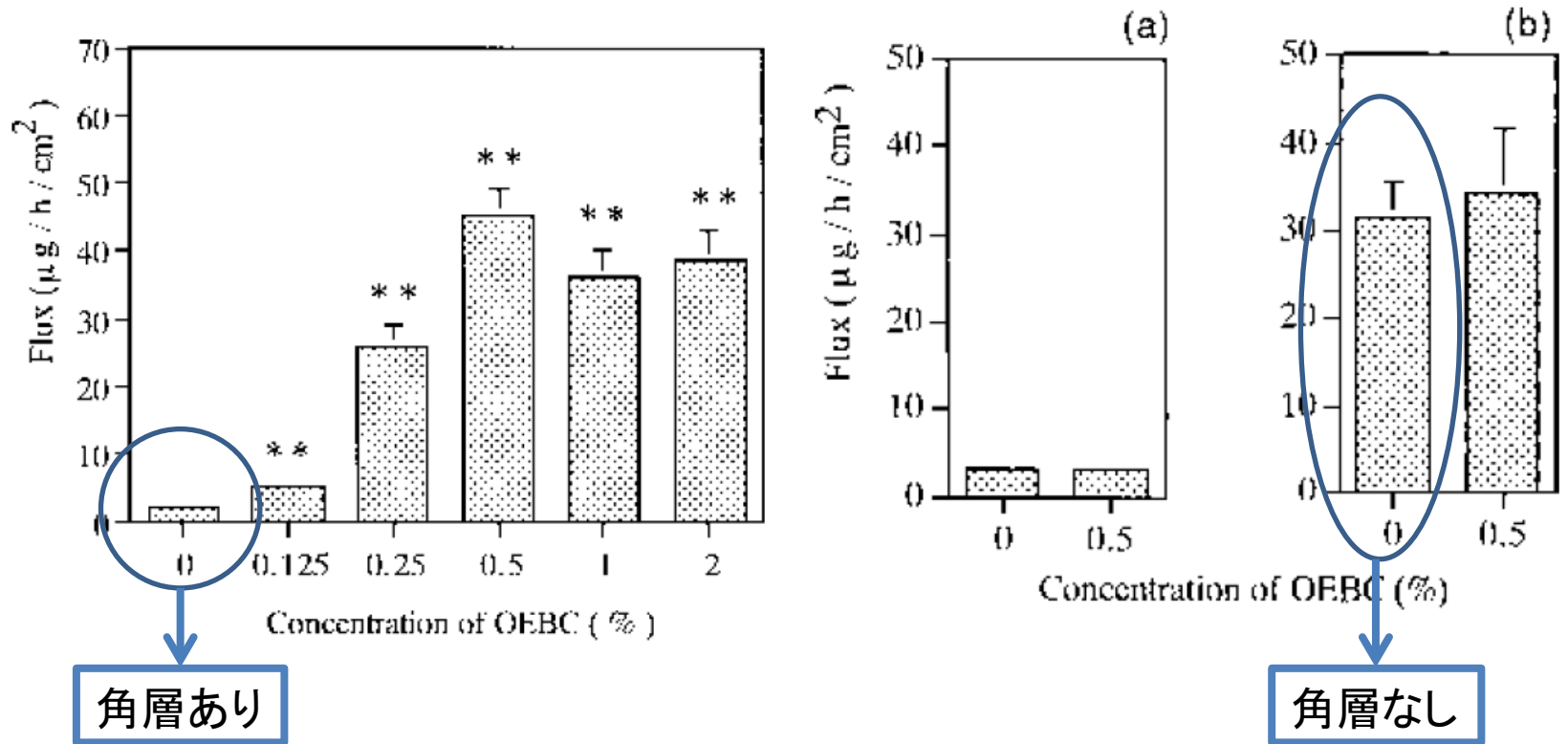
(x 160,000)



<http://mmh.banyu.co.jp/mmhe2j/sec18/ch201/ch201b.html>

P. W. Wertz, et al., *J. Invest. Derm.*, **89**, 419-425 (1987).

# 薬物皮膚透過における角層の役割



# 薬物の経皮吸収促進の方法

## 物理的促進法

- イオントフォレシス
- エレクトロポレーション
- ソノフォレシス
- ジェットインジェクション
- マイクロニードルアレイ

## 化学的促進法

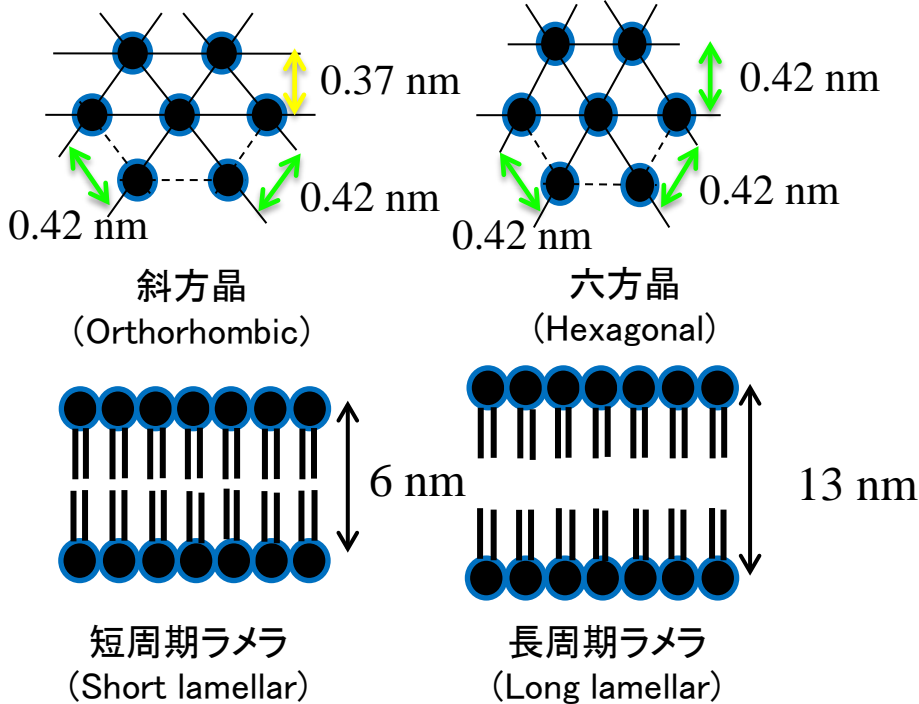
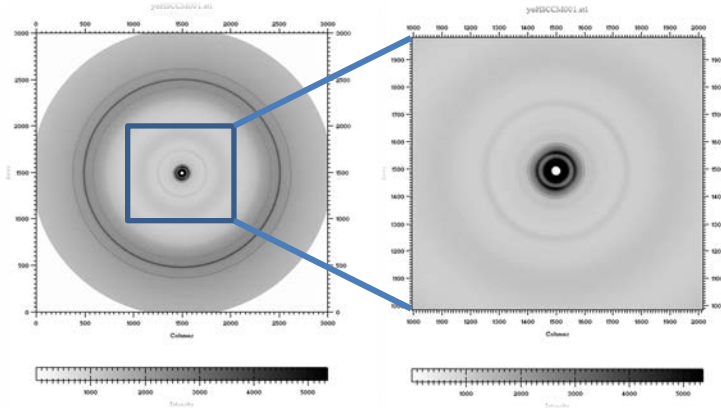
- プロドラッグ
- 経皮吸収促進剤

