Mean-Field Semantics for a Process Calculus for Spatially-Explicit Ecological Models

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We define a mean-field semantics for S-PALPS, a process calculus for spatially-explicit, individual-based modeling of ecological systems. The new semantics of S-PALPS allows an interpretation of the average behavior of a system as a set of recurrence equations. Recurrence equations are a useful approximation when dealing with a large number of individuals, as it is the case in epidemiological studies. As a case study, we compute a set of recurrence equations capturing the dynamics of an individual-based model of the transmission of dengue in Bello (Antioquia), Colombia.

1 Introduction

The collective evolution of a group of individuals is of importance in many fields; for instance, in system biology, ecology and epidemiology. When modeling such systems, we want to know the emergent behaviors of the whole population given a description of the low-level interactions of the individuals in the system. As an example, in eco-epidemiology the focus is on the number of individuals infected in a certain population and how a small number of individuals infected may lead to an epidemic.

Eco-epidemiology can be seen as a particular case of *population ecology*. The main aim of population ecology is to gain a better understanding of population dynamics and make predictions about how populations will evolve and how they will respond to specific management schemes. In eco-epidemiology, such management schemes can be a cure to a disease, mechanisms to prevent a disease such as vaccines, or mechanisms to prevent the *vector* (species infected with a disease) to spread a disease. To achieve these goals, scientists may construct models of ecosystems and management schemes (e.g., [33]).

Various formalisms have been proposed in the literature for the individual-based modeling of biological and ecological systems. Examples of such formalisms include the calculus of looping sequences [7] and its spatial extension [6], cellular automata [14, 11], Petri nets [17], synchronous automata [13], P systems [9, 8, 25] and process calculi (or process algebras) [28, 19].

In our work, we are interested in the application of process calculi for studying the population dynamics of ecological systems. Process calculi are formal frameworks to model and reason about concurrent systems and provide constructs to express sequential and parallel composition of processes, as well as different means of communication between processes. In contrast to the traditional approach to modeling ecological systems using ordinary differential equations which describe a system in terms of changes in the population as a whole, process calculi are suited towards the so-called "individual-based" modeling of populations. Process calculi enable one to describe the evolution of each individual of the population as a process and, subsequently, to compose a set of individuals (as well as their environment) into a complete ecological system. Process calculi include features such as time [27, 22], probability [29] and stochastic behavior [16]. Furthermore, following a model construction, one can use model-checking

tools for automatically analyzing properties of the models (e.g., [20, 31]) as opposed to just simulating trajectories, as it is typically carried out in most ecological studies.

In a previous work, we presented PALPS (Process Algebra with Locations for Population Systems), a process calculus developed for modeling and reasoning about spatially-explicit individual-based systems [24]. In PALPS, individuals are modeled using discrete time and probabilistic behavior, and space is modeled as a graph of discrete locations. We associated PALPS with a translation to the probabilistic model checker PRISM [3] to perform more advanced analysis of ecological models. Our experiments with PALPS [24, 23] delivered promising results via the use of statistical model checking provided by PRISM. Nonetheless, the results also revealed a limitation: the interleaving nature of the parallel composition operator led to a high level of nondeterminism and, thus, a very quick explosion of the state space. Moreover, the interleaving nature of PALPS comes in contrast to the usual approach of modeling adopted by ecologists where it is considered that execution evolves in phases during which individuals of a population engage *simultaneously* in some process, such as birth, dispersal and reproduction.

To alleviate the problem of the interleaving nature of parallel composition and the high degree of nondeterminism in PALPS, we proposed a new semantics of PALPS, which captures more faithfully the synchronous evolution of populations and removes as much unnecessary nondeterminism as possible. Our proposal consisted of a synchronous extension of PALPS, named *synchronous* PALPS (S-PALPS) [31]. The semantics of S-PALPS implements the concept of *maximum parallelism*: at any given time all individuals that may execute an action will do so simultaneously [31]. Furthermore, we proposed a new translation of S-PALPS to PRISM which implemented this synchronous semantics, as well as other features that removed the restrictions existing in the original framework. This led to a significant improvement regarding the size of S-PALPS models that can by analyzed via translation to PRISM in the range of hundreds of individuals. However, in epidemiological systems, components can number in millions.

