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Research Article

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Cyclopeptide self-assembly simulated epidemic sequential and synchronous complexity

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Abstract

Background: *Epidemic growth curve was one of the epidemiological characteristics, which included sequential and synchronous and their complexity*

Objectives: *Decoding the sequential and synchronous complexities of epidemic outbreaks will help guide the scientific response to the epidemic. Here, the complexities of epidemic sequential and synchronous were simulated from the perspective and method of cyclopeptide self-assembly, and the process of cyclopeptide self-assembly was observed by molecular fluorescence and morphological changes, reflecting the characteristics of the epidemic changes.*

Results: *The results showed that the cyclopeptide, namely cyclo (FWWYYF), self-assembly process took different forms under different concentrations and solvents. At lower concentrations, cyclopeptide molecules simulated the complexity of epidemic sequential and synchronous, while at higher concentrations, cyclopeptide molecules self-assembly also behaves as a non-sequential and non-synchronous composite multimodal model.*

Conclusions: *These results indicated that the complexity of the epidemic outbreaks was not only the complexity of sequential and synchronous, but also the emergence of non-sequential and non-synchronous complex multimodal models. Molecular simulations elucidated why the global pandemic required global solidarity and synchronization.*

Keywords: Cyclopeptide; Molecular Simulation; Sequential; Synchronous; Epidemic Complexity

Introduction

The development history of human epidemiology has proved that the outbreak of any newly emerging infectious disease can only be controlled by fully understanding its epidemiological characteristics and accurately grasping its internal epidemic law. Epidemic growth curve was one of the epidemiological characteristics, which included sequential and synchronous and their complexity (Figure 1). A common feature of many previous studies is that there is only one peak of infection density during each epidemic. However, real data from around the world suggest that in addition to the predominant unimodal feature of infection density, there are complex patterns consisting of two or more peaks [1-4]. The mechanism of the existence of the latter feature needs to be further elucidated. In addition, why can the epidemic spread sequentially in waves, which can only continuously delay the timeline of epidemic prevention and control, while the implementation of synchronous anti-epidemic action is conducive to the epidemic being controlled earlier, saving more lives, and restoring normal economic life? In this paper, the self-assembly of cyclic peptides was observed, the molecular simulation of epidemiological sequence and synchronization complexity, and the fluorescence change law of cyclic peptide molecules and its electron microscopy morphological changes reflected the sequential and synchronous mechanism of epidemiological epidemics, which was conducive to scientific guidance in anti-epidemic.