生体保護作用

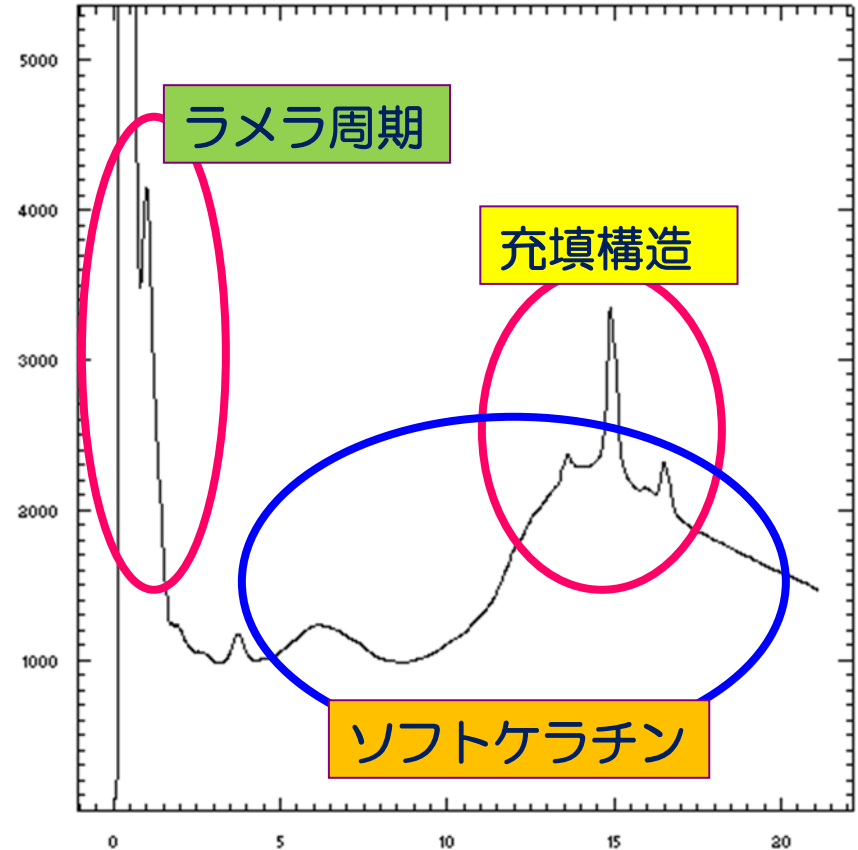
角層のバリア機能

薬物投与部位

# 角層細胞間脂質の構造解析

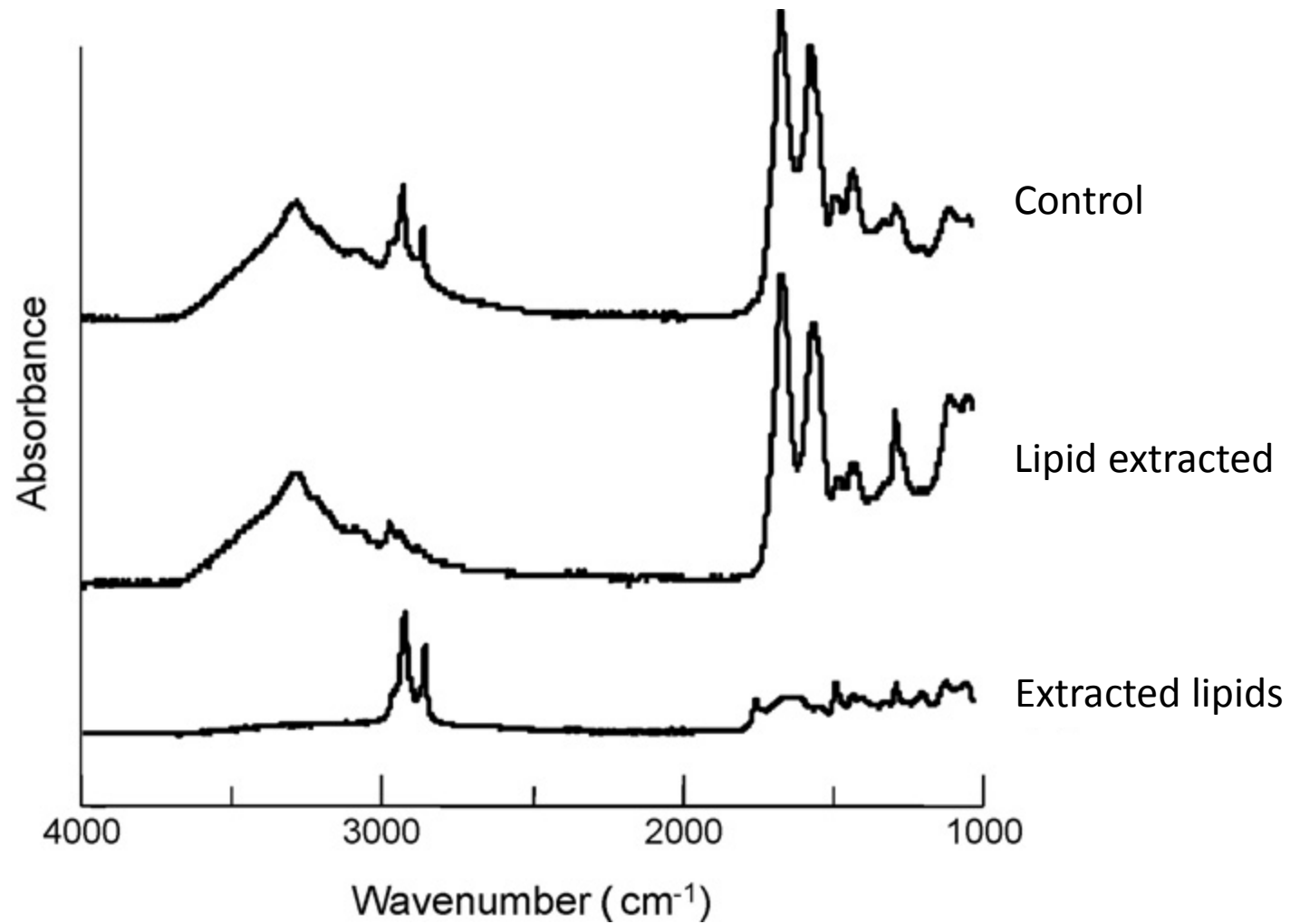


