Journal of Pharmaceutical and Biomedical Analysis 113 (2015) 163–180

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

journal homepage: www.elsevier.com/locate/jpba

Review

Analytical methods for kinetic studies of biological interactions: A review

Xiwei Zheng, Cong Bi, Zhao Li, Maria Podariu, David S. Hage*

Department of Chemistry, University of Nebraska, Lincoln, NE 68588, USA

ARTICLE INFO

Article history:
Received 9 December 2014
Received in revised form 16 January 2015
Accepted 19 January 2015
Available online 27 January 2015

Keywords:
Kinetics of biological interactions
Stopped-flow analysis
Surface plasmon resonance spectroscopy
Affinity chromatography
Capillary electrophoresis

ABSTRACT

The rates at which biological interactions occur can provide important information concerning the mechanism and behavior of these processes in living systems. This review discusses several analytical methods that can be used to examine the kinetics of biological interactions. These techniques include common or traditional methods such as stopped-flow analysis and surface plasmon resonance spectroscopy, as well as alternative methods based on affinity chromatography and capillary electrophoresis. The general principles and theory behind these approaches are examined, and it is shown how each technique can be utilized to provide information on the kinetics of biological interactions. Examples of applications are also given for each method. In addition, a discussion is provided on the relative advantages or potential limitations of each technique regarding its use in kinetic studies.

© 2015 Elsevier B.V. All rights reserved.

Contents

1. Introduction 164
2. Stopped-flow analysis 164
   2.1. General principles 164
   2.2. Applications involving single-molecule reactions 165
   2.3. Applications involving bimolecular reactions 165
   2.4. Applications involving competition studies 165
   2.5. Applications involving multistep reactions 167
   2.6. Advantages and potential limitations 168
3. Surface plasmon resonance 168
   3.1. General principles 168
   3.2. Data analysis methods 168
   3.3. Applications in kinetic studies 169
   3.4. Advantages and potential limitations 169
4. Affinity chromatography 170
   4.1. General principles 170
   4.2. Band broadening methods 170
   4.3. Peak fitting methods 171
   4.4. Split-peak method 172
   4.5. Peak decay method 172
   4.6. Ultrafast affinity extraction 173
   4.7. Advantages and potential limitations 173
5. Capillary electrophoresis 174
   5.1. General principles 174
   5.2. Analysis of slow biological reactions 174

* Corresponding author. Tel.: +1 402 472 2744; fax: +1 402 472 9402.
E-mail address: dhage1@unl.edu (D.S. Hage).

http://dx.doi.org/10.1016/j.jpba.2015.01.042
0731-7085/© 2015 Elsevier B.V. All rights reserved.

5.3. Kinetic capillary electrophoresis 174
5.4. Advantages and potential limitations 176
6. Conclusions 177
Acknowledgements 177
References 177

1. Introduction

Biological interactions are important in determining many of the processes that occur in living systems. For example, enzymes catalyze reactions by binding and modifying their substrates, transport proteins bind to and carry lipids, hormones or nutrients within the circulatory system, and antibodies are utilized by the immune system to bind and remove foreign substances from the body. Many of these events make use of non-covalent binding and may involve proteins, peptides, lipids, nucleic acids, lipids, metal ions, hormones or drugs [1–8]. Because of the widespread occurrence and importance of these interactions, various techniques have been developed to investigate and characterize such reactions [4–19]. The overall strength, or thermodynamics, of these processes is one item of interest in these studies; however, the rate of these interactions, or their kinetics, is also important to consider [1–8]. Obtaining such information can provide a better understanding of the function of individual interactions in a biological system, the mechanisms through which these interactions occur, and the effects that a change in conditions may have on these processes [1–8].

This review examines several analytical techniques that have been used in kinetic studies of biological interactions. The methods that will be discussed include common or traditional techniques such as stopped-flow analysis and surface plasmon resonance (SPR) spectroscopy, as well as separation-based approaches that make use of affinity chromatography or capillary electrophoresis (CE) [1,3,7,20]. The general principles and theory behind each of these techniques will be described, with particular attention being given to the use of each method for investigating the rates of biological interactions. An overview of the conditions and models that are used in each technique for kinetic studies will be provided, and examples of applications will be given to illustrate each approach. Finally, the advantages and possible limitations of each method will be discussed with regards to use of the technique in studying the rate of a biological interaction.

