

APPLICATION OF NETWORK PARTICLE TRACKING (NPT) IN OPEN
COMPARTMENTAL SYSTEMS: DYNAMIC STORAGE ANALYSIS, RESIDENCE TIME
DISTRIBUTION, TEMPORAL DISTRIBUTION

by

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(Under the direction of Caner Kazanci)

ABSTRACT

Compartment models are often used to represent and study biological and ecological systems. They are modeled as directed graphs, describing flows of a conserved quantity (eg. mass, energy, a specific molecule, etc.) among a set of compartments. Various measures have been defined to capture universal system-wide properties of these models.

An important system-wide property storage analysis quantifies how each environmental input gets shared among all compartments. Application of current storage analysis is restricted to steady-state models. It cannot be utilized to study dynamic systems. This is a major limitation as most ecosystems experience seasonal changes. Another property, residence time (RT), is a widely used concept representing the average time the flow material stays in a compartment (or the system) at equilibrium. Residence time distribution (RTD) offers more detailed information about the behavior of the flow material within the system. These properties get quite difficult to compute for large and complex networks. Tracing the movement of tagged flow material in the system, similar to tracer experiments, could be used study these essential properties.

In this thesis, we introduce a method that eliminates these shortcomings. Using a stochastic individual based algorithm called Network Particle Tracking (NPT), we come up with simulation-based definitions for storage analysis. While both definitions agree for steady-state systems, the NPT-based definition works for dynamic systems as well. We use the same methodology to study other interesting properties of mass and energy distribution within ecological networks.

INDEX WORDS: Storage analysis, Residence time distribution, Network Particle Tracking,
Compartmental systems

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DEDICATION

This thesis is dedicated to my dear grandparents and my dear parents, for their forever love and support.

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It would be difficult to acknowledge all those people who have contributed to this work without either making an omission or exceeding the proper page limits.

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1 Introduction

Compartmental models are mathematical models used to describe the way material or energy is transferred and distributed among the compartments of a system. Such models are often used to study biological and ecological systems, such as genetic networks, biological pathways, ecosystems, pharmacokinetic systems, etc. They are modeled as directed graphs, where edges represent an interaction or a relation between compartments, such as gene regulation, trophic interactions, or chemical reactions. Each compartment is assumed to be a homogeneous entity within which the entities being modeled are equivalent. For example, in a pharmacokinetic model, different sections of a body are represented by different compartments and the concentration of a drug in each compartment is assumed to be uniformly equal. Many software products [Clauset Jr et al., 1987, Ramsey et al., 2005, Kazanci, 2007] are developed to build such network models of real-life phenomena, with built in simulation and analysis tools. These models enable researchers to capture system-wide behavior, which may be counter-intuitive, and difficult to predict. Such behavior is generally due to the inherent complexity of network models. Often, effects of indirect connections and feedback cycles exceed the effects of direct connections, producing interesting behavior: A predator can have a significant positive effect upon its prey [Bondavalli and Ulanowicz, 1999], a protein may have a negative auto-regulatory role on its own expression [O'hare and Hayward, 1985]. Various measures have been defined that capture universal system-wide properties of network models, such as connectivity distribution [Jeong et al., 2000], response to perturbations [Ueda et al., 2004], cycling [Finn, 1976, Kazanci et al., 2008], indirect effects [Patten, 1985, Higashi and Patten, 1986], and ascendancy [Ulanowicz, 1986, Patten, 1995, Patrício et al., 2004], etc.

Storage analysis [Matis and Patten, 1981, Hearon, 1981, Fath and Patten, 1999], an important system-wide property, traces the storage value of a compartment back to boundary input. Storage analysis consists of a matrix S (storage-generation matrix), which is a linear map from system boundary inputs to compartment storage values. For a steady-state system, we can get the storage

value by multiplying S matrix with the vector of boundary inputs. For one element in the matrix, S_{ij} represents how much storage is generated in compartment i by a unit boundary input to compartment j . Such measures are extremely useful for research in environmental sciences [Mackay and MacLeod, 2002], pharmacokinetics [Cheng and Jusko, 1988, Plusquellec and Houin, 1990] and nutrition [Green and Green, 1990], where compartmental models are heavily utilized to assess the interaction between system boundary and internal compartments.

Traditional storage analysis has provided a way of studying systems at steady-state. However, this analysis is not applicable to evolving systems. This limits its application, as many interesting research areas involve change, such as environmental impact studies, effects of climate change, waste management, etc.

We construct a simulation based definition for storage-generation matrix S , which could also be applied to evolving systems, as well as steady-state models. Network particle tracking (NPT) is an individual based simulation method, where discrete “packets” of material or energy are labeled and tracked in time as they flow through the model compartments. Previously, it has been used to study Finn’s cycling index [Finn, 1976] and throughflow analysis [Patten, 1978]. Since NPT can simulate dynamic systems as well as steady state models, this method can overcome the shortcomings of traditional storage analysis, which was limited to steady state systems. This NPT based new method should agree with the current definition of storage analysis for steady state systems. This serves as a way to verify the accuracy of the NPT based storage analysis. Based on the verification, we compute the storage-generation matrix $S(t)$ for dynamic systems, which will be an evolving dynamic matrix function.

Residence time is another related property, which represents the amount of time the flow material spends in a particular compartment. This is what we call compartmental residence time, computed as the ratio of compartment storage value to throughflow (x_i/T_i). For each particle, NPT records its residence time in each compartment it goes through. By taking the average, we can compute NPT based compartmental residence time. Furthermore, because NPT is an individual based simulation method, it offers a way to investigate the residence time distribution. Besides compartmental

residence time, we are also interested in input based system residence time [Yu and Wehrly, 2004, Hearon, 1972] which has many important applications in areas such as drug delivery, toxicology, etc. Since NPT tracks complete pathways of individual particles, we can compute the system residence time and investigate its distribution as well. This distribution is essential for investigating issues such as the time it takes for 90% of a particular contaminant to leave the system.

Another property we investigate is the temporal distribution of material in each compartment. To be specific, we study how long it takes for particles to reach another compartment from an environmental input and stay in that compartment. Combining this information with storage analysis, one can compute a temporal distribution of residence time, which may have quite useful applications. For a specific compartment model, particles could represent a dose of medicine, or a certain kind of pollutant in the environmental system. Based on the temporal distribution of drug at the target organ or tissue, one can adjust dose size, interval and how the drug should be administered (oral or inject). Similar approach could be applied to toxicology and environmental impact studies.

2 Literature Review and Analysis

2.1 Storage analysis

Storage analysis [Matis and Patten, 1981] investigates the relation between input flows and compartment storage values. The storage-generation matrix S represents a linear mapping between the environmental input rates and the final storage values of each compartment. For instance, given one unit of mass or energy input to a system at compartment j , S_{ij} represents how much storage is generated at compartment i as a result of this input. The linear relationship between environmental input rates and storage values at steady state is described by the following equation:

$$Sz = x^*$$

where $z = [z_1, \dots, z_n]^T$ is the vector of environmental input flow rates to each compartment, and x^* is a vector of the steady-state storage values of all compartments.

Traditionally, storage analysis has provided a way of studying ecosystems models at steady state. This useful but limited application of storage analysis to systems with linear dynamics is due to the way the matrix is defined using linear algebra, as follows [Matis and Patten, 1981]:

$$\frac{dx}{dt} = Cx + z$$

where

$$C_{ij} = \begin{cases} F_{ij}/x_j & , i \neq j \\ -\sum_k F_{ki}/x_i & , i = j \end{cases}$$

Here, $F_{ij}(t)$ represents the flow rate from compartment j to i at time t . For donor controlled systems, C stays constant. For non-donor controlled systems, C is a function of x .

For an ecosystem model at steady state, the storage values of each compartment remain constant over time and the rate of change of these values is equal to zero ($\frac{dx}{dt} = 0$). This leads to the

Table 1: Storage Analysis matrix S shown for the intertidal oyster ecosystem model shown in figure 1.

	Filter Feeders	Deposited Detritus	Microbiota	Meiofauna	Deposited Feeders	Predators
Filter Feeders	48.07	0	0	0	0	0
Deposited Detritus	24.04	62.17	12.43	34.93	49.28	29.52
Microbiota	0.06	0.15	0.33	0.08	0.12	0.07
Meiofauna	0.58	1.50	0.72	3.69	1.19	0.71
Deposited Feeders	0.39	1.00	1.23	1.07	7.28	0.47
Predators	1.87	1.07	1.32	1.14	7.79	101.52

derivation of the storage matrix as a function of C , which also remains constant over time:

$$\begin{aligned}
 0 &= Cx^* + z \\
 -Cx^* &= z \\
 x^* &= \underbrace{-C^{-1}}_{=S} z
 \end{aligned}$$

Storage-generation matrix S is determined exclusively by the flow rates (F), boundary inputs (z), and steady-state storage values (x), and is independent of initial conditions.

EcoNet [Kazanci, 2007, 2006, 2009] uses this method for storage matrix computation. We demonstrate how to interpret the storage analysis matrix using the Oyster Reef model [Patten, 1986] shown in figure 1. By running Oyster Reef model in EcoNet, we get the S matrix shown in table 1. The first row of S contains all zeroes except for the first term because *Filter feeders* do not receive any input from other compartments. All other entries are non-zero, meaning that energy flows from any compartment to any other through direct or indirect pathways. $S_{12} = 24.04$ represents that a unit of input to *Filter feeders* contributes to *Deposited detritus* 24.04 units of storage over time. For further information on storage analysis or computation of S for steady state models is covered in Matis and Patten [1981], Patten [1978], Fath and Patten [1999].