## Human stratum corneum

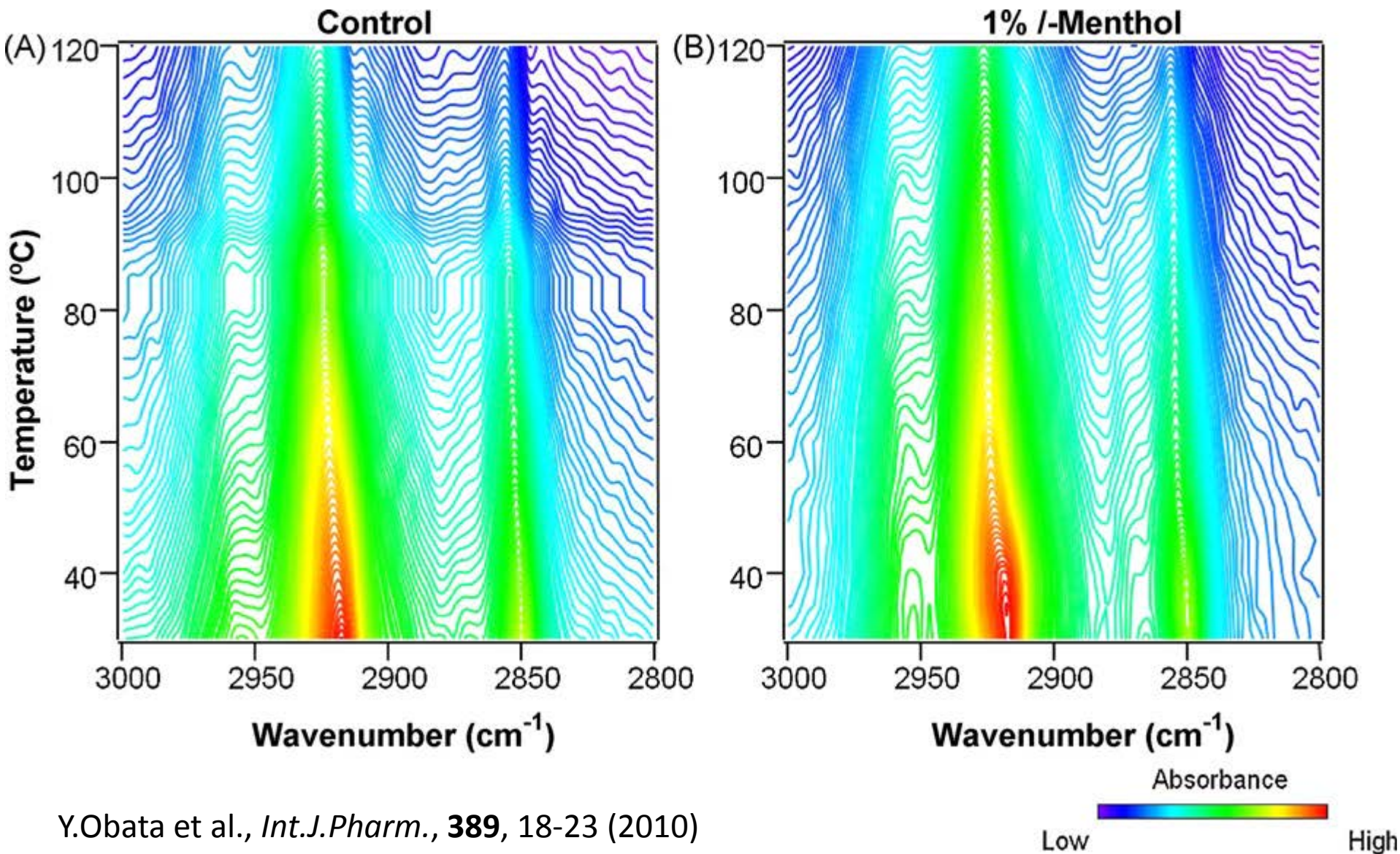


SPring-8 BL40B2  
 Imaging Plate; Exposure 30 s  
 Sample : Stratum corneum (2 mg)