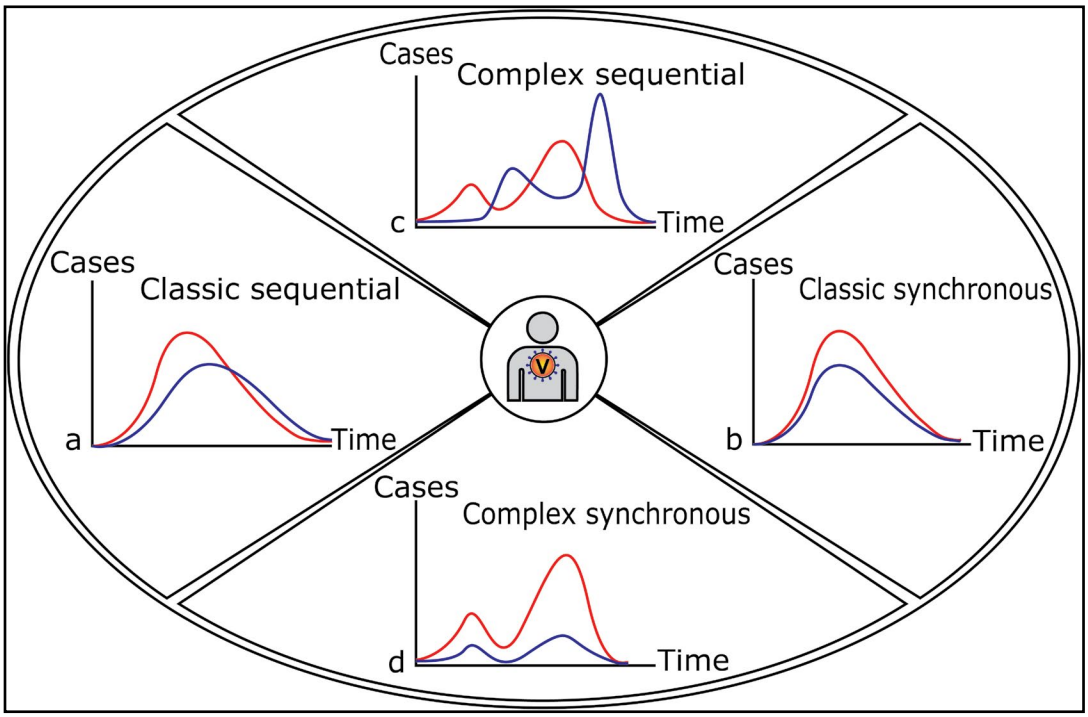

Figure 1: Epidemic sequential and synchronous complexity. a Unimodal sequential model of epidemic classical trend; b. Unimodal synchronous model of epidemic classical trend; c. Multimodal sequential model of epidemic complex trend; d. Multimodal synchronous model of epidemic complex trend.

Materials and Methods

(1) Cyclopeptide design and synthesis: based on the analysis results of mass spectrometry and nuclear magnetic resonance (NMR), the synthetic product was determined to be cyclo(FWWYYF), which was synthesized by Nanjing Peptide Biotechnology Co., LTD.

(2) Self-assembly method: Since cyclopeptide molecules could not be dissolved by heating in pure water, dissolution dilution method was adopted to induce cyclopeptide self-assembly. The cyclopeptide was first dissolved in ethanol for detection and observation, and then diluted with pure water to obtain the cyclopeptide mixed solution of ethanol/water (v/v = 1:1) for detection and observation. In this process, due to the rapid change of solvent polarity, the cyclic peptides will self-assemble under different interaction forces.

(3) The fluorescence spectrum of cyclopeptide was detected by F-7000 fluorescence spectrophotometer.

(4) Scanning electron microscope observation: 10 μL cyclopeptide solution was taken with pipetting gun and then dropped on the surface of the silicon wafer after ultrasonic cleaning and dried naturally at room temperature. After the solvent was fully developed, a layer of platinum metal was plated on the surface of the sample to increase the electrical conductivity of the sample, and then the surface morphology of the sample is observed by scanning electron microscope (SEM).

Results

In order to simulate the epidemic sequential and synchronous complexity model, the cyclopeptide, cyclo(FWWYYF), composed of three aromatic amino acids, was synthsized and experimented, and the cyclopeptide self-assembly varied with different concentrations and solvent environments. Figure 2 showed the fluorescence and electron microscope results of cyclo(FWWYYF). The S1 and S3 cyclopeptides were dissolved in anhydrous ethanol at concentrations of 0.01 mg/ml and 1.0 mg/ml, respectively. With the increase of concentration, the self-assembly of cyclopeptides changed from fibrous to globular; The fluorescence spectrum presented a sequential multimodal complex model; The S2 and S4 were added water on the basis of S1 and S3, where ethanol/water (v/v = 1:1) . With the change of solvent polarity, the self-assembly of cyclopeptides changed from scattered fibrous or globular form to aggregation form; The fluorescence spectrum presented a synchronous multimodal complex model. The S1 and S2 showed that the fluorescence spectra of cyclopeptide presented a synchronous multimodal complex model at a low concentration of 0.01 mg/ml. The S3 and S4 showed that the cyclopeptide self-assembly changed from spontaneous type to trigger type at a relatively high concentration of 1.0 mg/ml, and the fluorescence spectra showed a non-sequential and non-synchronous composite multimodal model.

