Classification of two-site exchange models for DCE-MRI

S. Sourbron[1], and D. L. Buckley[1]
[1]Division of Medical Physics, University of Leeds, Leeds, United Kingdom

PURPOSE: The Tofts models have long been regarded as a standard approach to tracer-kinetic analysis of DCE-MRI [1]. However, recent technological advances such as parallel imaging and higher field strengths have improved DCE-MRI data quality to a point where more complex models are required [2]. For tissues with a bidirectional exchange of tracer between intra- and extravascular spaces, a number of alternative two-site exchange models have been proposed [3-6]. Each imposes different constraints on the tissue, but due to their complicated algebraic structure the relation between the models is poorly understood [7]. As a result it remains unclear which is more accurate in general or in particular applications, and how such a choice can be made operationally. Here we propose a generalised model which exposes the architectural differences between the models and allows transparent handling of model-comparison and -selection issues.

METHODS: We define the class of two-site exchange models as models that describe the tissue as consisting of a plasma space P with volume V_p and an extravascular extracellular space E with volume V_E. The tracer exchange rate between P and E is the permeability-surface area product PS which is equal to the exchange rate from E to P. Plasma enters P at a flow rate F_P and is evacuated from P at the same rate F_P. E does not exchange tracer directly with the environment. The majority of proposed models for generic tissue types have this architecture [1,3-6]. The tissue-homogeneity model (TH) [3] models E as a compartment and P as a plug flow system. Since it has no analytical solution, it is often approximated with the adiabatic approximation (AATH) [4,7]. Koh's model [5] also models P as a plug flow system, but forbids tracer transport in E parallel to the capillary. The 2-compartment exchange model (2CXM) [6] models both P and E as compartments. The Tofts model [1] is a special cases of TH and 2CXM, so it does not need to be considered separately.

RESULTS: The generalised two-site exchange model is depicted in fig 1. It describes E and P as n identical compartments ($n \geq 1$) with volumes V_P/n and V_E/n, respectively. PS is distributed uniformly over the pairs of compartments. Tracer transport in P is unidirectional at a rate F_P, but transport in E is bidirectional and characterised by a new rate constant $D \geq 0$, which is proportional to the diffusion coefficient in E. Hence this generalised model has two new additional parameters (n,D): n characterises the geometry of each space, and D the tracer transport rate in E. The 3 special cases can be defined by fixing the values of (n,D): Koh's model [5] is defined by D=0 and 1/n=0; TH [3] by 1/D=0 and 1/n=0; 2CXM [6] by n=1. Since the model is discrete and finite, the residue function can be generated by calculating the exponential of the system's characteristic matrix [8]. Koh's model and TH can be approximated to arbitrary precision be performing this simulation at large n. Fig 2 shows an example in two different conditions with n=50. The results change only marginally at higher n.

CONCLUSION: The generalised model (fig 1) offers a physically insightful way of representing the different assumptions inherent in the most common two-site exchange models. Being finite, it also offers a method to approximate models such as the TH which do not have an analytical solution in the time domain. It enables the investigation of the differences between all models and the accuracy of approximations such as the AATH (fig 2). Finally, it has a broader scope than any of the existing models, as it allows modelling of realistic tissue structures that are intermediate between the ideal cases of a single compartment (n=1) or a plug flow model (1/n=0). With sufficient data quality, this offers the hope that new parameters such as diffusion in E can be determined in tissues where none of the existing models offers an accurate fit to the data.

REFERENCES: [1] Tofts et al 1999 JMRI 10: 223-232 **[2]** Donaldson et al 2010 MRM 63: 691-700 **[3]** Johnson & Wilson 1966 Am J Physiol 210: 1299-1303 **[4]** St Lawrence and Lee 1998 JCBFM 18: 1365-77 **[5]** Koh et al 2003 IEEE Trans Biomed Eng 50: 159-167 **[6]** Brix et al 2004 MRM 52: 420-429 **[7]** Kershaw et al 2010 MRM Aug 16 (Epub) **[8]** Jacquez 1985; Compartmental analysis in biology and medicine; University of Michigan Press.

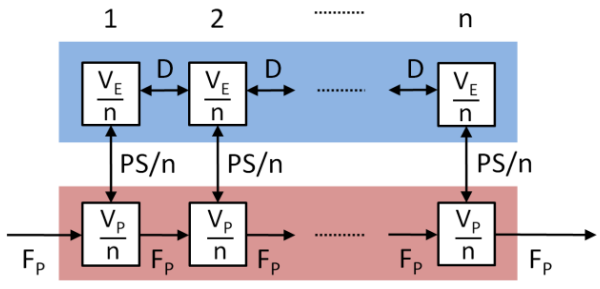

Fig 1. The generalised two-site exchange model. Interstitial and intravascular components are in the blue and red rectangles, respectively.

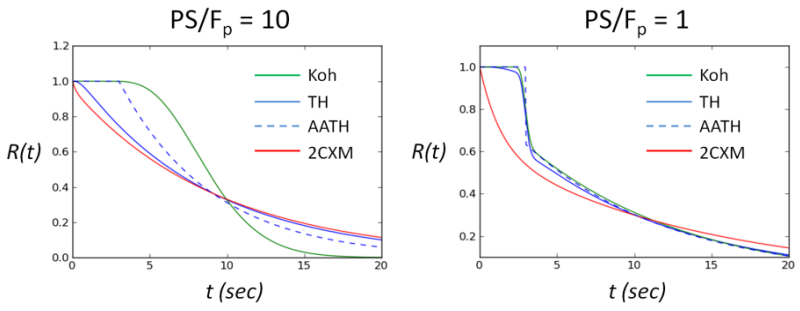

Fig 2. Residue functions for the four special cases in the flow-limited regime (left) and intermediary flow regime (right). In each case, v_p=5%, v_e=10%, F_p=1ml/min/ml.