# 角層の赤外分光測定(1)

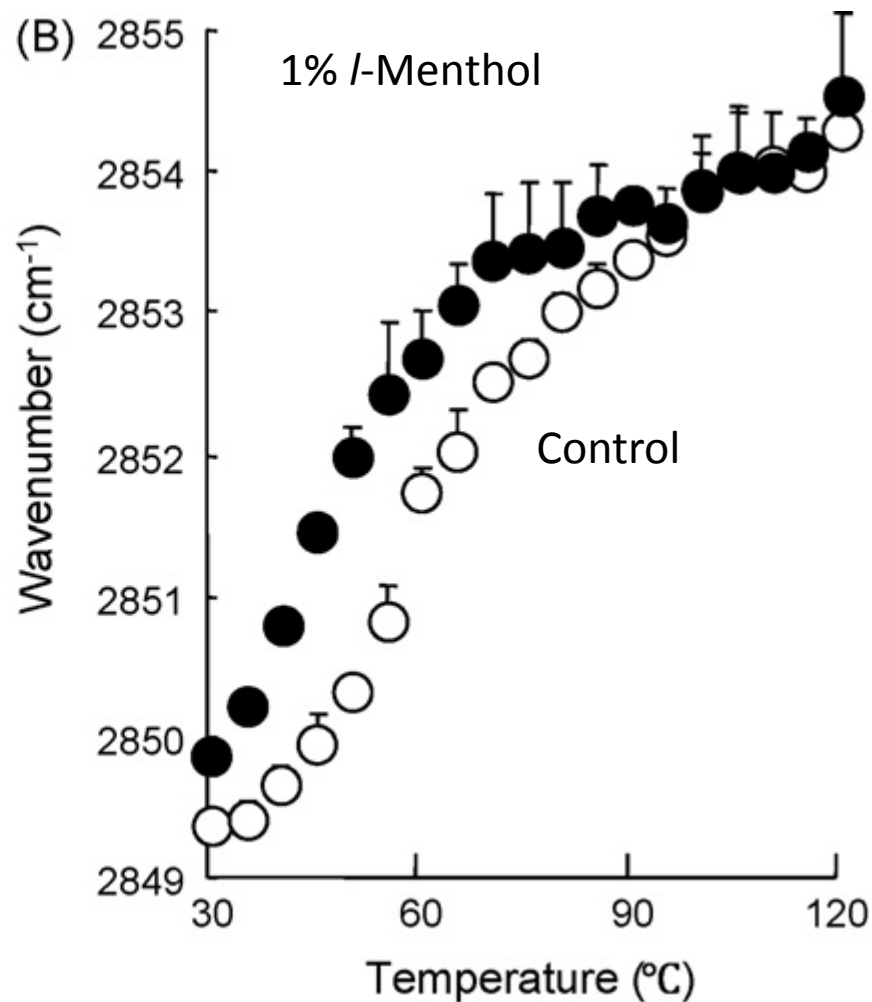
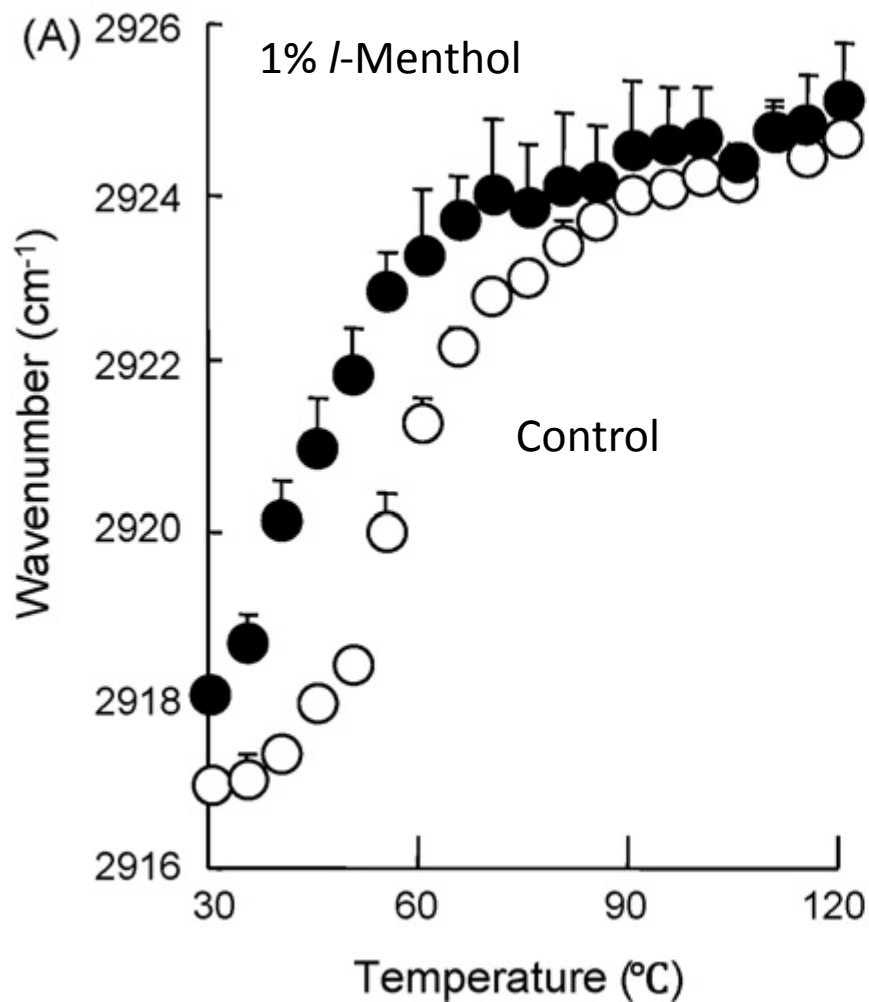