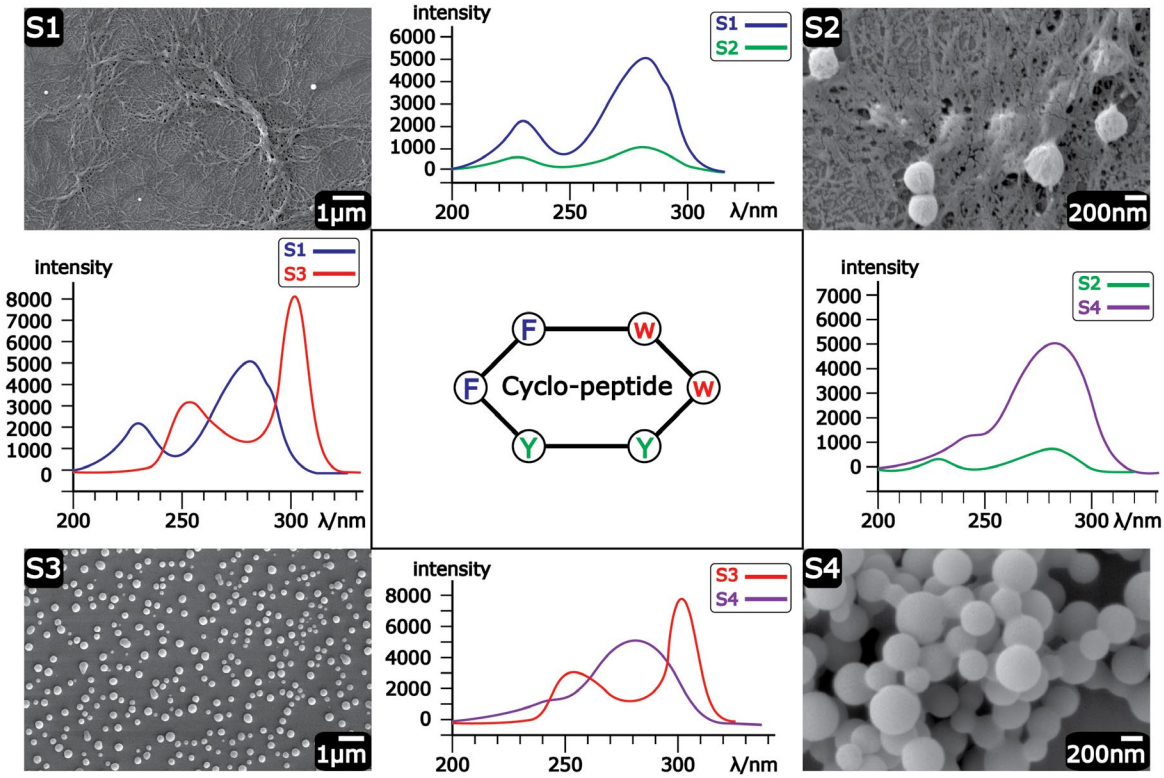

Figure 2: Cyclopeptide self-assembly simulated epidemic sequential and synchronous complex multimodal models. The intensity and wavelength of the cyclopeptide self-assembly fluorescence curve reflected the number of cases and time of the epidemic curve. The electron microscope observation of molecular diffusion and molecular aggregation reflected the sequential and synchronous of the macro behavior of the epidemic model.

Discussion

The results of the cyclopeptide self-assembly fluorescence curve showed that, on the one hand, the aromatic amino acid groups in the cyclopeptide molecules, namely tryptophan, tyrosine and phenylalanine, were in microenvironments with different concentrations. Due to the non-covalent weak force, the absorption peaks of different aromatic amino acid groups showed a bimodal pattern. This non-covalent weak force molecular simulation explained that the epidemic transmission curve might show a bimodal pattern. It has been reported that a bimodal pattern might occur with different time delays of epidemic transmission between the two layers, which further proved that the basic component was caused by weak coupling conditions between the layers 2. On the other hand, the concentration of cyclopeptide molecules and free diffusion dominated the fluorescence sequential curve, and the change of solvent polar environment determined the fluorescence synchronous curve. The fluorescence synchronous curve was the result of molecular transformation from free diffusion to molecular polymerization. The results showed that the regulation of cyclopeptide self-assembly was related to the change of molecular concentration and solvent polarity. Nanofibers and nanospheres could be assembled through hydrogen bonding, π-π stacking, hydrophobic interaction, van der Waals interaction, etc. When the solution environment changed rapidly, the hydrophobic interaction becomed very strong instantly, which led to the self-assembly behavior and rapid phase transition of cyclopeptide. Through the characteristics of cyclopeptide self-assembly behavior changes, the sequential and synchronous complex models of epidemics could be simulated [5-6]. The intensity and wavelength of the cyclic peptide self-assembly fluorescence curve reflected the number of cases and time of epidemic curve. The change of solvent polarity environment did not significantly change the self-assembly of low-concentration cyclic peptides, and the self-assembly of fluorescence detection of low-concentration cyclic peptides showed a synchronization curve (S1 and S2), and the synchronization curve flattened significantly, reflecting that if the number of epidemic patients is not large, it is easier to control the epidemic growth synchronously and quickly, and flatten the curve. The formation of disordered nanospheres with high concentration of cyclopeptides was accompanied by rapid self-assembly, which was observed by electron microscopy to form nanosphere aggregates. Fluorescence detection showed that the sequential and synchronous curves were significantly different from the results of low concentration cyclopeptide, reflecting the complexity of the epidemic. However, in the cyclopeptide self-assembly, the low concentration synchronous curve was consistent with the high concentration synchronous curve. The results showed that regardless of the degree of outbreak, as long as the global synchronous action was taken, the epidemic would be controlled earlier. The experimental results here were consistent