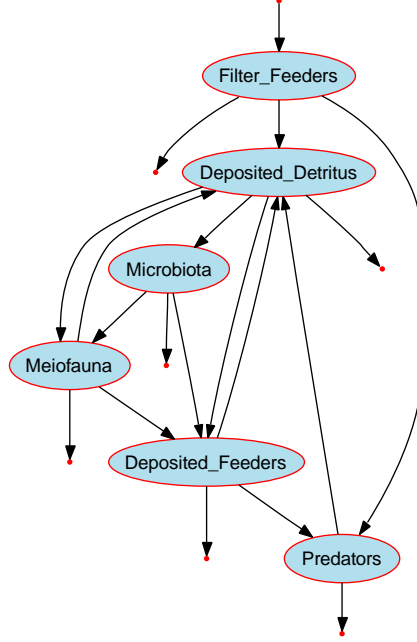


Figure 1: Network diagram of the intertidal oyster reef ecosystem model [Dame and Patten, 1981]. There are 6 compartments including Filter Feeders, Deposited Detritus, Microbiota, Meiofauna, Deposited Feeders and Predators. The diagram is created by EcoNet [Kazanci, 2007, 2009].

Before constructing the NPT-based definition, perhaps we need to clarify the meaning of “dynamic storage analysis matrix”, and study why it is cumbersome to extend the conventional definition to evolving ecosystem models. Repeating the steps in computing S for steady-state models to derive S for an evolving ecosystem, we get:

$$\begin{aligned}\dot{x}(t) &= C(x)x(t) + z(t) \\ -C(x)x(t) &= z(t) - \dot{x}(t) \\ x(t) &= [-C(x)^{-1}] (z(t) - \dot{x}(t))\end{aligned}$$

Assume that we define the “dynamic” storage analysis matrix as $S(t) = -C(x(t))^{-1}$, similar to the steady-state definition. Note that $S(t)$ no longer maps boundary inputs to compartment storages because of the extra $-\dot{x}(t)$ term. In fact, $S(t)$ maps the difference between the environmental input and the change in storage values, to storage values, which is hardly a practical measure. What we need is a matrix function $S(t)$, where $S_{ij}(t)$ represents the instantaneous storage contribution to

compartment i by unit boundary input at compartment j .

One issue with this definition is that all off-diagonal entries of $S(t)$ will be zeroes ($S_{ij}(t) = 0$ for all $i \neq j$), because it takes some time for any boundary input to travel to another compartment, and then contribute to its storage. An instantaneous approximation to a phenomenon that takes a finite, non-zero amount of time to occur will never be accurate. An example is trying to capture a snapshot of a moving scene with a camera at 10^{-6} seconds. The end result will be a completely dark picture, since 10^{-6} seconds is not enough for accurate exposure in ambient light. In fact, any steady-state measure that depends on indirect effects, such as Finn's cycling index [Finn, 1976, Kazanci et al., 2008] or Throughflow analysis [Patten et al., 1976, Matamba et al., 2009], will have the same issue if we try to extend their definitions to dynamic systems using instantaneous approximations.

Another issue with this definition is the inherent assumption that storage occurs instantaneously. On particle level, storage depends not only on the amount of particles that reside in a compartment, but also on the residence time of those particles. The same amount of storage can be created by 10 particles staying in a compartment for a day, or 240 particles staying for an hour. Therefore we revise the previous definition by applying the instantaneous approximation only to the boundary input:

Let $S_{ij}(a, b)$ represent the amount of storage created at compartment i **over time** ($a < t < \infty$), by a unit input into compartment j over the time interval $[a, b]$. Then we define

$$S(t) = \lim_{h \rightarrow 0} S(t - h, t + h)$$

In this latter definition, we do not care when the storage contribution occurs. It can be at any time. However, since we are dealing with open systems, all particles will leave the system sooner or later. Therefore we can revise the definition above and use $a \leq t < M$ (instead of $a < t < \infty$) where M is a very large finite value.

2.2 Residence time

Residence time quantifies how long a given substance remains in a particular compartment of a biogeochemical cycle and other models. For ecosystems, residence time represents the amount of time the flow material spends in a certain compartment before leaving, which is associated with storage value of this compartment and flow rate with connected compartments. It is traditionally computed as the ratio of storage value to throughflow (x_i/T_i). Throughflow is the sum of inflows or outflows at each compartment or the system. Note that inflow equals outflow at steady state. Residence time distribution (RTD) is a probability distribution function that describes the amount of time the flow material spends in the system or a particular compartment. The concept of RTD was proposed and used early in [MacMullin and Weber, 1935] and [Danckwerts, 1953]. RTDs have interesting applications in life sciences, in particular, toxicology, environmental sciences, drug delivery and nutrition. For example, it is widely used to study flow and mixing behavior of components in a reactor [Iliuta et al., 1996, Zhang et al., 2005]. Since each compartment is regarded as homogeneous, compartmental RTD is exponential. However, system RTD is not the case because of the inter-structure within the system.

In experimental studies, RTD is usually measured by stimulus-response technique. Adding tracer to flow material, RTD is derived by recording the tracers distribution. It is assumed tracer has no effect on the flow material and they have the same path as flowing through the system. RTD has also been studied through numerical computations. RTD has been computed by statistical probability. Yu and Wehrly [2004] use saddlepoint approximation to investigate RTD, a method based on deriving the moment generating function of the variable of interest. Their method is specific to a two-compartment model. However, real systems are various and can be quite complex. So this approach for computing RTD has several disadvantages. First, the procedure is rather involved and difficult to understand, especially for those who have limited mathematics and statistics background. Second, the method is model specific, and difficult to generalize.

Another issue we are interested in is how the flow material is distributed in the system temporally. In other words, we investigate how long it takes for a boundary input to reach a specific compartment within the system, and how the density of the flow material changes over time in each

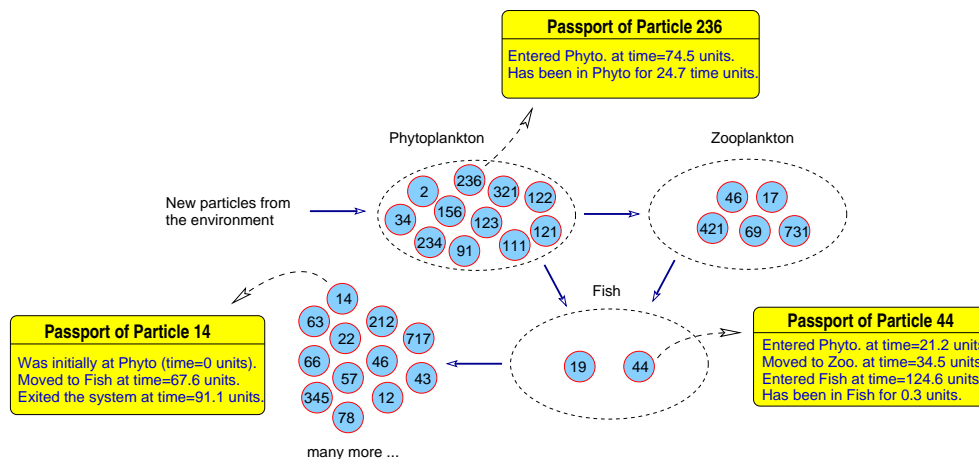


Figure 2: Three-compartment model depicting particles and their transport information. A record of the trajectory and timing of each particle from its point and time of entry to (potentially) its point and time of exit is given in the particle “passports”.

compartment. We call this measure temporal residence time distribution, and refer to it as temporal distribution (TD) for simplicity. TD is essential in various fields, including environmental and toxicological studies, drug delivery, and nutrition.

2.3 Network Particle Tracking

Network particle tracking [Kazanci and Tollner, 2009, Tollner and Kazanci, 2007, Kazanci et al., 2008] is an individual based simulation method, where discrete “packets” of material or energy are labeled and tracked in time as they flow through the model compartments (Figure 2). In addition to tracking the storage values of model compartments over time (as occurs in a differential equation model), NPT identifies which individual particles represent the storage values of each compartment. The method is particularly useful at steady state, where differential equation simulations give constant values for storage values over time, giving the illusion that the system has “stopped”, whereas NPT will show continuous movement of particles.

What sets NPT apart from other similar algorithms is: (1) NPT deduces its rules on how an individual particle will move directly from the differential equation representation of the model. This eliminates the need for extra parameters or decisions that are required to build most individual-based models. Therefore causality is preserved. (2) NPT is a stochastic method that is compatible

with the so called “master equation” [Gillespie, 1992, 2000]. In other words, the mean of many NPT results agree with the differential equation solution.

NPT starts with breaking initial stocks or input flows into discrete packets which we call particles. For example, for a Nitrogen flow model, a particle could represent a Nitrogen atom. Next, based on flow rates, NPT determines which flow is likely to occur and when. A particle is then chosen randomly from the donor compartment and introduced to the recipient compartment. Ecosystem models are open systems and therefore new particles enter the system continuously. So if the chosen flow is an environmental input, a new particle is labeled and introduced to the recipient compartment. NPT output records the history of all particles when it flows through the network.

In figure 3, we show a sample NPT output for the intertidal oyster reef ecosystem model [Patten, 1986]. The results include *pathway*, *flow time* and *residence time* data. We define the *pathway* of a particle as an ordered list of compartments visited by that particle. *Flow time* indicates the exact time when a particle flows from one compartment (or the environment) to another one (or the environment). Simulation start time is set as the reference ($t = 0$). Time units are defined by the model, therefore depend on the model. For the oyster reef model, time units are days. This paper does not focus on a particular model. Therefore, we simply use the term *time units* (tu) for sake of generality. *Residence time* represents how long a particle stays in a particular compartment it visits. Therefore it is defined as the difference between two consecutive flow time values. For example, data in figure 3 indicate that *Particle 144* enters *Compartment 1* at $t = 0.5tu$ and leaves at $t = 9.7tu$. Hence its residence time at *Compartment 1* is 9.2 time units.