# 角層の赤外分光測定(2)





# 角層の赤外分光測定(3)

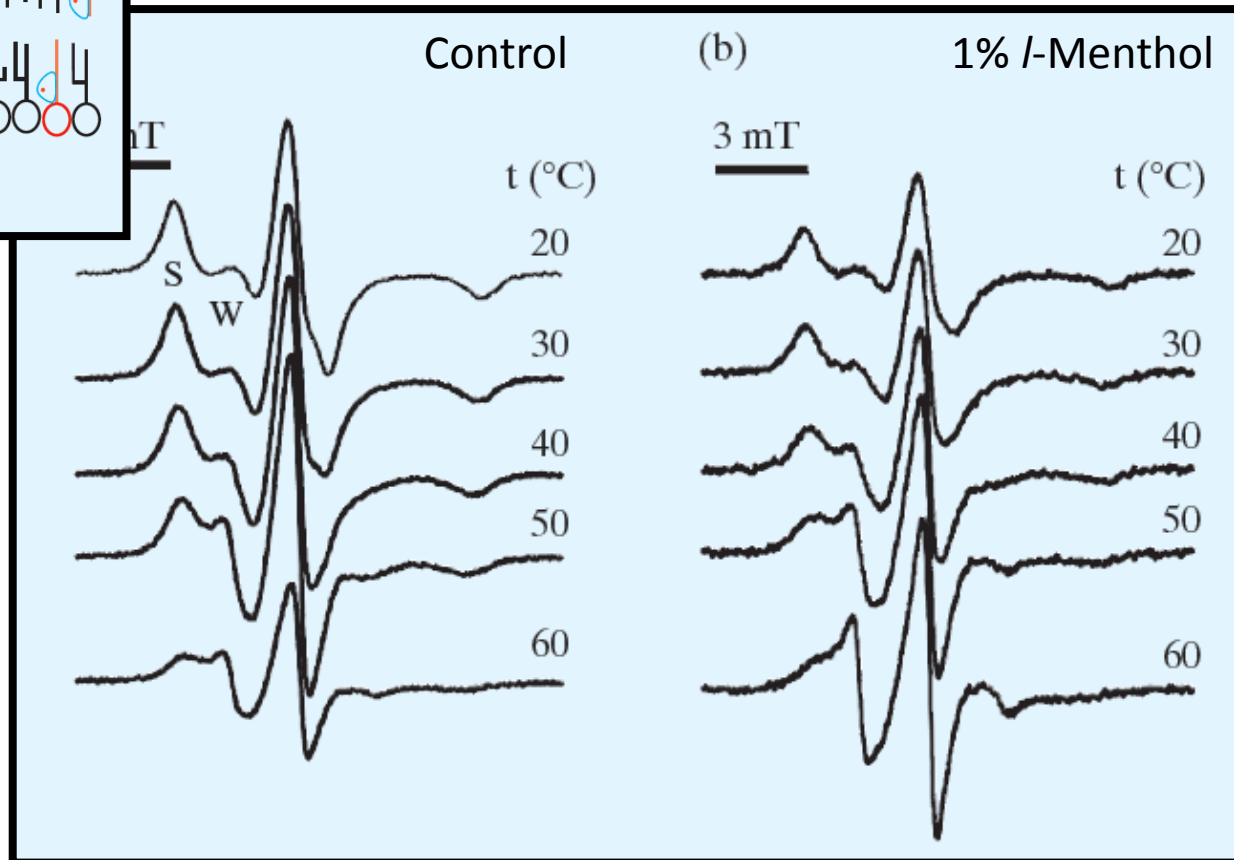
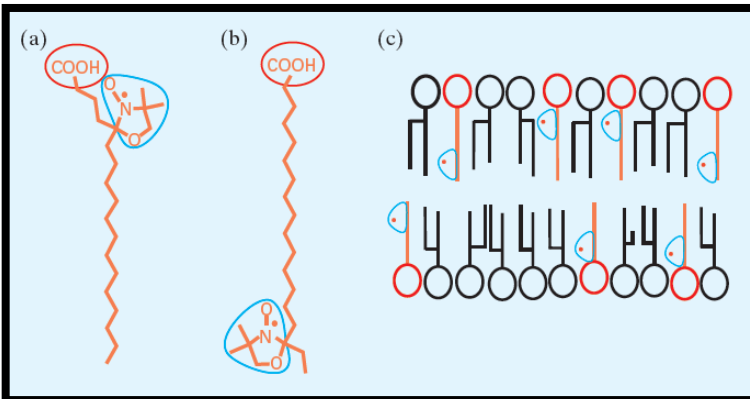


# 角層の赤外分光測定(4)

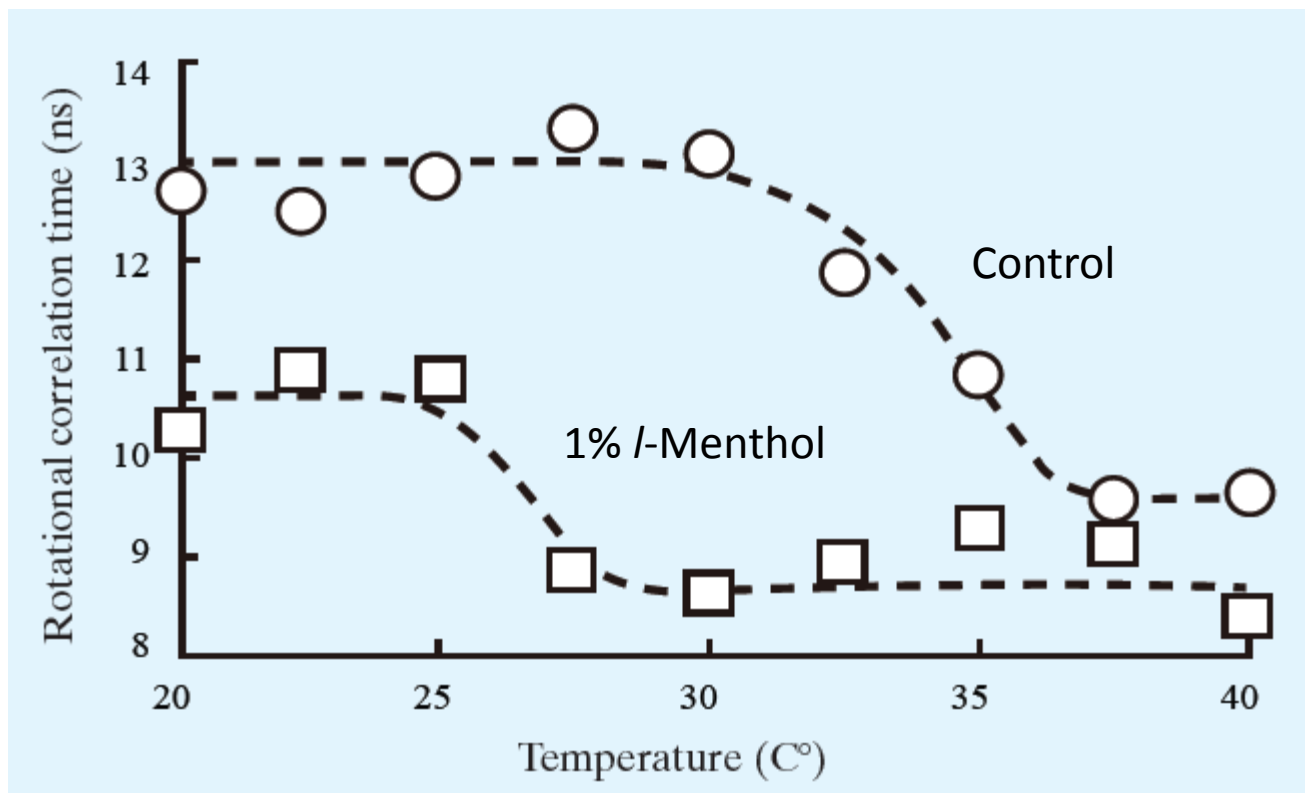
The corresponding temperature required to influence stratum corneum obtained from pretreated stratum corneum at 30 °C.