To deal with this challenge, in this paper, we present a *mean-field semantics* to represent the average behavior of S-PALPS systems for populations of potentially millions of individuals. Mean-field semantics gives a deterministic approximation of the average behavior of a system, given low-level specifications at the individual level in terms of discrete-time and discrete-space mean-field equations. In this work we propose an algorithm of polynomial-time complexity for producing the mean-field equations given an S-PALPS model of a system. The algorithm avoids computing the complete state-space of a system and its complexity is independent of the size of the populations. Rather, given the stochastic nature of the systems in question, the accuracy of the method relies on the fact that the numbers of each agent in the system are sufficiently large. We illustrate the application of our semantics for the construction of mean-field equations of an S-PALPS model of the transmission of dengue in Bello, Colombia.

Mean-field semantics have been proposed for a number of process calculi including PEPA [16, 32] and WSCCS [29, 20]. The former line of work differs from our semantics since the underlying model is continuous time. Instead, our work is closely related to that of [20] for WSCCS. Our semantics extends that of [20] in two ways. First, we extend the semantics of S-PALPS to deal with locations, since S-PALPS includes an explicit notion of discrete space not present in WSCCS. Second, the nature of our calculus and, specifically, the presence of an explicit probabilistic operator, as opposed to weights, and the absence of nondeterminism at the level of individuals, yields a simpler semantics, as well as the lifting of some of the restrictions imposed in [20]. As related work, we also mention the mean-field semantics proposed for reactive networks in [12] which, however, is not directly related with our aim of providing this analysis capability to the spatially-explicit process calculus S-PALPS.

The remainder of the paper is as follows. In Section 2 we present the syntax and the semantics of S-PALPS. In Section 3 we present a mean-field semantics for S-PALPS. We apply our techniques to study the population dynamics of dengue in Section 5. Section 6 presents conclusions and future work.

2 Synchronous PALPS

In S-PALPS, we consider a system as a set of individuals operating in space, each belonging to a certain species and inhabiting a location. Individuals who reside at the same location may communicate with each other upon channels (e.g., for preying) or they may migrate to a new location. S-PALPS models probabilistic events with the aid of a probabilistic operator.

The syntax of S-PALPS is based on the following basic entities: (1) **S** is a set of species ranged over by **s**, **s'**. (2) **Loc** is a set of locations ranged over by ℓ , ℓ' . The habitat is then implemented via a relation **Nb**, where $(\ell, \ell') \in \mathbf{Nb}$ exactly when ℓ and ℓ' are neighbors. (3) **Ch** is a set of channels ranged over by lower-case strings. The syntax of S-PALPS is given at two levels, the individual level ranged over by P and the system level ranged over by S which are defined as follows:

$$P ::= \mathbf{0} \mid \eta.P \mid \sum_{i \in I} p_i : P_i \mid \gamma? (P_1, P_2) \mid P_1 \mid P_2 \mid C$$

$$S ::= \mathbf{0} \mid P : \langle \mathbf{s}, \ell, q \rangle \mid S_1 \parallel S_2 \mid S \setminus L$$

where $L \subseteq \mathbf{Ch}$, I is an index set, $p_i \in (0,1]$ with $\sum_{i \in I} p_i = 1$, C ranges over a set of process constants \mathscr{C} , each with an associated definition of the form $C \stackrel{\mathrm{def}}{=} P$, and the actions that a process can perform are

$$\eta ::= a \mid \overline{a} \mid go \ell \mid \sqrt{\qquad} \gamma ::= a \mid \overline{a}$$

Beginning with the *individual level*, *P* can be one of the following:

- Process 0 represents the inactive individual, that is, an individual who has ceased to exist.
- Process $\eta.P$ describes the action-prefixed process which executes action η before proceeding as P. An activity η can be an input action on a channel a, written simply as a; an output action on a channel a, written as \overline{a} ; a movement action to location ℓ , $go\ell$; or the tick action $\sqrt{}$ that indicates a discrete-time unit on a global tick action, $\sqrt{}$. Actions of the form a, and \overline{a} , $a \in \mathbf{Ch}$, are used to model activities performed by an individual; for instance, preying and reproduction.
- Process $\sum_{i \in I} p_i : P_i$ represents the probabilistic choice between processes P_i , $i \in I$. The process randomly selects an index $i \in I$ with probability p_i , and then evolves to process P_i . We write $p_1 : P_1 \oplus p_2 : P_2$ for the binary form of this operator.
- Process γ ? (P_1, P_2) depends on the availability of a communication on a certain channel as described by γ . If a communication is available according to γ then the communication is executed and the flow of control proceeds according to P_1 . If not, the process proceeds as P_2 . This operator is a deterministic operator as, in any scenario, the process γ ? (P_1, P_2) proceeds as either P_1 or P_2 but not both, depending on the availability of the complementary action of γ in the environment in which the process is running.