NPT has been used to study Finn’s cycling index [Finn, 1976, Kazanci et al., 2008], throughflow analysis [Patten, 1978, Matamba et al., 2009], effects of consumers in stream nutrient dynamics [Small et al., 2009]. Using NPT, we can simulate both dynamic and steady-state models and get the trace of all particles. For each particle that enters the system at one particular compartment, by tracing its pathway, we can get its storage contribution to every compartment. This can be

Particle	Pathway	* → 1 → 2 → 4 → 5 → 6 → *								
144	Flow time	0.5	9.7	16.8	20.4	27.2	34.8			
	Residence time	9.2	7.1	3.6	6.8	7.6				
Particle	Pathway	* → 1 → 2 → 5 → 2 → 4 → *								
145	Flow time	1.2	10.3	19.8	28.0	33.5	41.6			
	Residence time	9.1	9.5	8.2	5.5	8.1				
Particle	Pathway	* → 1 → 2 → 4 → 2 → 3 → 4 → 5 → 6 → *								
146	Flow time	2.3	9.2	13.4	17.2	24.2	33.5	39.6	44.1	50.8
	Residence time	6.9	4.2	3.8	7.0	9.3	6.1	4.5	6.7	

Figure 3: Partial output of a Network Particle Tracking (NPT) simulation is shown for the intertidal oyster reef ecosystem model [Dame and Patten, 1981] (Figure 1). Numbers 1 through 6 correspond to compartments *Filter Feeders*, *Deposited Detritus*, *Microbiota*, *Meiofauna*, *Deposited Feeders* and *Predators* respectively. The output includes *pathway*, *flow time* and *residence time* data for each particle. * represents the environment. NPT tracks all particles starting from their entrance to the ecosystem, until they leave back out to the environment. A typical NPT simulation contains more than 10^5 particle pathways. Such a simulation takes a couple of seconds to run on a typical desktop computer.

regarded as storage analysis on particle level. By taking the average of these data for large number of particles, we can compute the S matrix. Using NPT, we can compute residence times and the associated distributions regardless of size or complexity. We can classify particles with respect to their input compartments, and compute the input-based system residence time. We can factor time into our computations, and build a temporal distribution (TD). These distributions provide new opportunities to study and understand how living systems function.

3 Methods

In this section, we use a sample NPT simulation output to demonstrate how we compute the S matrix, compartmental residence time, input based system residence time and temporal distribution. Based on these ideas, we apply this methodology to specific models in the next section.

3.1 NPT based storage analysis

3.1.1 NPT based storage analysis for steady-state systems

Recall that S_{ij} represents the amount of storage generated at compartment i by a unit of environmental input into *compartment* j . The storage amount contributed by a particle at a compartment is proportional to the total residence time of that particle at that compartment. To compute the storage analysis matrix S using NPT, we need both the pathway and the residence time data. Let's compute S_{61} using the NPT output shown in figure 3:

Note that all three particles enter the ecosystem at *Filter feeders* (compartment 1), and S_{61} represents how much storage is created by these particles at *Predators* (compartment 6). Only two particles (144 and 146) end up visiting *Predators* (compartment 6), and they stay for 7.6 and 6.7 time units respectively. Therefore:

$$S_{61} = \frac{7.6 + 6.7}{3} \approx 4.77$$

Deposited detritus (compartment 2) is much more popular than *Predators* (compartment 6), and all three particles visit this compartment at least once before they exit the system. Therefore we can compute S_{21} as follows:

$$S_{21} = \frac{(7.1) + (9.5 + 5.5) + (4.2 + 7.0)}{3} \approx 11.1$$

There is a significant discrepancy between the values we have just computed above ($S_{61} \approx 4.77$, $S_{21} \approx 11.1$) and the values given in table 1 ($S_{61} = 24.04$, $S_{21} = 1.87$). This is mainly due to our

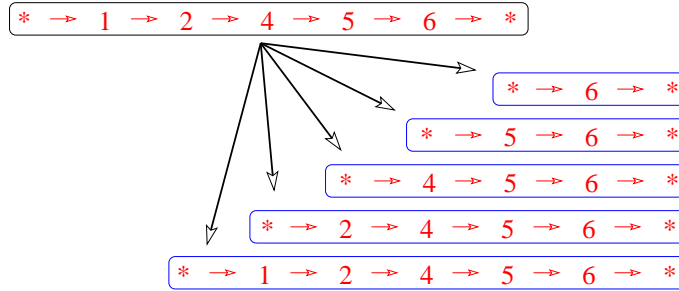


Figure 4: To compute storage analysis matrix S , each pathway in NPT output is viewed as multiple pathways as shown above. Here, pathway of *particle 144* from figure 3 is expanded into five separate pathways. Such expansion enables us to compute S_{ij} even if there is no environmental input into compartment j .

computation above being based on only three pathways. NPT is a stochastic simulation method, therefore the NPT based computation of S is an approximation. However, any desired accuracy can be achieved by using more pathways.

Actually, the process of computing the matrix S is slightly more involved, because rarely an ecosystem model will have environmental inputs into all its compartments. For example, how can we compute S_{42} for the oyster reef ecosystem model when no particle enters *Deposited Detritus* (compartment 2) from the environment?

To be able to compute the full S matrix, we use that fact that whether a particle enters a compartment from the environment, or from another compartment, it will behave the exact same way afterwards. In other words, we need not make any distinction between environmental inputs, or inter-compartmental inputs to compute S using NPT output. As a result, we can treat each particle pathway as multiple particle pathways as shown in figure 4. This increase in effective number of pathways also increases the accuracy of computation of S . Applying this expansion to all three pathways in 3 results in 15 new pathways, yielding 18 pathways in total. We name this new set contracted pathways.

We carry out the computation of S on contracted pathways. Since any compartment receives either an environmental input, or at least one inter-compartmental input, it is possible to compute the full

S matrix for any ecosystem model. Let's compute S_{42} using the contracted pathways:

First we determine how many contracted pathways start with *Deposited Detritus* (Compartment 2). Note that *Deposited Detritus* (compartment 2) appears five times in figure 3, therefore five extended pathways will start with *Deposited Detritus*. Then we add up the total residence time at *Meiofauna* (Compartment 4) for these five (contracted) pathways, and compute S_{42} as follows:

$$S_{42} = \frac{(3.6) + (8.1) + (8.1) + (3.8 + 6.1) + (6.1)}{5} = 7.16$$

In general, we compute S as follows:

$$S_{ij} = \frac{1}{|\mathcal{P}_j|} \sum_{\mathcal{P}_j} \text{sum of residence times at compartment } i$$

where \mathcal{P}_j is a list of contracted pathways that start with compartment j , and $|\mathcal{P}_j|$ represents the number of extended pathways in this list. The larger the number of pathways $|\mathcal{P}_j|$, the more accurate the computation of NPT based S .

3.1.2 NPT based dynamic storage analysis

For steady-state models, we can use all the pathways from NPT output and compute an average S matrix. However, for dynamic systems, we expect that S matrices will be a functions of time, and represent it with $S(t)$.

To compute this dynamic $S(t)$, let $S_{ij}(a, b)$ represent the amount of storage created at compartment i over time ($a < t < \infty$), by a unit input into compartment j over the time interval $[a, b]$. We define

$$S(t) = \lim_{h \rightarrow 0} S(t - h, t + h)$$

In this latter definition, we do not care when the storage contribution occurs. It can be at any time. However, since we are dealing with open systems, all particles will leave the system sooner or later. Therefore we can revise the definition above and use $a \leq t < M$ (instead of $a < t < \infty$) where M is a large finite value.

The $S(t)$ matrix is calculated as follows:

Step 1: Simulate the model using NPT until all the particles that flow within the system during the time window $[t - h, t + h]$ leaves the system.

Step 2: We utilize contracted pathways to compute $S(t)$. First, we find out all the contracted pathways of the form “* $\rightarrow j \rightarrow \dots$ “ whose first flow time sit exactly between $[t - h, t + h]$.

Step 3: We add up all residence times for i in each contracted pathway, and divide this sum by the number of contracted pathways, to get an estimated value for $S_{ij}(t)$.

For example, we compute $S_{61}(1)$ over $[0.5, 1.5]$ with the NPT output provided in figure 3. By extending these three pathways, we get totally 18 contracted pathways (5 for particle 144, 5 for particle 145, 8 for particle 146). Only 3 (1 for particle 144, 1 for particle 145, 1 for particle 146) of them start with compartment 1. Among these 3 extended pathways, 2 of them enter compartment 1 during $[0, 2]$. For one extended pathway, the particle enters compartment 1 at 0.5 time units (tu) and stay in compartment 6 for 7.6 tu , and for the other one, the particle enters compartment 1 at 1.2 tu and does not visit compartment 6 at all. Therefore:

$$S_{61}(1) = \frac{(7.6) + (0)}{2} = 3.8$$

In general, we compute S as follows:

$$S_{ij}(t) = \lim_{h \rightarrow 0} S(t - h, t + h) = \frac{1}{|\mathcal{P}_j(t - h, t + h)|} \sum_{\mathcal{P}_j(t - h, t + h)} \text{sum of residence times at compartment } i$$

where $\mathcal{P}_j(t - h, t + h)$ is a list of extended pathways that start with compartment j and particle enters j during $[t - h, t + h]$, and $|\mathcal{P}_j(t - h, t + h)|$ represents the number of elements in this list. The larger the value $|\mathcal{P}_j(t - h, t + h)|$, the more accurate our computation of S will be.

