



Real-time multiple-particle tracking: applications to drug and gene delivery

Junghae Suh^a, Michelle Dawson^b, Justin Hanes^{a,b,*}

^aDepartment of Biomedical Engineering, The Johns Hopkins University, 3400 N. Charles St., Baltimore MD, 21218, USA

^bDepartment of Chemical and Biomolecular Engineering, The Johns Hopkins University, 3400 N. Charles St., Baltimore MD, 21218, USA

Received 12 May 2004; accepted 5 August 2004

Abstract

Complex biological environments, such as the cell cytoplasm or the mucus lining the airways of the lungs, can pose significant barriers to efficient therapeutic drug and gene delivery. Biological barriers are particularly important in controlled drug delivery applications that utilize a large carrier particle, such as a liposome or a polymer micro- or nanosphere. The dynamic transport of particulate drug and gene delivery vehicles through these barriers is poorly understood, having been primarily studied with static methods in the past. Recently, the transport of synthetic drug and gene carriers has been investigated quantitatively with real-time particle tracking technology, providing new insight into particle behavior in complex biological environments that is guiding rational improvements in particle design. This review briefly highlights basic principles of particle tracking and its application to elucidate important phenomena that limit effective particulate drug and gene delivery. © 2004 Elsevier B.V. All rights reserved.

Keywords: Drug delivery; Gene delivery; Multiple-particle tracking; Intracellular; Mucus; Diffusion; Transport; Rheology

Contents

1. Introduction.	64
2. Intracellular barriers	65
2.1. Properties of cell cytoplasm.	65
2.2. Active transport of nonviral vectors.	66
2.3. Subdiffusive and immobile vectors	66
2.4. Rapid perinuclear accumulation of gene vectors	67

* Corresponding author. Department of Chemical and Biomolecular Engineering, The Johns Hopkins University, 3400 N. Charles St., Baltimore MD, 21218, USA. Tel.: +1 410 516 3484; fax: +1 410 516 5510.

E-mail address: hanes@jhu.edu (J. Hanes).

3.	Extracellular barriers	68
3.1.	Particle transport in human cystic fibrosis (CF) mucus	68
3.1.1.	Properties of CF mucus	68
3.1.2.	Heterogeneous particle transport through CF mucus	68
3.1.3.	Micro- and macrorheology of CF mucus.	68
3.1.4.	Effects of mucolytic agents.	70
3.2.	Particle transport in gastrointestinal mucus	70
4.	Other applications	71
4.1.	Viral gene delivery vectors	71
4.2.	Characterizing cell cytoplasm	71
4.3.	Motion of plasma membrane components	71
5.	Particle tracking technology: a brief tutorial	71
5.1.	Time scale	72
5.2.	Individual vs. ensemble transport properties	73
5.3.	Transport modes	73
5.3.1.	Simple diffusion	74
5.3.2.	Anomalous subdiffusive transport	74
5.3.3.	Corralled motion	74
5.3.4.	Active transport	74
5.3.5.	Immobile	74
5.4.	Diffusivities	75
5.4.1.	Microscopic diffusion	75
5.4.2.	Mesosopic diffusion.	75
5.4.3.	Macroscopic diffusion	76
5.5.	2D v. 3D tracking	76
5.6.	Tracking resolution	76
6.	Conclusions	77
	References	77

1. Introduction

Effective drug and gene delivery to target cells is often limited by inefficient particle transport through complex extra- and intracellular biological environments [1]. For example, drug/gene particulate carriers delivered to the gastrointestinal (GI) tract or to the lungs via inhalation must be capable of traversing mucus barriers designed to trap foreign particulates and prevent their transport to underlying cell surfaces [2,3]. Mucus depletion of cell monolayers typically dramatically improves gene transfection of cells with nonviral vectors [4], underscoring the importance of the mucus barrier. Once in cells, gene vectors must traverse the highly crowded cytoplasm, congested with macromolecules and organelles, to reach the nucleus [5]. The sparse quantitative investigations of these barriers have focused largely on bulk particle transport properties.

In these studies, individual particle interactions with their biological environment remain a black box. Additionally, the dynamic interaction of drug/gene delivery vectors with components in the extra- and intracellular environments have often been overlooked. Limited understanding of barriers to efficient delivery hampers the rational design of improved vectors.

To address these issues, real-time multiple-particle tracking (MPT) technology has recently been applied to the study of drug and gene carrier delivery through biological environments [2,3,5,6]. As the name implies, multiple-particle tracking involves tracking the microscopic motion of tens of individual particles simultaneously in real-time using video microscopy. Particle tracking technology is valuable in obtaining information on how, and how fast, particles move in various environments. Data obtained at the individual particle level can be

Download English Version:

<https://daneshyari.com/en/article/10883858>

Download Persian Version:

<https://daneshyari.com/article/10883858>

[Daneshyari.com](https://daneshyari.com)