	Asymmetric stretching	Symmetric stretching
40% ethanol	37.8	36.5
0.5% L-menthol	42.8	38.1
1.0% L-menthol	46.0	43.4

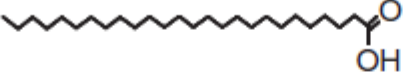
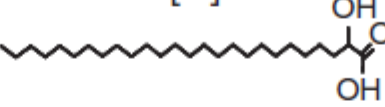
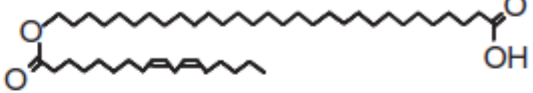
# 電子スピン共鳴による測定(1)



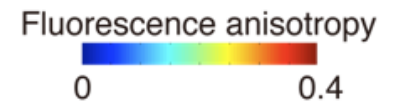
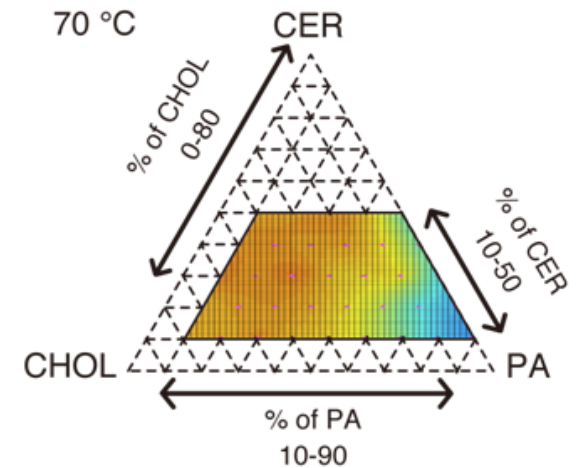
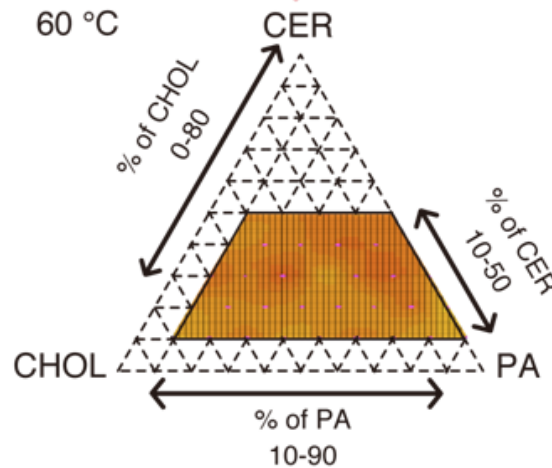
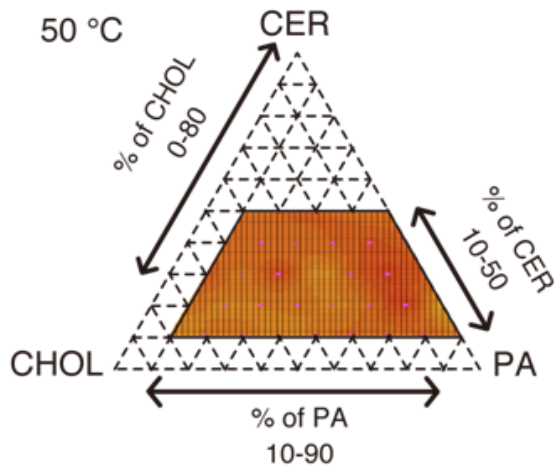
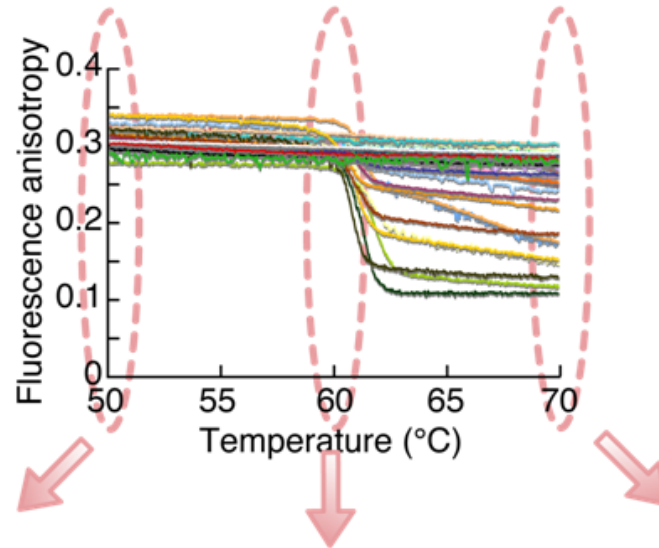
# 電子スピン共鳴による測定(2)