with the "whole society as one" and "whole government as one" as the most important measures [7, 8]. Molecular simulations elucidated why the global pandemic required global solidarity and synchronization.

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Author contributions: Conceive the project and experiment: Z.F.X.; Cyclopeptide determination and experiment: Y.W. ; Scanning electron microscope observation: Q.W.

Competing interest declaration: The authors declare no competing interests.

Additional information: Cyclopeptide HPLC-MS and Cyclopeptide NMR

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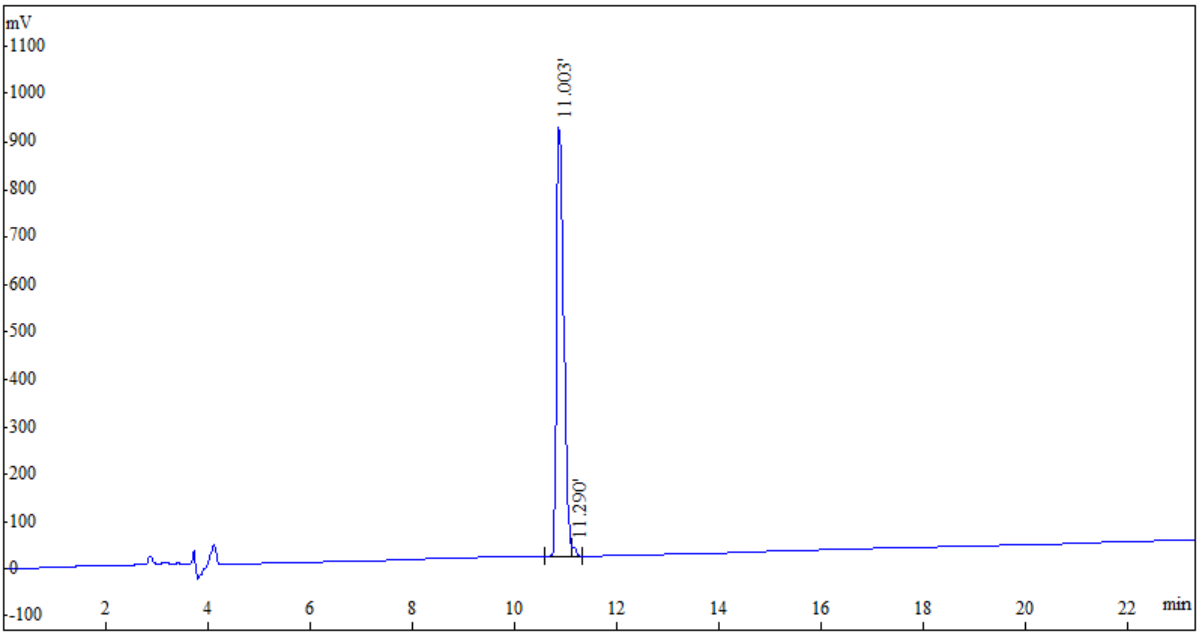
HPLC REPORT