Moving on to the *population level*, population systems are built by composing in parallel sets of located individuals. A set of q individuals of species \mathbf{s} located at location ℓ is defined as $P:\langle \mathbf{s},\ell,q\rangle$. In a composition $S_1\|S_2$ the components may proceed while synchronizing on their actions following a set of restrictions. These restrictions enforce that probabilistic transitions take precedence over the execution of other actions and that time proceeds synchronously in all components of a system. That is, for $S_1\|S_2$ to execute a $\sqrt{}$ action, both S_1 and S_2 must be willing to execute $\sqrt{}$. Action $\sqrt{}$ measures a tick on a global clock. These time steps are abstract in the sense that they do not necessarily have a defined length and, in practice, $\sqrt{}$ is used to separate the rounds of an individual's behavior. In the case of multi-species systems these actions must be carefully placed in order to synchronize species with possibly different time scales.

System $S \setminus L$ models the restriction of channels in L within S. This construct is important to define *valid systems*: We define a *valid* system to be any process of the form $S \setminus L$ where, for all of S's subprocesses of the form a?(P,Q) and $\overline{a}?(P,Q)$ we have that $a \in L$. Hereafter, we consider only valid systems.

Example 1. Let us consider a species **s** where individuals cycle through a dispersal phase followed by a reproduction phase. Further, suppose that the habitat is a ring of size m where the neighbors of location ℓ are $\ell \pm 1$. In S-PALPS, we may model **s** by P_0 , where

$$P_0 \stackrel{\text{def}}{=} \sum_{\ell \in \mathbf{Nb}(\mathsf{myloc})} \frac{1}{2} : go \, \ell. \sqrt{.P_1} \qquad P_1 \stackrel{\text{def}}{=} p : \sqrt{.(P_0|P_0)} \, \oplus \, (1-p) : \sqrt{.(P_0|P_0|P_0)}$$

According to the previous definition, during the dispersal phase, an individual moves to a neighboring location which is chosen probabilistically among the neighboring locations of the *current location* (myloc) of the individual. Subsequently, the flow of control proceeds according to P_1 which models the probabilistic production of one offspring (case of $P_0|P_0$) or two offspring (case of $P_0|P_0|P_0$). A system that contains two individuals at a location ℓ and one at location ℓ' can be modeled as

System
$$\stackrel{\text{def}}{=} P_0: \langle \mathbf{s}, \ell, 2 \rangle | P_0: \langle \mathbf{s}, \ell', 1 \rangle$$
.

The semantics of S-PALPS is defined operationally via two transition relations, the *non-deterministic* transition relation and the *probabilistic transition relation* yielding transition systems that can be easily translated into *Markov decision processes* [26]. The main features of the semantics is that probabilistic transitions take precedence over all other actions and that all processes must synchronize on timed actions. Finally, at any given time, all individuals that may execute an action will do so simultaneously. A full account of the semantics can be found in [31].

3 Mean-field semantics for S-PALPS

Using the operational semantics of S-PALPS, we can study the transient dynamics of a system: the time series evolution of the model. This is necessary for the simulation of models that can be obtained by translating S-PALPS to PRISM. Using PRISM it is also possible to use model checking or approximated model checking (i.e., statistical model checking). Although this approach can be effective for S-PALPS models with fairly large state spaces (consisting of populations in the range of a few hundreds of individuals), the size of a state space is exponential in the number of components and locations, and, in epidemiological systems, components can number in millions. To address this challenge, in this section we develop a mean-field semantics for S-PALPS which can be used for reasoning about systems with very large populations. To compute the mean-field semantics, we proceed in 3 steps: (1) compute the initial-state matrix, (2) compute the state-transition table and (3) compute the mean-field equations. In particular, we begin by assuming an S-PALPS model of the form:

$$System = (\Pi_{1 \leq j \leq m} P_1: \langle \mathbf{s}_1, \ell_j, q_{1,j} \rangle | \dots | \Pi_{1 \leq j \leq m} P_n: \langle \mathbf{s}_n, \ell_j, q_{n,j} \rangle) \setminus L$$

where P_1, \ldots, P_n , is the set of all processes the populations may evolve into, $\mathbf{s}_1, \ldots, \mathbf{s}_n \in \mathbf{S}, \ell_1, \ldots, \ell_m \in \mathbf{Loc}$ is the set of all locations in the system, and the $q_{i,j} \geq 0$ are the sizes of the population of individuals at state P_i at location ℓ_j where, if a location-state pair (P_i, ℓ_j) for some species \mathbf{s} is not present in the initial configuration then *System* includes the component $P_i:\langle \mathbf{s}, \ell_j, 0 \rangle$.

Restrictions for our method are the following: as usual, the numbers of the agents q_i must be sufficiently large and process constants must be guarded. That is, we do not allow definitions of the form $C \stackrel{\text{def}}{=} P|C$, since these yield infinite-sized systems.

- **1. Initial-state matrix** (*Init*). This matrix, *Init*, captures the initial configuration of the system under study by noting the number of individuals of each type at each location. It is a matrix of size $n \times m$, where n is the number of all accessible process-states and m the number of distinct locations in the system (see the definition of *System* above) and it is obtained directly from the definition of *System*. Specifically, Init[i, j] = q where q is the number of individuals of state P_i at location ℓ_i .
- **2. State-transition table** (*STT*). This 3-dimensional table, *STT*, shows how processes evolve from one state to another and how their locations change. Each entry in the state-transition table is an expression that captures the average evolution, after the execution of a single action of a process P at a location ℓ to some process Q at a location ℓ' . This is expressed as a function of the size of the population of process P. Formally, matrix STT is of size $n \times n \times m$. We point out again that n is the number of different states individuals may engage in and m the number of locations in a system. Note that while these quantities may be big, if we are considering a detailed model of a system (many process states and large number of locations), typically, they are fairly small and, most importantly, they are independent of the size of the populations considered as well as the size of the system under consideration. This matrix captures the evolution after one action step and not necessarily after a time unit, since actions under study may include actions such as $go \ \ell$, communication actions and probabilistic actions. The entries of the matrix are expressions that capture the number of processes of a certain type that have evolved at a location as a function of the number of various processes at different locations that may evolve into the specific state-location pair, in the previous step of the system.

In order to capture the evolution in a manner compatible with the original S-PALPS semantics, we employ the following notions: timed(S) captures whether S may engage in a timed action (all its active components may execute $\sqrt{}$); prob(S) captures whether S may engage in a probabilistic actions (at least one of its components may execute a probabilistic action). These notions are essential to capture that probabilistic actions take precedence over all other actions and that $\sqrt{}$ actions may take place only if all components of the system are willing to synchronize on a timed step. In particular, given a system S, to construct the values of the transition matrix STT capturing the evolution of its components $P_i:\langle \mathbf{s}_i, \ell_i, q_i \rangle$ we use a function $[\![\cdot]\!]: \mathbf{Proc} \times \mathbf{Act} \to \mathscr{P}(\mathbf{Expr}: \mathbf{Proc})$, where \mathbf{Proc} is the set of all processes of the form $P:\langle \mathbf{s}, \ell, q \rangle$ and \mathbf{Expr} is an expression capturing the evolution in question. In particular, given a process $P:\langle \mathbf{s}, \ell, q \rangle$ and an action α , $[\![P:\langle \mathbf{s}, \ell, q \rangle, \alpha]\!]$ returns a set of expressions $e_i: P_i:\langle \mathbf{s}, \ell_i, q_i \rangle$ capturing the set of processes in which $P:\langle \mathbf{s}, \ell, q \rangle$ may evolve and the concentration e_i for each of these processes as a function of the concentration of $P:\langle \mathbf{s}, \ell, q \rangle$. We proceed to define this function. We begin with the evolution according to probabilistic transitions and timed actions, where we have:

$$\begin{split} & \llbracket P{:}\langle \mathbf{s},\ell,q\rangle,a) \rrbracket &= \langle \rangle, & \text{if } \mathsf{prob}(S) \\ & \llbracket P{:}\langle \mathbf{s},\ell,q\rangle,prob \rrbracket &= \langle p_i \cdot P_t : P_i{:}\langle \mathbf{s},\ell,q\rangle|i \in I\rangle, & \text{if } P = \sum_{i \in I} p_i{:}P_i \\ & \llbracket P{:}\langle \mathbf{s},\ell,q\rangle,\sqrt{\rrbracket} &= \langle P_t : P'{:}\langle \mathbf{s},\ell,q\rangle\rangle, & \text{if } P = \sqrt{.P'} \text{ and } \mathsf{timed}(S) \\ & \llbracket P{:}\langle \mathbf{s},\ell,q\rangle,\sqrt{\rrbracket} &= \langle \rangle, & \text{if } P = \sqrt{.P'} \text{ and } \neg \mathsf{timed}(S) \end{split}$$

Thus, no communication on channel a may take place if a process occurs within a system satisfying prob(S). Similarly, a $\sqrt{}$ action may not take place if the process does not occur within a system satisfying timed(S). On the other hand, probabilistic transitions may take place freely and so do $\sqrt{}$ actions within timed systems. Note that in the above, we write P_t for the number of agents P at step t.

Moving on to the execution of a movement action, we define:

$$[P:\langle \mathbf{s},\ell,q\rangle,\tau_{go,\ell}] = \langle P_t:P':\langle \mathbf{s},\ell',q\rangle\rangle, \text{ if } P=go\ell'.P'$$

This leaves us with the execution of channel-based actions where we distinguish the following cases:

• If $P = \eta . P'$, where $\eta \in \{a, \overline{a}\}$ and $a \notin L$, that is a does not belong to the set of restricted channels, then we have

$$[P:\langle \mathbf{s}, \ell, q \rangle, \eta] = \langle P_t: P':\langle \mathbf{s}, \ell, q \rangle \rangle, \text{ if } P = \eta.P'$$

• If $P = \eta . P'$ where $\eta \in \{a, \overline{a}\}$ and $a \in L$, then the number of agents evolving to P' depends on the number of agents co-located with P and available to execute action η and the complementary action $\overline{\eta}$. Let us write X_t for the number of co-located agents able to execute η and Y_t for the number of co-located agents able to execute the complementary action $\overline{\eta}$. If $Y_t \ge q + X_t$ then all agents of type P will proceed to state P'. If not, then the mean change in agent P is expressed as

$$\frac{\sum_{k=1}^{q} k \binom{q}{k} \binom{X_t}{Y_t - k}}{\sum_{k=1}^{q} \binom{q}{k} \binom{X_t}{Y_t - k}}$$

This term can be simplified using *Vandermonde's Convolution* and standard theory regarding the binomial coefficient to $\frac{q \cdot Y_t}{X_t}$ [15]. Thus, we have:

$$\llbracket \eta.P:\langle \mathbf{s},\ell,q\rangle,\eta \rrbracket = \langle \min(q,\frac{q\cdot Y_t}{X_t}):P':\langle \mathbf{s},\ell,q\rangle\rangle$$

• Finally, we have to consider the evolution of a $P = \gamma?(P_1, P_2)$ process. In such processes, we know that $\gamma \in \{a, \overline{a}\}$ where $a \in L$. Thus, the evolution is similar to the previous case. The point in which this case differs is when there is not a sufficient number of collaborating agents to provide the complementary $\overline{\gamma}$ actions. In such a case, a number of instances of the process will evolve to P_2 thus, giving:

$$\llbracket \gamma?(P_1, P_2) : \langle \mathbf{s}, \ell, q \rangle, \boldsymbol{\eta} \rrbracket = \langle \min(q, \frac{q \cdot Y_t}{X_t}) : P_1 : \langle \mathbf{s}, \ell, q \rangle, (q - \min(q, \frac{q \cdot Y_t}{X_t})) : P_2 : \langle \mathbf{s}, \ell, q \rangle \rangle$$

3. Mean-field equations (MFEs). Using the state-transition table and the initial-state matrix, we can derive a set of recurrence equations that represent the mean-field semantics of a system. The system of recurrence equations contains one variable for each different process and at each location in a system. A variable $P_i(t)@\ell_j$ represents the mean number of individuals of process $P_i:\langle \mathbf{s},\ell_j,m'\rangle$, at time t and location ℓ_j and a variable $P(t-1)@\ell_j$ represents the number of individuals of process P_i at location ℓ_j during time t-1. Formally, $P_i(t)@\ell_j$ is defined by

$$P_i(t) @ \ell_j = \begin{cases} Init[i, j] & t = 0 \\ \sum_{1 \le k \le n} STT[k][i][\ell_j] & \text{otherwise} \end{cases}$$

