Amphiphilic Homochiral Oligopeptides Generated via Phase Separation of Non-Racemic \(\alpha\)-Amino Acid Derivatives and Lattice-Controlled Polycondensation in a Lipid Environment

I. Weissbuch, I. Rubinstein, M. J. Weygand\textsuperscript{1} K. Kjaer\textsuperscript{1} and M. Lahav

Department of Materials and Interfaces, The Weizmann Institute of Science, 76100-Rehovot, Israel
\textsuperscript{1}Materials Research Department, Risø National Laboratory, 4000 Roskilde, Denmark

An accepted scenario for the early formation of the biopolymers of Life from abiotic atomic or molecular components invokes an essential role played by early membrane-like materials. It does not, however, consider the formation of homochiral polymers from racemates or from non-racemic amphiphilic activated \(\alpha\)-amino acids. Our model environment consists of self-assembled monolayers of 1,2-dipalmitoyl-\textit{rac}-glycerol (DPG) or 1,2-dipalmitoyl-\textit{rac}-phosphatidyl-ethanolamine (DPPE) at the air-water interface. The process of phase separation and polycondensation of the racemic thioethyl esters of \textit{N}\textsuperscript{\textit{\epsilon}}-stearoyl-lysine (C\textsubscript{18}-TE-Lys) and of \(\gamma\)-stearyl-glutamic acid (C\textsubscript{18}-TE-Glu) occurring within monolayers of \(R,S\)-DPG and \(R,S\)-DPPE at the air-water interface was studied by grazing incidence X-ray diffraction (GIXD), corroborated with a determination of the diastereoisomeric composition of the oligopeptide (oligo-C\textsubscript{18}-Lys and oligo-C\textsubscript{18}-Glu) products by matrix-assisted laser-desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) using deuterium enantio-labeling.\textsuperscript{[1]}

The GIXD patterns measured from 1:1 (mol) mixtures of either \(R,S\)-DPG or \(R,S\)-DPPE with \(R,S\)-C\textsubscript{18}-TE-Lys (Fig. 1a, b) demonstrate phase separation. One phase corresponds to the self-assembled (\(R,S\))\textsuperscript{\textit{\epsilon}}-TE-Lys crystallites, very similar to that measured in the absence of DPG (Fig. 1c). The second phase arises from either the DPG (Fig. 1d) or DPPE (Fig. 1f) crystallites and only one Bragg peak is visible, when compared to the corresponding patterns measured from the pure lipids (Fig. 1d, f). The surface occupancy of the (\(R,S\))-C\textsubscript{18}-TE-Lys crystallites was only one third of the monolayer total area and their crystalline coherent lengths were affected, being reduced by the presence of the lipid.

Lattice-controlled polycondensation within the 2D crystallites was catalyzed by aqueous solutions of Ag\textsuperscript{+} or I\textsubscript{2}/KI injected beneath the monolayer and yielded mixtures of diastereoisomeric oligopeptides (up to six to eight repeat units) with enhanced relative abundance of those containing homochiral sequences, as analyzed by MALDI-TOF MS.\textsuperscript{[2]} The GIXD pattern of the film was measured also two hours after injection of the Ag\textsuperscript{+} aqueous solution of the catalyst beneath the film (Fig. 1e) showing again phase separation between product phase and the DPPE phase. The reason for selecting DPPE was that it was anticipated (and indeed experimentally found) that its primary amine group would be a nucleophile that would initiate the polycondensation of the C\textsubscript{18}$^\text{\textit{\epsilon}}$-TE-Lys to yield oligopeptides covalently-linked at the carboxylate end with a DPPE molecule. These results provide evidence that the 2D crystallites of the monomer are embedded within the phospholipid film.

![Chemical Structures](image-url)
Figure 1: GIXD patterns, $I(q_{xy}, q_z)$, measured from the self-assembled 2D crystallites of: (a, b) 1:1 (mol) mixtures of $R,S$-C$_{18}$-TE-Lys with $R,S$-DPG and $R,S$-DPPE; (c) pure $R,S$-C$_{18}$-TE-Lys; (d) pure DPG; (e) 1:1 mixtures of $R,S$-C$_{18}$-TE-Lys with DPPE after 2hrs reaction in the presence of Ag$^+$ catalyst; (f) pure DPPE.

The GIXD patterns measured from 1:1 mixtures of either $R,S$-DPG or $R,S$-DPPE with $R,S$-C$_{18}$-TE-Glu (Fig. 2a,b) demonstrate again the occurrence of the phase separation. One phase corresponds to the self-assembled $(R,S)$-C$_{18}$-TE-Glu 2D crystallites and is very similar to that measured in the absence of DPG (Fig. 2c). The second phase arises from the $(R,S)$-DPG (Fig. 1d) or $R,S$-DPPE crystalline phase (Fig. 1f). Within the lipid environment, the crystalline coherent length of $(R,S)$-C$_{18}$-TE-Glu was reduced.

Figure 2. GIXD patterns, $I(q_{xy}, q_z)$, measured on water at 4 $^\circ$C, from the self-assembled 2D crystallites of: (a, b) 1:1 (mol) mixtures of $R,S$-C$_{18}$-TE-Glu with $R,S$-DPG and $R,S$-DPPE; (c) pure $R,S$-C$_{18}$-TE-Glu. The Bragg peaks are labeled $\{h,k\}$ Miller indexes and the subscripts RS refer to the C$_{18}$-TE-Glu phase.

This work was supported by the IHP-Contract HPRI-CT-1999-00040/2001-00140 of the European Commission.

References