

IDENTIFIABILITY OF LINEAR COMPARTMENT MODELS: THE SINGULAR LOCUS

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ABSTRACT. This work addresses the problem of identifiability, that is, the question of whether parameters can be recovered from data, for linear compartment models. Using standard differential algebra techniques, the question of whether a given model is generically locally identifiable is equivalent to asking whether the Jacobian matrix of a certain coefficient map, arising from input-output equations, is generically full rank. We give a formula for these coefficient maps in terms of acyclic subgraphs of the model's underlying directed graph. As an application, we prove that two families of linear compartment models, cycle and mammillary (star) models with input and output in a single compartment, are identifiable, by determining the defining equation for the locus of non-identifiable parameter values. We also state a conjecture for the corresponding equation for a third family: catenary (path) models. These singular-locus equations, we show, give information on which submodels are identifiable. Finally, we introduce the *identifiability degree*, which is the number of parameter values that match generic input-output data. This degree was previously computed for mammillary and catenary models, and here we determine this degree for cycle models. Our work helps shed light on the question of which linear compartment models are identifiable.

1. INTRODUCTION

This work focuses on the identifiability problem for linear compartment models. Linear compartment models are used extensively in biological applications, such as pharmacokinetics, toxicology, cell biology, physiology, and ecology [2, 3, 7, 9, 12]. Indeed, these models are now ubiquitous in pharmacokinetics, with most kinetic parameters for drugs (half-lives, residence times, and so on) based at least in part on linear compartment model theory [13, 18].

A mathematical model is *identifiable* if its parameters can be recovered from data. Using standard differential algebra techniques, the question of whether a given linear compartment model is (generically locally) identifiable is equivalent to asking whether the Jacobian matrix of a certain *coefficient map* (arising from certain *input-output equations*) is generically full rank. Recently, Meshkat, Sullivan, and Eisenberg gave a general formula for the input-output equations of a linear compartment model [11]. Using this formula, it is easy to check whether a given model is (generically locally) identifiable. Nevertheless, we would like to bypass this formula. That is, *can we determine whether a model is identifiable by simply inspecting its underlying directed graph?* Or, as a first step, *if a model is identifiable, when can we conclude that a given submodel is too?* Our interest in submodels, obtained by removing edges, has potential applications: the operation of removing an edge in a model may correspond to a biological intervention, such as a genetic knockout or a drug that inhibits some activity. Identifiable submodels have been studied by Vajda and others [14, 16].

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