3.2 Residence time analysis

3.2.1 NPT based compartmental residence time analysis

We can utilize NPT simulation output to compute residence time (RT) for each compartment as well. This requires a simpler computation than the S matrix, as individual particle residence times

Table 2: Computing of RT_2 with sample NPT results.

	Sum of residence time at compartment 2	Number of 2 in each pathway
Particle 144	(7.1)	1
Particle 145	(9.5) + (5.5)	2
Particle 146	(4.2) + (7.0)	2
\sum_{pathways}	33.3	5

are a direct output of NPT simulations. Therefore all we need to do is to take an average of these individual residence times.

$$RT_i = \sum_{\text{pathways}} \frac{\text{sum of residence time at compartment } i \text{ for each pathway}}{\text{number of } i \text{ in each pathway}}$$

For example, using the data in Figure 3, we show how to compute RT_2 in Table 2:

From table 2, we get

$$RT_2 = 33.3/5 = 6.66tu$$

Besides the averaged value, NPT based methodology enables us to investigate the distribution of these individual residence times, providing more detail on how flow material is managed within the system. We demonstrate the residence time distribution in Section 4.

3.2.2 Input based system residence time analysis using NPT

System residence time for open systems is the average time the flow material spends in the system, which can be computed as $\frac{\text{total system storage}}{\text{total system input (or output)}}$ [Han, 1997] at steady state. However, a compartmental system may have multiple inputs. Based on where the material enters, there might be more than one system RT for the same model, which we call input based system RT. In this case, the ratio of stock to throughflow fails to compute the input based system residence time, let alone the distribution of system RT. Using NPT simulation output, we can compute the input based system RT as the time difference of when the particle enters and leaves the system, and compute its distribution as well. Depending on where the particles enter the system, their mean system residence times and distributions may vary.

From the sample NPT output in figure 3, all the three particles enter the system at compartment 1, so we do not need to specify where the input occurs. By taking the difference of entrance and exit time, we get the total residence time for these three particles, which are 34.3, 40.4, and 48.5. To see the distribution of system residence time, we need to run the model for a long time, allowing enough particles to go through the system and generating enough pathways.

If there are multiple inputs for a particular system, we need to differentiate them and compute their distributions separately. Since different entry points contribute different pathways, these distributions may differ significantly.

3.3 Temporal distribution

Residence time and storage analysis is mostly concerned with how much of a boundary input will end up in other compartments within the system. However, in certain cases, we are also concerned with “when” as well as “how much”. Questions like “When will a certain drug be disposed of from the body?” or “When will a certain part of the ecosystem be free of a contaminant?” need temporal information. Even for systems at steady-state, this temporal information is inherently present. For example, assume 100 kcal energy enters compartment 2 on the 1st day. How much of this energy will reach compartment 5 on the following days? Temporal distribution (TD) is a matrix function that addresses this question directly.

Table 3 shows how to compute TD_{21} with the sample NPT output in figure 3. Three particles enter compartment 1 in 10 days. TD_{21} will show us how many of these 3 particles will be in compartment 2 during the following days. To save spaces, we count the number of particles in compartment 2 every other day. For each particle, we check where it resides every other day. To compute TD, we count the total number of particles in compartment 2 and plot the total number of particles with respect to time. Only three particles are traced in this example, and the time interval of two days is rather large, providing a coarse plot. For better accuracy, we may choose a smaller time interval and trace thousands of particles. In the following two sections, we show the application of TD on two specific models.

Table 3: NPT results show when each particle reach compartment 2 and how long it stays there. Every two days, we check where is each particle. “Y” represents it is in compartment 2, and “N” is not. At the end, we count the total number of particles in 2 over time. This is the 3 particles’ distribution in compartment 2 from this sample NPT output.

	Time (day)																
Particle #	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34
144	N	N	N	N	Y	Y	Y	Y	N	N	N	N	N	N	N	N	N
145	N	N	N	N	N	Y	Y	Y	Y	N	N	N	N	Y	Y	Y	N
146	N	N	N	N	Y	Y	N	N	Y	Y	Y	Y	N	N	N	N	N
Particle # in compartment 2	0	0	0	0	2	3	2	2	2	1	1	1	0	1	1	1	0

4 Results

4.1 NPT based storage analysis

4.1.1 Verification and Accuracy

To verify the accuracy of this new method for computing the S matrix, we compare its results with that of the conventional methodology. Since current methodology is limited to steady state or donor-controlled systems, we choose the Oyster Reef ecosystem model for comparison.

We compute the S matrix for Oyster Reef model using NPT simulation output. As we increase the simulation time, more particle pathway data accumulates, and the stochastic S matrix gradually gets closer to the conventional S matrix, shown in table 1.

To demonstrate this fact, we ran the Oyster Reef model for 1000 times with NPT and computed S_{42} ¹. Figure 5a shows the distribution of S_{42} for three different simulation times. We observe that the variance in S_{42} decreases with longer simulation times, and the NPT-based S_{42} converges to the conventional S_{42} .

To make sure all entries of NPT-based S converge to conventional S , we compute Frobenius norm² of the difference of the two S matrices computed using different methodologies. Frobenius norm of $m \times n$ matrix A is defined as the square root of the sum of absolute squares of its elements.

$$\|A\|_F = \sqrt{\sum_{i=1}^m \sum_{j=1}^n |a_{ij}|^2}$$

In our example, A matrix is the difference between stochastic S and conventional S matrices. Since we use relative error to show the difference, its element a_{ij} is computed as the following:

¹The choice of S_{42} is arbitrary.

² Frobenius norm is a component-wise L^2 -norm, and is more suitable for error analysis in our case compared to the standard L^2 (induced) matrix norm.

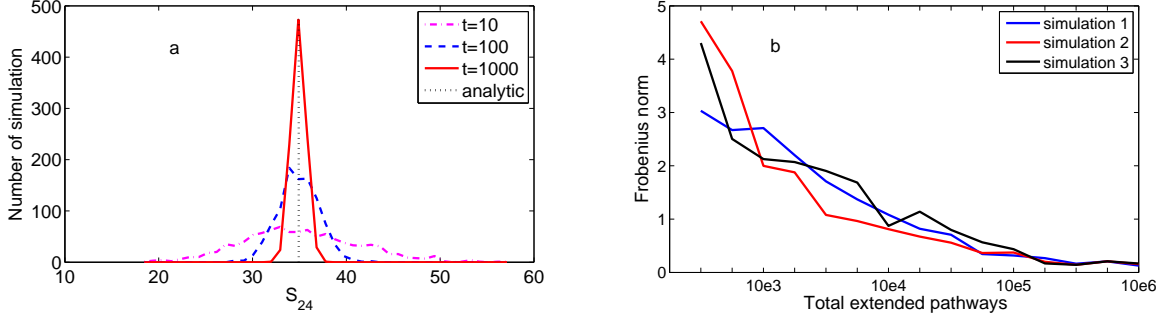


Figure 5: The stochastic storage-generating matrix S is computed for the Oyster Reef model. (a) S_{42} is computed for 1000 NPT simulations. Distribution of one entry, S_{42} is shown for three simulation times. (b) Frobenius norm of difference between stochastic and conventional S matrix is shown for three NPT simulations.

$$a_{ij} = \frac{\text{stochastic } S_{ij} - \text{conventional } S_{ij}}{\text{conventional } S_{ij}}$$

To make the equation easier, we use \mathbb{S} to represent stochastic S matrix and S is conventional S matrix. So we get

$$E(S, \mathbb{S}) = \left\| \frac{\mathbb{S} - S}{S} \right\|_F = \sqrt{\sum_{i=1}^m \sum_{j=1}^n \left| \frac{\mathbb{S}_{ij} - S_{ij}}{S_{ij}} \right|^2}$$

$E(\mathbb{S}, S)$ is the square root of sum of $\left| \frac{\mathbb{S}_{ij} - S_{ij}}{S_{ij}} \right|^2$. In figure 5b, we show a plot of $E(\mathbb{S}, S)$ vs. total extended pathways for 3 NPT running of the same model. We observe that the difference between stochastic and conventional S matrix converges to 0 with the increased simulation time (and number of extended pathways), despite the stochastic behavior of NPT simulation.

4.1.2 Dynamic storage analysis

We have previously discussed the accuracy and convergence properties of NPT based storage analysis definition for steady state ecosystem models 5. Next we do dynamic storage analysis for a simple lake model (see figure 6). The purpose of this model is to convey our method, not to discuss and replicate realistic lake ecosystem dynamics. Here, we simulate the annual changes of biomass in a simple lake model. *Phytoplankton* gets variable environmental input, which represents the availability of nutrients with seasonal variation. Flows between compartments are donor-recipient

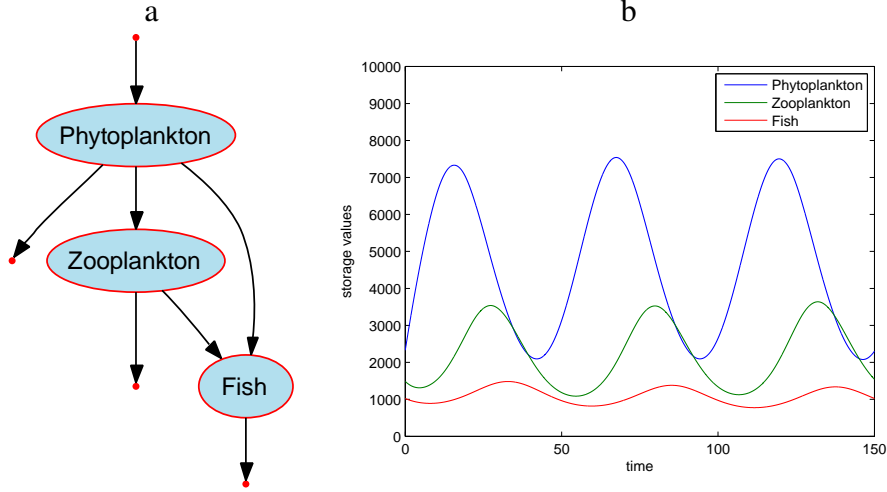


Figure 6: (a) Simple lake model network graph and (b) Evolution of compartmental storage value over time.

controlled.