Sample:	Cyclo(FWWYYF)	Analyzed date:	2019-11-20
Analyst:	HXH	Reconstitution:	100%Ethanol
Lot. No.:	NJP21039-191008		
Column:	4.6×250mm,Venusil MP C18-5		
Solvent A	A: 0.1% Trifluoroacetic Acid in 100% Acetonitrile		
Solvent B	B: 0.1% Trifluoroacetic Acid in 100% Water		

Gradient:

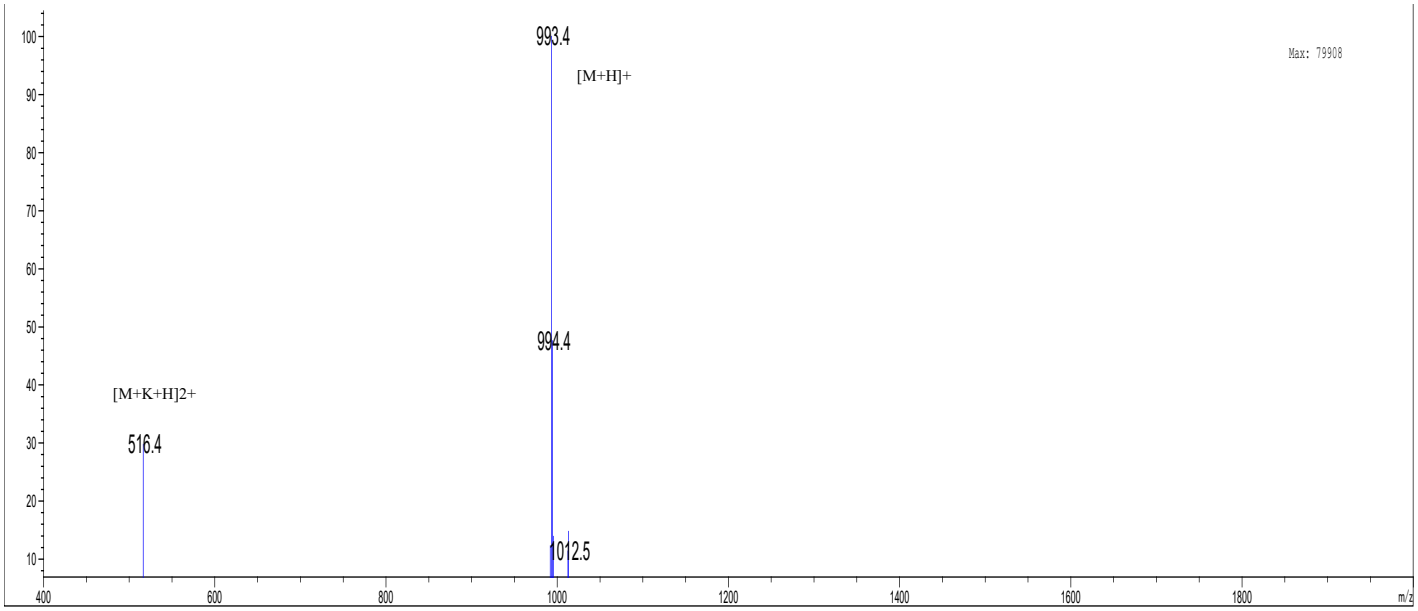
	A	B
0.0min	50%	40%
25.0min	90%	10%
25.1min	100%	0%
30.0min	Stop	

Volume:	5μl
Wavelength:	220nm
Flow rate:	1.0ml/min



Rank	Time	Conc.	Area	Height
1	11.003	98.6191	7965091	900221
2	11.290	1.3809	111532	18985
Total		100	8076623	919206

MASS SPECTROMETRY REPORT



Sample Description		Instrument	Agilent-6125B		
Analyzed date:	2019-10-31	Probe:	ESI	Probe Bias:	+4.5kv
Analyst:	YU	Nebulizer Gas Flow:	1.5L/min	Detector:	1.5kv
Sample:	Cyclo(FWWYYF)	CDL:	-20.0v	T. Flow:	0.2ml/min
M.W.:	993.12	CDL Temp.:	250 °C	B. Conc.:	50%H2O/50%ACN
Lot. No.:	NJP21039-191008	Block Temp.:	200 °C		