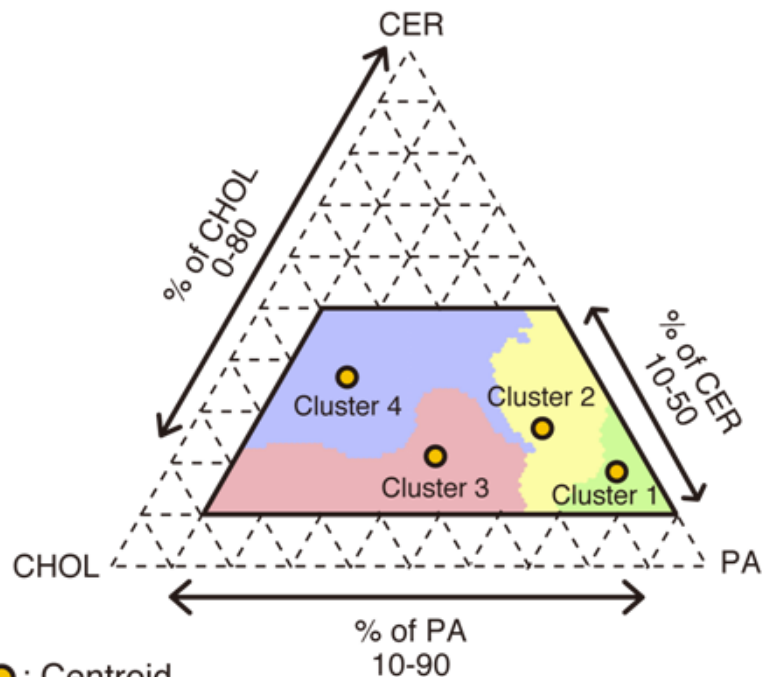
# ヒト細胞間脂質のセラミドの分類

Fatty acid	Non-hydroxy fatty acid [N]	$\alpha$ -Hydroxy fatty acid [A]	Esterified $\omega$ -hydroxy fatty acid [EO]
Sphingoid			
Dihydrosphingosine [DS]	CER[NDS] <span style="background-color: #92d050; padding: 2px 5px;">10</span>	CER[ADS] <span style="background-color: #92d050; padding: 2px 5px;">11</span>	CER[EODS] <span style="background-color: #92d050; padding: 2px 5px;">12</span>
Sphingosine [S]	CER[NS] <span style="background-color: #92d050; padding: 2px 5px;">2</span>	CER[AS] <span style="background-color: #92d050; padding: 2px 5px;">5</span>	CER[EOS] <span style="background-color: #92d050; padding: 2px 5px;">1</span>
6-Hydroxy sphingosine [H]	CER[NH] <span style="background-color: #92d050; padding: 2px 5px;">8</span>	CER[AH] <span style="background-color: #92d050; padding: 2px 5px;">7</span>	CER[EOH] <span style="background-color: #92d050; padding: 2px 5px;">4</span>
Phytosphingosine [P]	CER[NP] <span style="background-color: #92d050; padding: 2px 5px;">3</span>	CER[AP] <span style="background-color: #92d050; padding: 2px 5px;">6</span>	CER[EOP] <span style="background-color: #92d050; padding: 2px 5px;">9</span>

# 脂質モデルの蛍光異方性



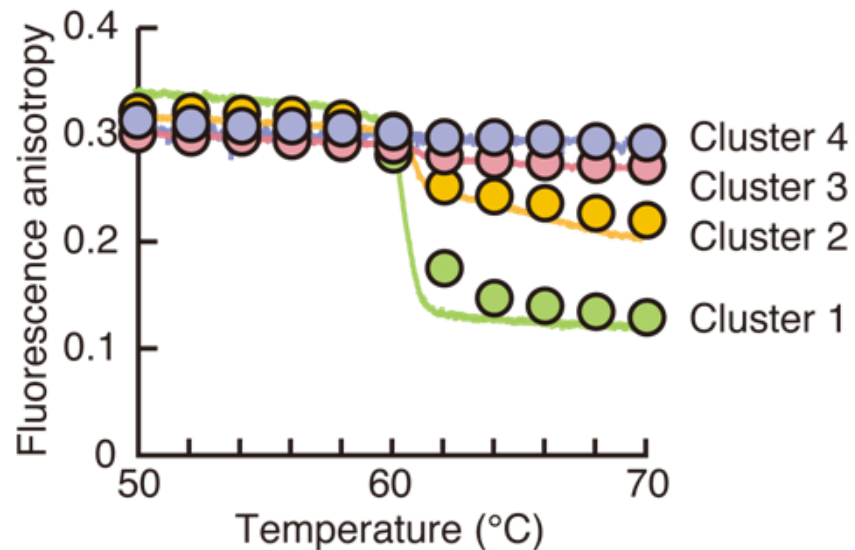
# 特徴的な脂質モデルの抽出



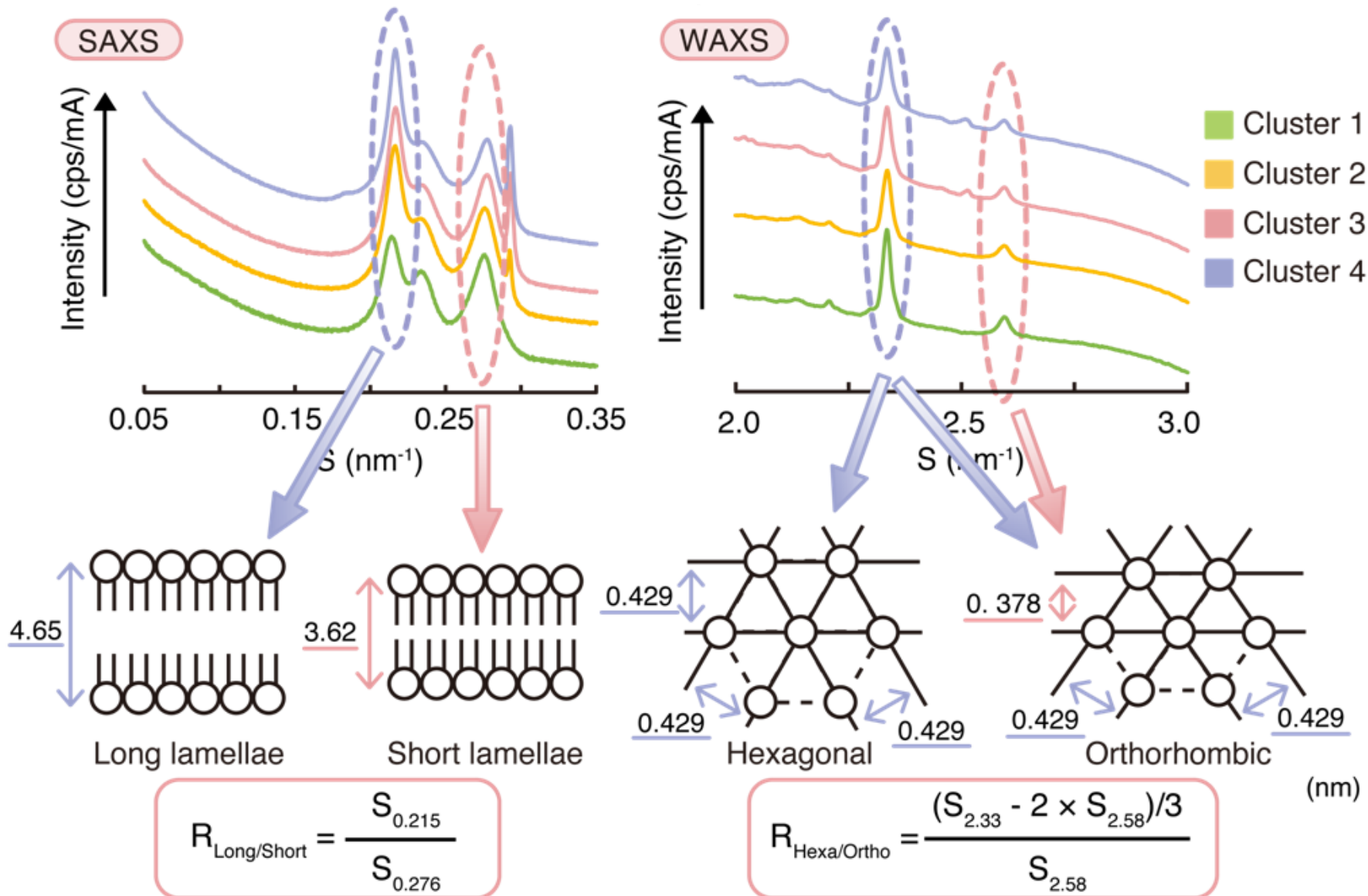
●; Centroid

	CER	CHOL	PA
Cluster 1	17.8	5.5	76.6
Cluster 2	26.4	13.9	59.5
Cluster 3	20.9	35.1	43.8
Cluster 4	36.6	42.7	20.6