This model has three compartments: *Phytoplankton*, *Zooplankton*, *Fish*. The equations for this simple lake model are as follows:

$$\dot{P} = 1000 + 600 * \sin(t/8.3) - 0.000025 * P * Z - 0.000025 * P * F - 0.15 * P$$

$$\dot{Z} = 0.000025 * P * Z - 0.000015 * Z * F - 0.1 * Z$$

$$\dot{F} = 0.000025 * P * F + 0.000015 * Z * F - 0.08 * F$$

\dot{P} , \dot{Z} , \dot{F} represent the storage changing rate of *Phytoplankton*, *Zooplankton*, *Fish*. $1000 + 600 * \sin(t/8.3)$ is the only seasonal changing environmental input to *Phytoplankton*. $0.000025 * P * F$ represents consumption of *Phytoplankton* by *Zooplankton*. $0.000015 * Z * F$ represents consumption of *Zooplankton*. Those two flows are donor-recipient controlled, which is determined by the storage value of donor and recipient. $0.15 * P$, $0.1 * Z$, $0.08 * F$ represent the death rate of *Phytoplankton*, *Zooplankton*, and *Fish*.

Figure 6(b) show the time course of compartmental storage values. Storage value of *Zooplankton* performs the similar changes after *Phytoplankton* and *Fish* perform after *Zooplankton*, which is

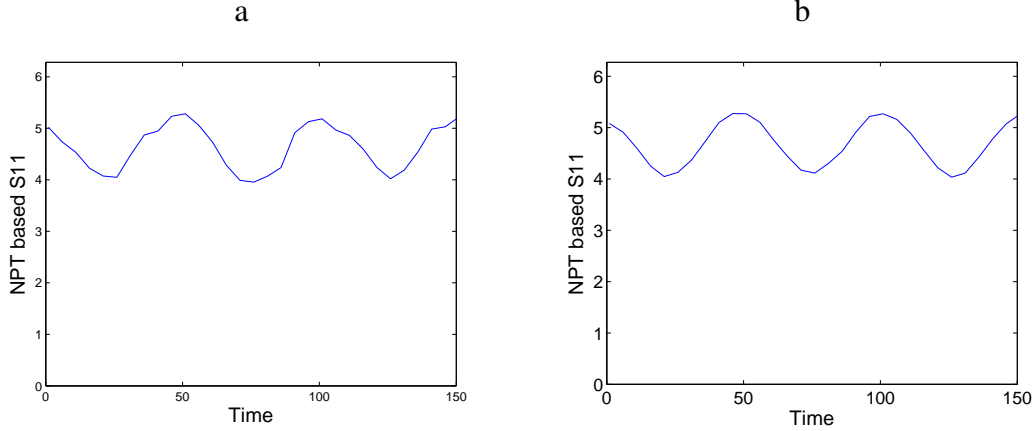


Figure 7: The NPT based dynamic $S_{11}(t)$ (a) based on one NPT simulation. (b) Smoother $S_{11}(t)$ plot is based on the average over 100 NPT simulations.

in accordance with the changing of different trophic levels in a real lake system. The oscillation is driven by the non-linear donor-recipient dynamics and the oscillating environmental input. Because of the oscillating storage values, we expect to observe a changing $S(t)$ matrix for this system.

In figure 7, we show NPT based $S_{11}(t)$. Comparing these two figures with figure 6(b), they have the same cycling period, which is around $50tu$. The oscillating $S(t)$ matrix shows that particles entering the system at different times may have different storage contributions.

It is rather difficult to verify if this new definition of $S(t)$ is correct, as there is no other similar dynamic storage analysis description to compare it to. However, there is one property of $S(t)$ that enables us to check the validity of this new definition. In section , we mention that $S = -C^{-1}$ is constant if all flows in the model are donor controlled, that is, $f_{ij} = c_{ij}x_j$ where c_{ij} is constant for all i, j . Note that this is true for even dynamic ecosystem models. So, if we compute $S(t)$ for a dynamic ecosystem model with donor controlled flows, $S_{ij}(t)$ should stay constant over time, for all i, j .

To verify our definition of $S(t)$, we build a similar lake model, which has the same network graph and similar storage changes over time with the lake model in figure 6. For the lake model in figure 6, we change the flow type to donor-controlled and keep the seasonal changing input. Although the

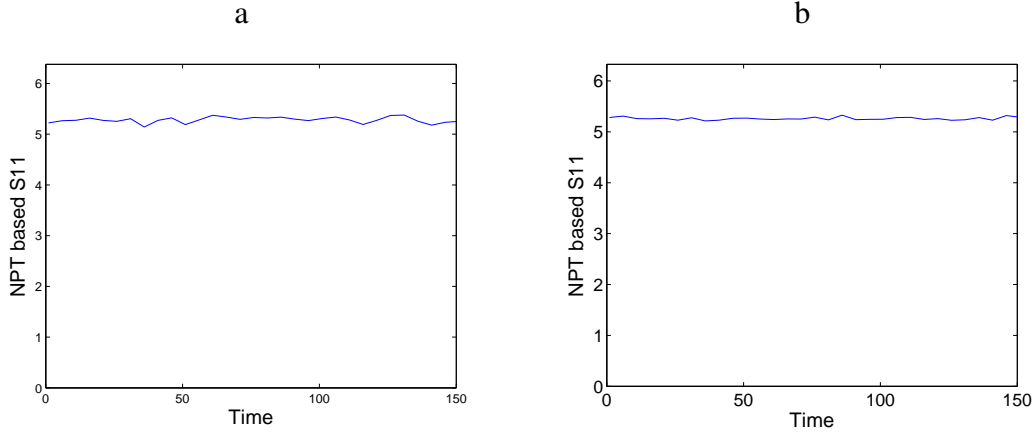


Figure 8: The NPT based dynamic $S_{11}(t)$ value. (a) Based on a single NPT simulation. (b) Smoother $S_{11}(t)$ plot is based on an average of 100 NPT simulations.

flow dynamics are different, we adjusted the parameters of this new model so that the time course plots of these two models are very similar.

Here is the equation for this model:

$$\dot{P} = 1000 + 600 * \sin(t/8.3) - 0.08 * P - 0.01 * P - 0.1 * P$$

$$\dot{Z} = 0.08 * P - 0.05 * Z - 0.1 * Z$$

$$\dot{F} = 0.01 * P + 0.05 * Z - 0.1 * F$$

Except the seasonal changing input, all the compartmental flows are donor controlled.

We perform NPT-based dynamic storage analysis for this new lake model. As all the compartmental flows are donor controlled, we expect to see constant values for $S(t)$ that do not change over time, despite the fact that storage values of all compartments will be changing over time. Result in figure 8 shows that no matter when the particles enter the system, their storage contribution remains constant, as expected.

NPT has excellent convergence properties, and NPT based S can be feasibly computed with arbitrary accuracy. The same results are valid for the dynamic definition as well. However, our

computation of $S(t)$ includes one more parameter (h) which is related to the following approximation:

$$S(t) = \lim_{h \rightarrow 0} S(t-h, t+h) \approx S(t-h, t+h) \text{ when } h \text{ is small}$$

How small should we choose h so that $S(t)$ is computed accurately? This is an important concern, especially if $S(t-h, t+h)$ changes rapidly as $h \rightarrow 0$. Fortunately, it is exactly the opposite. Note that

$$S(t-h, t+h) = \frac{1}{2h} \int_{t-h}^{t+h} S(t) dt$$

Therefore the error term $|S(t-h, t+h) - S(t)|$ is going to be exactly zero if the change in $S(t)$ is linear. In other words, no matter how fast or steep the change in S is, as long as it is linear, NPT based $S(t)$ will be exact. Accuracy will be of concern only if $\frac{d^2S(t)}{dt^2}$ is significantly large. This only happens for extremely sudden changes, and are rather rare for ecosystems. Even in such rare cases, choosing smaller h values guarantees accurate results.

For example, for the dynamic lake model in figure 6, the periods of storage value changes were around 50 time units. Figure 7 was created for $h = 10$.

4.2 Residence time distribution

We expect that the average residence time from each NPT simulation will be around x_i/T_i . And with the increase of total running time, the number of pathways we used for computing residence time increases, and therefore the results get closer to x_i/T_i . We expect that the compartmental residence time distribution will be exponential.

For a system with one environmental input, we are interested in investigating the distribution of system residence time. If the system has multiple environmental inputs, we need to compare the difference between these input based system residence times. Regardless of the number of inputs, we expect to see a large variation depending on the system structure and topology, as was observed in [Yu and Wehrly, 2004].

In this section, we show compartmental and system RTD for the Georgia salt marsh model [Teal,

Table 4: Compartmental stock, throughflow and residence time for eight compartments. These data are from running the Georgia salt marsh model in EcoNet [Kazanci, 2007].

	Stock (kcal/m ²)	Throughflow (kcal/m ² /day)	Residence time (day)
Spartina	520.26	94.74	5.49
Algae	35.21	4.93	7.14
Insects	2.97	1.04	2.86
Detritus	652.07	26.08	25.00
Bacteria	7.22	6.57	1.10
Spiders	0.99	0.15	6.67
Nematodes	9.01	7.30	1.23
Mudcrabs	0.60	0.09	6.67

1962], figure 9.