2. Stopped-flow analysis

2.1. General principles

Many methods for kinetic studies are based on the measurement of a change in the concentration of a reagent or product as a function of time after the reagents have been mixed [21–27]. This approach requires that the process of interest be slow enough to give a reaction time that is longer than the time needed for reagent mixing and instrument activation. However, many biological interactions can occur within seconds (s) or milliseconds (ms), a fact which has limited the application of many traditional kinetic methods to such systems [21].

Stopped-flow analysis is one technique that can be employed to study the kinetics of biological interactions. The mixing time for samples and reagents in stopped-flow analysis can be as short as 1-2 ms, making this approach useful for examining interactions that occur even on the millisecond-to-second timescale. Examples of biological interactions that have been investigated with this method in kinetic studies are protein folding [28–30], enzyme inhibition [31,32], and the binding of proteins or DNA to hormones, drugs, or small molecules [33–40]. The reactants that can be used in stopped-flow analysis include proteins, DNA, drugs, hormones, and metal ions, among others [28–80].

In this technique, a small volume of each desired reagent is rapidly applied by a device such as a syringe and passed through a mixer to initiate the reaction (see Fig. 1). This mixture is then moved into an observation chamber, and the flow is stopped. Data acquisition of a signal that is produced by one of the components in the observation chamber is begun at this time. The time interval between the mixing of the reagents and the beginning of signal observation is usually only 1-2 ms and is referred to as the “dead time” [21,24].

Detection in stopped-flow analysis can be accomplished by using various methods that are able to selectively monitor a reagent or product in the reaction. Absorbance and fluorescence are two common detection methods that are employed for this type of experiment [21,25,28]. For instance, reactants or products with a specific chromophore or fluorophore (e.g., NADH, pyridoxal phosphate, or tryptophan residues on a protein) can be used to follow the rate of a biological reaction [21]. Alternatively, a tag such as fluorescein can be added to one of the reagents to monitor the progress of the reaction [21]. Circular dichroism has also been used in stopped-flow analysis for studies involving protein folding and unfolding [28–30]. In addition, fluorescence lifetime measurements [47,48], nuclear magnetic resonance spectroscopy [41,42,49,50], and small-angle X-ray scattering [51] have been coupled with stopped-flow analysis to study the kinetics of protein folding or drug metabolite degradation.

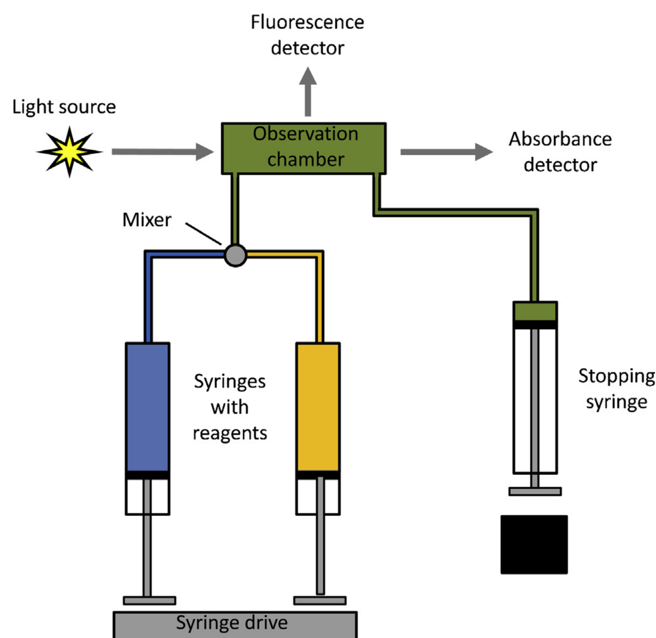

Fig. 1. General design of an instrument for carrying out stopped-flow analysis, as illustrated here for a device that can be used with either fluorescence or absorbance detection. This figure is based on information that was obtained from Refs. [22–24].

Download English Version:

https://daneshyari.com/en/article/1220282

Download Persian Version:

https://daneshyari.com/article/1220282

Daneshyari.com