(mol%)



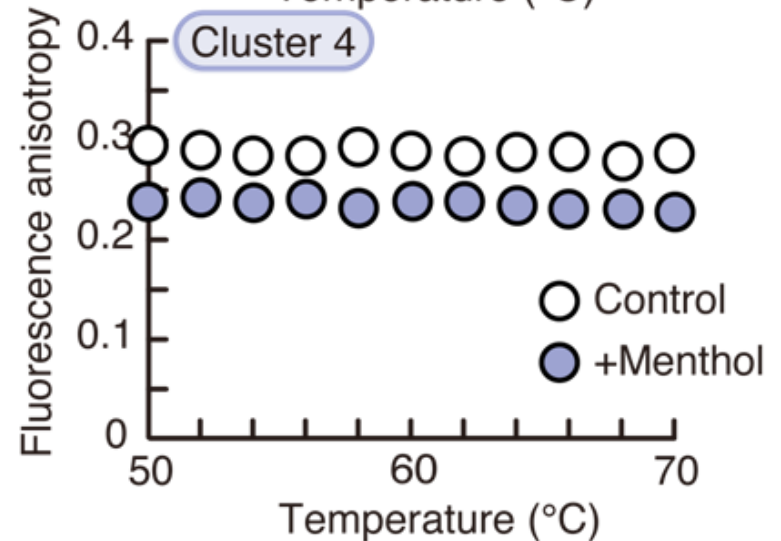
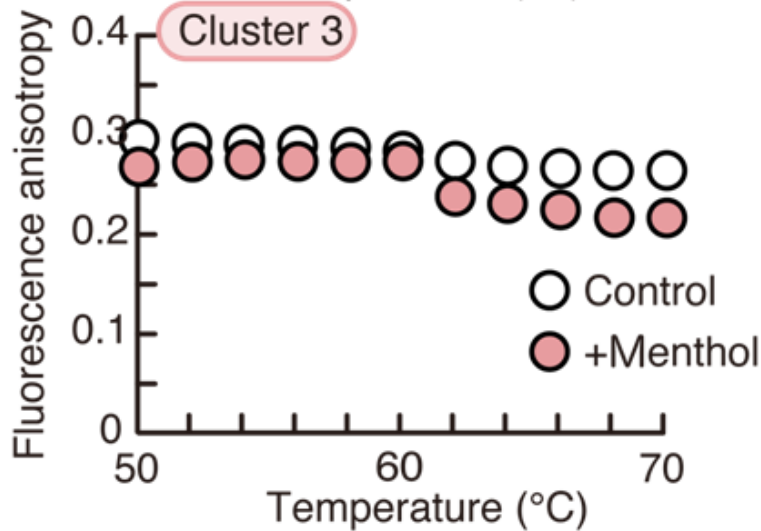
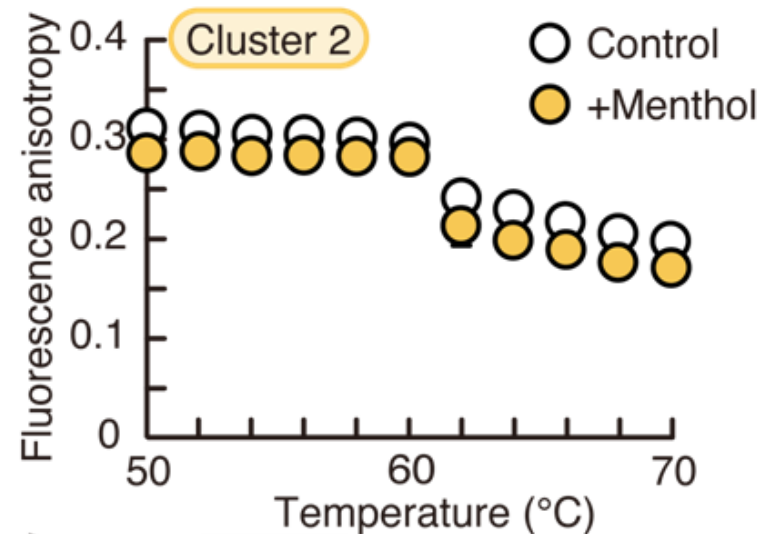
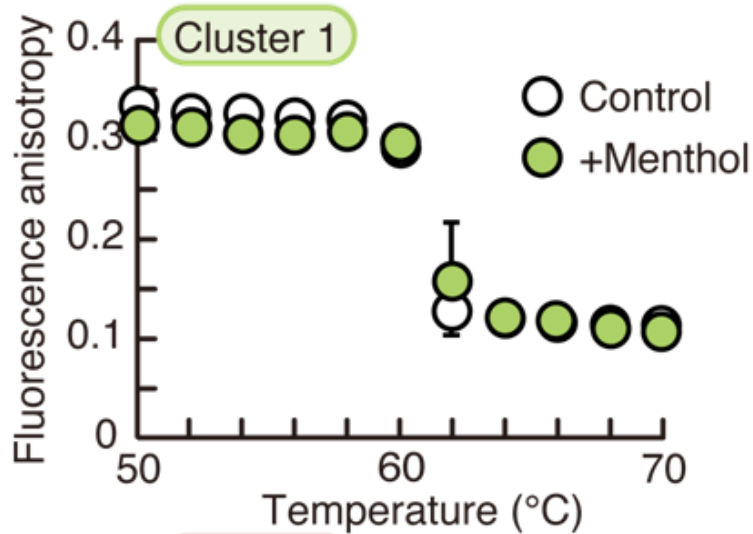
# 脂質モデルのX線回折プロファイル



S; Area of diffraction peak



# 脂質モデルの蛍光異方性



Each point represents mean  $\pm$  S.D. (n = 3)

# 充填構造に及ぼすメントールの影響