Running this model in EcoNet [Kazanci, 2007], we got the stock, throughflow, and average residence time at steady state, shown in table 4. We arbitrarily choose two compartments, *Spartina* and *Detritus*, and compute their compartmental RTD using NPT simulations.

Using NPT, we tracked 1,000,000 particles, recorded their residence times in *Spartina* and *Detritus*, and plotted RTD for these two compartments, as shown in figure 10. Mean residence time for *Spartina* and *Detritus* are equal to 5.50 days and 25.06 days, which agree with results in table 4 from EcoNet.

In figure 10, NPT approximation of compartmental RTD coincides with the exponential distribution ($P(t) = \frac{1}{RT} e^{-\frac{t}{RT}}$) as expected. Although the average residence time is 5.50 days, it takes more than 40 days for 99% of the particles to leave compartment *Spartina*, and 150 days for *Detritus*.

System residence time can be computed by taking the ratio of total system storage to total system input (or output):

$$\frac{520.26 + 35.21 + 2.97 + 652.07 + 7.22 + .99 + 9.01 + 0.60}{94.74 + 4.93} = 12.32 (day) \quad (1)$$

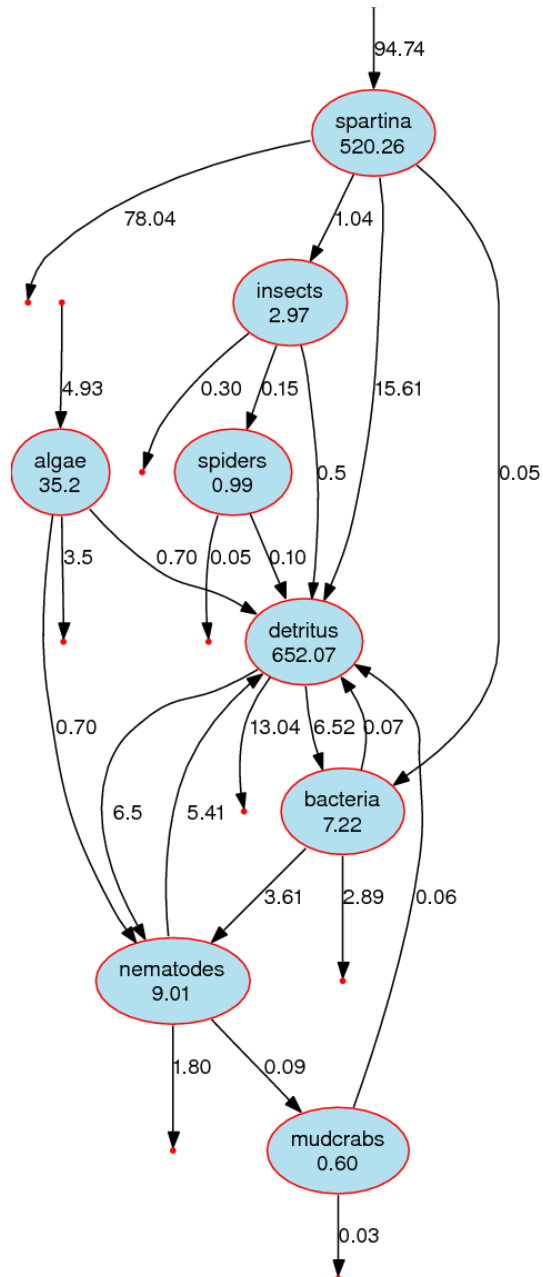


Figure 9: Georgia salt marsh energy flow model with eight compartments and two environmental inputs at *Spartina* and *Algae*. Numbers in circles show storage value for each compartment. Numbers around arrows are flow values between one compartment and another (or the environment).

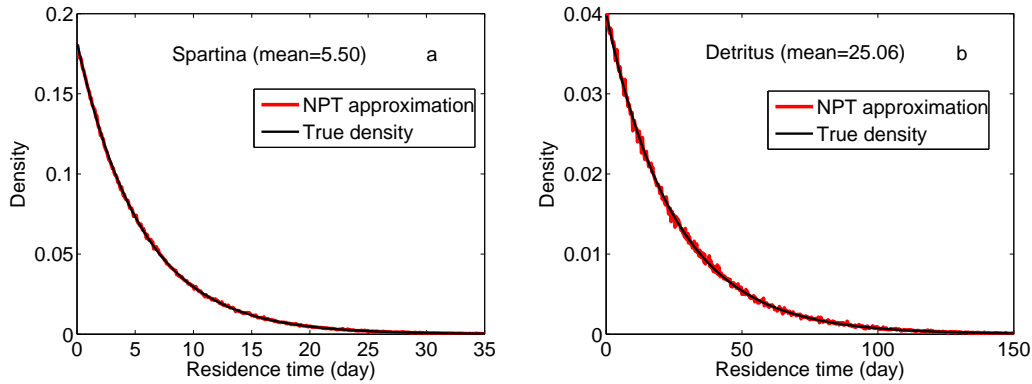


Figure 10: Residence time distribution for *Spartina* and *Detritus* compartments for the Georgia Salt Marsh model shown in figure 9. a & b show density of residence time for the compartments *Spartina* and *Detritus*. Both of them show the comparison of NPT approximation with the numerically approximated true density.

However, unlike the compartmental RTD, computation of system RTD is not trivial, as the distribution need not be exponential. Furthermore, the GA salt marsh ecosystem model receives two environmental inputs. Particles entering the system through different compartments will have different pathway profiles, resulting in different system residence times. Finding the residence times and the associated distribution based on the input location is not an easy task without using NPT simulations. On the contrary, using NPT simulations, computing the system RTD of flow material that enter the system through *Algae* is not any difficult than computing any compartmental RTD. In figure 11, we show the two system RTDs, based on two different environmental inputs at *Algae* and *Spartina*. The computations are based on the same NPT simulation we have used for the compartmental RTD in figure 10.

We observe that the flow material entering the system through *Spartina* and *Algae* have different residence times, 12.11 and 16.87 respectively. Note that 95% of energy enters the GA salt marsh system at *Spartina*, so if we take a weighted average of these two RT's, we get

$$12.11 \times 95\% + 16.87 \times 5\% = 12.34 \approx 12.32$$

which coincides with the average system RT computed without using NPT 1.

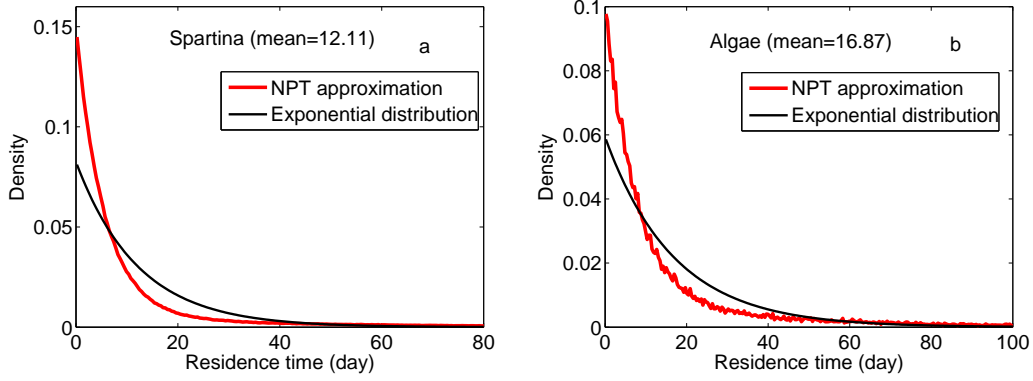


Figure 11: System RTD of energy for the Georgia Salt Marsh model. a & b separately show the RTD for two different environmental inputs: *Spartina* and *Algae*. In each of them, we provide both the results from NPT approximation and the exponential distribution. Exponential distributions are plotted with $\frac{1}{\mu}e^{-t/\mu}$, where $\mu = 12.11$ and 16.87 for these two inputs. The difference clearly demonstrates that the system residence times are not exponentially distributed because of the system structure and topology.

4.3 Temporal distribution

We expect that temporal distribution of material will be affected by residence time in each compartment. The larger the residence times, the longer it takes for particles to reach another compartment. We expect to see various distributions depending on network topology, such as damped oscillations for compartments with high cycling indexes.

4.3.1 NPT based temporal distribution for Oyster Reef model.

We simulate the Oyster Reef model Dame and Patten [1981] with NPT and compute its temporal distribution over time ($TD(t)$). At steady state, this system receives $41.5 \text{ kcal } m^{-2}$ per day from environment at compartment 1 (*Filter Feeders*). Let's consider $TD_{21}(t)$ as an example. First, we set a time window, say $[0, 100]$. During 100 days, $4150 \text{ kcal } m^{-2}s$ energy enters *Filter Feeders*. This part of energy is labeled as 4150 particles and they are tracked until they exit the system. Some of these labeled particles will reach compartment 2 later. As shown in section , we set small time intervals. For each small time interval, we record the number of labeled particles in compartment 2 and plot how the number of particles changes over time. Similarly, we also compute TD_{ij} for $1 \leq i, j \leq 6$.

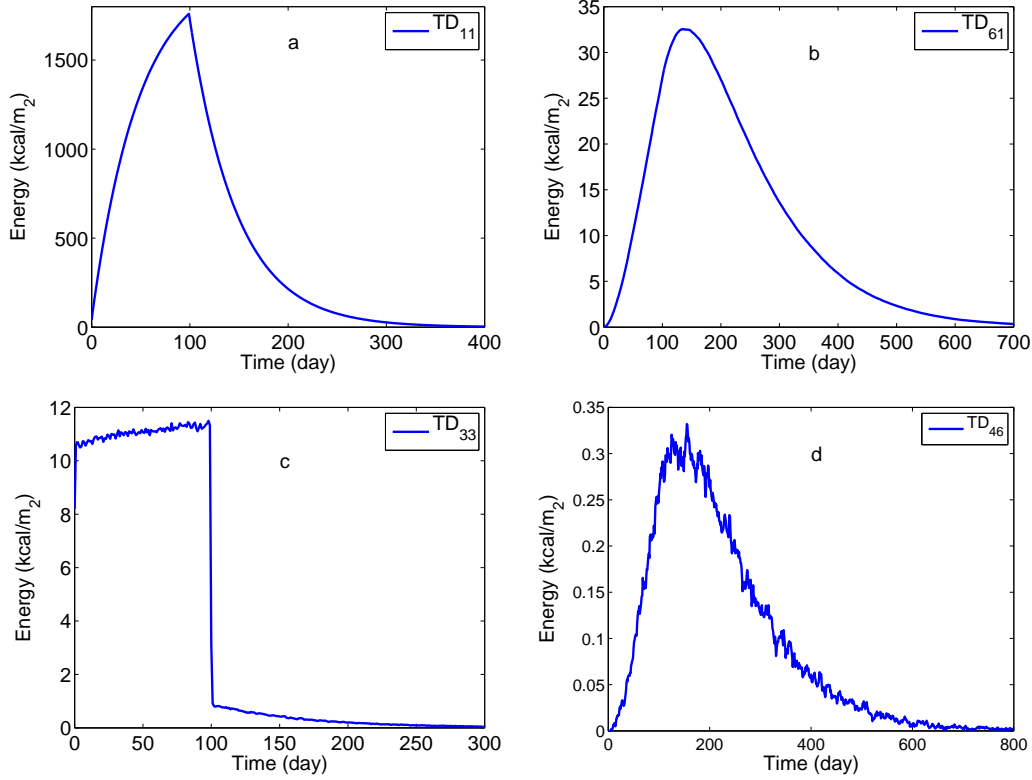


Figure 12: Temporal distribution over time for Oyster Reef model. Four of 36 plots are picked to demonstrate various properties of these distributions. We record this part of energy entering compartments during the first 100 days. In each plot, X and Y-axes represent time and energy amount respectively. For example, figure c (TD_{61}) shows energy amount over time in compartment 6 for the energy entering 1 during the first 100 days.

To get a smoother line, we run the model for 2000 times and take the average of 2000 NPT results. Oyster Reef model has 36 TD plots in total. Below, we summarize some interesting points regarding figure 12.

1. In figure 12a TD_{11} and 12c TD_{33} , the number of particles keeps increasing during $[0, 100]$ and reaches the peak at $t = 100$, and then decreases. After $t = 100$, the TD_{11} goes down much more slowly than TD_{33} . This is because the residence time of compartment 1 is higher than that of compartment 3.
2. In figure 12b TD_{61} , The number of particles keeps increasing and reaches its peak after $t = 100$, at around $t \approx 150$. Time is needed for particles to reach compartment 6 from compartment 1, hence

the time lag.

3. In figure 12 TD_{46} , the number of particles fluctuate, which may be due to cycling. For this model, the fluctuation is not very obvious, which might be related to the low Finn's cycling index [Finn, 1976, 1980] value (0.11).

4. Some of the plots look smooth, e.g. TD_{11} and TD_{61} . And some of them look noisy, e.g. TD_{33} and TD_{46} . We can say that particles entering 6 from compartment 1 are numerous, and those from compartment 6 to 4 are few. So, the fluctuation is much more obvious when there are fewer particles present.

4.3.2 NPT based temporal distribution for drug delivery model

Drugs could be administered through different routes such as oral, intravenous injection, and muscle injection. Figure 13 is a compartment model showing pharmacokinetics of pravastatin [Hatanaka et al., 1998] after single intravenous and oral administration in rats. The deep compartment mainly represents muscle, and the shallow compartment reflects the liver, the target compartment. And absorption compartment is required after oral administration, while there is no absorption for intravenous injection.

We show how the drug is distributed in the rat's system after taking pravastatin. For the same drug amount, we compare the difference between single intravenous and oral administration. The TD plots will be helpful in choosing the more effective administration method.

For each administration method, 5 mg pravastatin is inserted into the rat. We simulated the model with NPT and computed TD over time in each compartment. Figure 14 shows the amount of pravastatin over time in these four compartments, and figure 15 is for intravenous injection. Since injected drug will not reach the *Absorption* compartment, only drug distributions for the other three compartments are shown here.

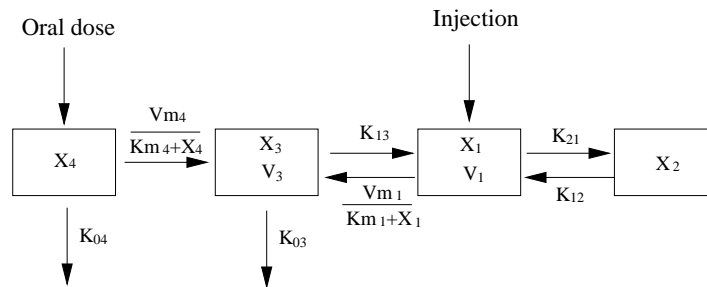


Figure 13: Pharmacokinetic model for pravastatin in a rat [Hatanaka et al., 1998]. Pravastatin is a drug administered to reduce blood cholesterol levels. Four compartments 1, 2, 3, 4 represent *Central*, *Deep*, *Shallow* and *Absorption* compartments, respectively. Drug is administered orally or through intravenous injection.

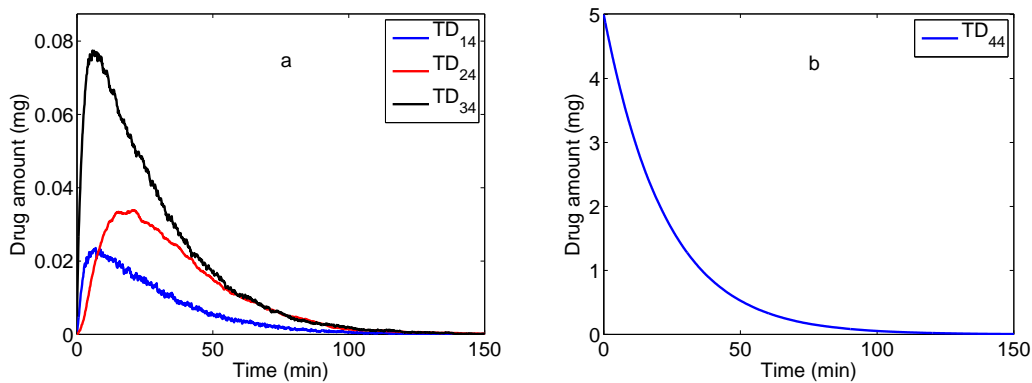


Figure 14: Temporal distribution for oral pravastatin administration. 1, 2, 3, 4 represent *Central*, *Deep*, *Shallow* and *Absorption* compartments, respectively. For this case, the drug is taken orally and enters the system through the absorption system. We plot the drug's amount in all the four compartments. TD_{44} shows the drug's distribution over time in the *Absorption* compartment. Only a small part of the drug stays through absorption and most leaves the system quickly. Similarly, TD_{14} , TD_{24} , TD_{34} show the TD for *Central*, *Deep*, and *Shallow* compartments.

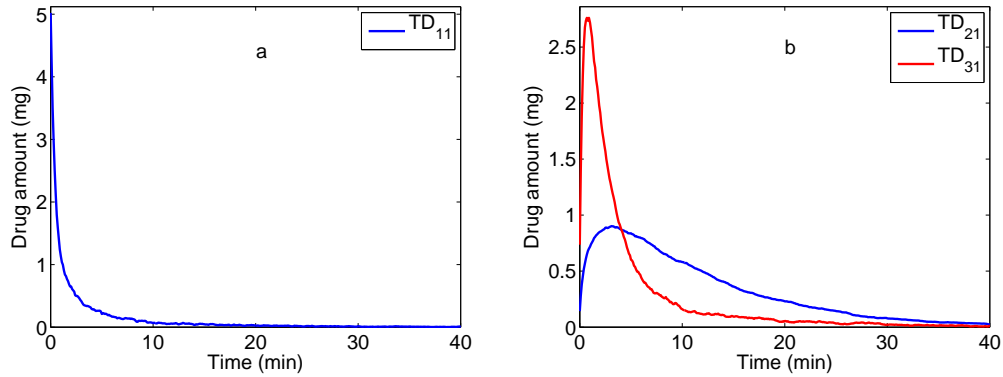


Figure 15: Temporal distribution for intravenous injection administration. 1, 2, and 3 represent *Central*, *Deep*, and *Shallow* compartments, respectively. For this case, the drug is taken injected and enters the system through central system. The drug never goes to *Absorption* compartment in this case. So we plot the drug's density in the other three compartments. TD_{11} shows the drug's distribution over time in *Central* compartment. Similarly, TD_{21} , TD_{31} show the TD for *Deep*, *Shallow* compartments.

Comparing these two figures, orally administered drug stays much longer time in the rats, because it takes time for the drug to be absorbed in the *Absorption* compartment. However, as a result of the low absorption efficiency, most of the drug leaves the system at the absorption process and little enters the other three compartments. On the other hand, the injected drug reaches *Deep*, *Shallow* compartments quicker in higher amounts, but stays there for a relatively shorter time.

We could conclude that oral administration has a longer effect than injection in the *Deep*, *Shallow* compartments, and injection administration takes effect faster.

These plots demonstrate the TD for a single dose with two different administration methods. We could also plot TD for drug administration at regular intervals for a more realistic case study.

5 Discussion

In this thesis, we present the Network Particle Tracking (NPT) based storage analysis and compare this with traditional methods and results. Both methods agree for steady-state systems. Since our simulation-based definition is applicable to both steady-state and dynamic models, we can extend its applicability to many interesting research areas, such as environmental impact studies, effects of climate change, waste management, etc.

By doing storage analysis for dynamic models, we found the following conclusions: For donor controlled models, even compartmental storage values are changing with variable environmental input, S matrix for the system are constant over time. However, if we replace the donor controlled flows with donor-recipient controlled flows, S matrix for these systems will also show dynamic changes.

We extended the definition of a steady-state measure, storage analysis, to evolving ecosystem models. The same procedure can be applied to other steady-state measures that depend on indirect relations among compartments, such as throughflow analysis, Finn's cycling index, indirect effects ratio and utility analysis, etc.

In this project, we also demonstrate the NPT based method to plot residence time distribution (RTD) and temporal distribution (TD). And several applications to specific models are demonstrated.

We already know the compartmental RTD is exponential, which agrees with what we get from NPT outputs. Furthermore, NPT allows us to investigate system RTD, which is not easy to compute. Based on different inputs, we may have more than one system RTD for a given model, which offers a new angle for comparison between different environmental inputs. Most system RTD computation methods are involved and model specific. NPT is general and applicable regardless of model size and complexity. In the future, we plan to investigate system RTD further, and study the relation between network topology and distribution type.

We discussed three system-wide properties separately in this thesis: storage analysis, residence time, temporal distribution. For a unit input, storage analysis represents the stock value it generates at compartment i , residence time represents the average time it remains in compartment i , and temporal distribution shows the time-course of stock generated at compartment i . These related measures complement each other in describing a similar phenomenon from different aspects, providing a comprehensive analysis methodology for understanding storage in complex compartmental models of living systems.

References

- C. Bondavalli and R. E. Ulanowicz. Unexpected effects of predators upon their prey: the case of the american alligator. *Ecosystems*, 2(1): 49–63, 1999.
- H. Cheng and W. J. Jusko. Mean residence time concepts for pharmacokinetic systems with nonlinear drug elimination described by the michaelis menten equation. *Pharmaceutical research*, 5(3):156–164, 1988.
- K. H. Clauset Jr, C. C. Rawley, and G. C. Bodeker. STELLA - software for structural thinking. *Collegiate Microcomputer*, 5(4):311–319, 1987.
- R. F. Dame and B. C. Patten. Analysis of energy flows in an intertidal oyster reef. *Marine Ecology Progress Series*, 5(2):115–124, 1981.
- P. V. Danckwerts. Continuous flow systems : Distribution of residence times. *Chemical Engineering Science*, 2(1):1–13, 1953.
- B. D. Fath and B. C. Patten. Review of the foundations of network environ analysis. *Ecosystems*, 2:167, 1999.
- J. T. Finn. Measures of ecosystem structure and function derived from analysis of flows. *Journal of Theoretical Biology*, 56(2):363–80, 1976.
- J. T. Finn. Flow analysis of models of the hubbard brook ecosystem. *Ecology*, 61(3):562–571, Jun 1980.
- D. T. Gillespie. A rigorous derivation of the chemical master equation. *Physica A*, 188(3):404–425, 1992.
- D. T. Gillespie. The chemical Langevin equation. *The Journal of Chemical Physics*, 113(1):297,

2000.

M. H. Green and J. B. Green. The application of compartmental analysis to research in nutrition.

Annual Review of Nutrition, 10(1):41–61, 1990.

B. P. Han. Residence time of matter and energy in econetworks at steady state. *Ecological*

Modelling, 95:301–310, 1997.

T. Hatanaka, S. Honda, S. Sasaki, K. Katayama, and T. Koizumi. Pharmacokinetic and

pharmacodynamic evaluation for tissue-selective inhibition of cholesterol synthesis by

pravastatin. *Journal of Pharmacokinetics and Pharmacodynamics*, 26(3):329–347, 1998.

J. Z. Hearon. Residence times in compartmental systems and the moments of a certain

distribution. *Mathematical Biosciences*, 15:69–77, 1972.

J. Z. Hearon. Residence times in compartmental systems with and without inputs. *Mathematical*

Biosciences, 55:247–257, 1981.

M. Higashi and B. C. Patten. Further aspects of the analysis of indirect effects in ecosystems.

Ecological Modelling, 31(1):69–77, 1986.

I. Iliuta, F. C. Thyron, O. Muntean, and M. Giot. Residence time distribution of the liquid in

gas-liquid cocurrent upflow fixed-bed reactors. *Chemical Engineering Science*, 51(20):4579 –

4593, 1996.

H. Jeong, B. Tombor, R. Albert, Z. N. Oltvai, and A. L. Barabasi. The large-scale organization of

metabolic networks. *Nature*, 407(6804):651–654, 2000.

C. Kazanci. EcoNet 2.0. University of Georgia, Athens, GA, USA., 2006. URL [http://eco.](http://eco.engr.uga.edu)

[engr.uga.edu](http://eco.engr.uga.edu).

C. Kazanci. Econet: A new software for ecological modeling, simulation and network analysis.

Ecological Modelling, 208(1):3–8, 2007.

- C. Kazanci. *Handbook of Ecological Modelling and Informatics*, chapter Network calculations II: a user's manual for EcoNet, pages 325–350. WIT Press, 2009.
- C. Kazanci and E. W. Tollner. Network particle tracking (NPT): An individual based simulation algorithm compatible with the differential equation representation for network models. In Preparation, 2009.
- C. Kazanci, L. Matamba, and E.W. Tollner. Cycling in ecosystems: An individual based approach. *Ecological Modelling*, In Press, 2008. doi:10.1016/j.ecolmodel.2008.09.013.
- D. Mackay and M. MacLeod. Multimedia environmental models. *Practice Periodical of Hazardous, Toxic, and Radioactive Waste Management*, 6:63, 2002.
- RB MacMullin and M. Weber. The theory of shortcircuiting in continuous-flow mixing vessels in series and the kinetics of chemical reactions in such systems. *Trans. Amer. Inst. Chem. Engng*, 31:409–458, 1935.
- L. Matamba, C. Kazanci, J. R. Schramski, M. Blessing, P. Alexander, and B.C. Patten. Throughflow analysis: a stochastic approach. *Ecological Modelling*, 2009.
- J. H. Matis and B. C. Patten. Environ analysis of linear compartmental systems: the static, time invariant case. *Bulletin International Statistics Institute*, 48:527–565, 1981.
- P. O'hare and G. S. Hayward. Three trans-acting regulatory proteins of herpes simplex virus modulate immediate-early gene expression in a pathway involving positive and negative feedback regulation. *Journal of Virology*, 56(3):723–733, 1985.
- J. Patrício, R. Ulanowicz, M. A. Pardal, and J. C. Marques. Ascendancy as an ecological indicator: a case study of estuarine pulse eutrophication. *Estuarine, Coastal and Shelf Science*, 60(1):23–35, 2004.
- B. C. Patten. Systems approach to the concept of environment. *Ohio Journal of Science*, 78(4):

206–222, 1978.

B. C. Patten. Energy cycling, length of food chains, and direct versus indirect effects in ecosystems. *Can. Bull. Fish. Aqu. Sci.*, 213:119–113, 1985.

B. C. Patten. Energy cycling, length of food chains, and direct versus indirect effects in ecosystems. *Ecosystem Theory for Biological Oceanography*. *Can. Bull. Fish. Aquat. Sci.*, 213:119–138, 1986.

B. C. Patten. Network integration of ecological extremal principles: exergy, emergy, power, ascendancy, and indirect effects. *Ecological Modelling*, 79:75–84, 1995.

B. C. Patten, R. W. Bosserman, J. T. Finn, and W. G. Cale. *Systems Analysis and Simulation in Ecology*, volume 4, chapter Propagation of cause in ecosystems, pages 457–579. Academic Press, New York., 1976.

Y. Plusquellec and G. Houin. Analytical study of open four compartment pharmacokinetic models: concentrations, area under curves, mean residence times. *Journal of biomedical engineering*, 12(4):358, 1990.

S. Ramsey, D. Orrell, and H. Bolouri. Dizzy: stochastic simulation of large-scale genetic regulatory networks. *Journal of bioinformatics and computational biology*, 3(2):415–436, 2005.

G. Small, A. Helton, and C. Kazanci. Can consumer stoichiometric regulation control nutrient spiraling in streams? *Journal of the North American Benthological Society.*, 2009.

J. M. Teal. Energy flow in the salt marsh ecosystem of Georgia. *Ecology*, 43:614–624, 1962.

E. W. Tollner and C. Kazanci. Defining an ecological thermodynamics using discrete simulation approaches. *Ecological Modelling*, 208(1):68–79, 2007.

H. R. Ueda, S. Hayashi, S. Matsuyama, T. Yomo, S. Hashimoto, S. A. Kay, J. B. Hogenesch, and M. Iino. Universality and flexibility in gene expression from bacteria to human. *Proceedings of*

the National Academy of Sciences, 101(11):3765–3769, 2004.

R. E. Ulanowicz. Growth and development: *ecosystems phenomenology*. Springer New York et al., 1986.

J. Yu and T. E. Wehrly. An approach to the residence time distribution for stochastic multi-compartment models. *Mathematical biosciences*, 191(2):185–205, 2004.

T. Zhang, T.Wang, and J.Wang. Mathematical modeling of the residence time distribution in loop reactors. *Chemical Engineering Processing*, 44(11):1221–1227, 2005.