In the first case, for t=0, the value is obtained from the initial-state matrix. The second case, for t>0, the value is obtained from state-transition from all the processes in the system. According to the state-transition table, processes that do not derive into $P':\langle \mathbf{s},\ell,m'\rangle$ are said to produce 0 individuals of process $P':\langle \mathbf{s},\ell,m'\rangle$ in the next time unit.

Algorithm 1 is the pseudocode to construct the state-transition table *STT*. For simplicity, we assume that the entries of the state-transition table are expressions over the number of individuals of each process.

Algorithm 1 Algorithm to compute the state-transition table (STT) of a S-PALPS model

```
1: procedure COMPUTE_STT(System)
             STT = \text{matrix of dimension } n \times n \times m \text{ initialized with } 0
 3:
             for each P_i, \ell_i \in System do
                   if P = \sum_{i \in J} p_i : P_i then STT[i][j][\ell_i] + p_i \cdot P_i@(t-1), \forall j \in J
 4:
                    else if P_i = \sqrt{P_i} and timed(System) then STT[i][j][\ell_i] + P_i@(t-1)
 5:
                    else if P_i = go \ell_k . P_j then STT[i][j][\ell_k] + e P_i@(t-1)
 6:
                    else if \eta ==a or \eta ==\overline{a}, a \notin L and P_i ==\eta . P_i then STT[i][j][\ell_i] +=P_i@(t-1)
 7:
                    else if \eta ==a or \eta ==\overline{a}, a \in L and P_i == \eta . P_i then
 8:
                          X_{t-1} = number of co-located agents executing \eta
 9:
                          Y_{t-1} = number of co-located agents executing \overline{\eta}
10:
                   STT[i][j][\ell_j] += \min(P_i@(t-1), \frac{P_i@t-1\cdot Y_{i-1}}{X_{i-1}})
STT[i][i][\ell_j] += P_i@(t-1) - \frac{P_i@t-1\cdot Y_{i-1}}{X_{i-1}})
else if \eta \in \{a, \overline{a}\} and a \in L and P_i == \gamma?(P_j, P_k) then
11:
12:
13:
                          X_{t-1} = number of co-located agents executing \eta
14:
                         \begin{split} Y_{t-1} &= \text{number of co-located agents executing } \frac{1}{\eta} \\ STT[i][j][\ell_j] + &= \min(P_i@(t-1), \frac{P_i@t-1\cdot Y_{t-1}}{X_{t-1}}) \\ STT[i][k][\ell_j] + &= P_i@(t-1) - \frac{P_i@t-1\cdot Y_{t-1}}{X_{t-1}}) \end{split}
15:
16:
17:
18:
             end for
19:
20: end procedure
```

Theorem 1. The complexity of Algorithm 1 is $O(n^2 \cdot m)$ where n is the number of different states individuals may engage in and m the number of different locations in the system.

Proof. The algorithm consists of a loop that fills in the positions of the 3-dimensional matrix STT. Assuming that by some preprocessing we have the set of processes executing the actions η and $\overline{\eta}$ of interest, each value of the matrix can be computed at constant time, yielding the result.

Example 2. In what follows we present the mean-field semantics of Example 1. In this example, we have a total of 7 process states: $R_1 = P_0$, $R_2 = go(\text{myloc} + 1).R_4$, $R_3 = go(\text{myloc} - 1).R_4$, $R_4 = \sqrt{.P_1}$, $R_5 = P_1$, $R_6 = \sqrt{.(P_0|P_0)}$ and $R_7 = \sqrt{.(P_0|P_0|P_0)}$. Furthermore, let us assume that the habitat is a ring of size 4.

1. In the initial-state, there are 2 individuals of process P_0 at location 1 and 1 individual of process P_0 at location 2. This is represented in the following 4×7 initial-state matrix:

2. Using the methodology defined above, the transition matrix for the example is given below. Note that in fact this is a 3-dimensional matrix, the third dimension being the location dimension. To capture this in two dimensions we write $@\ell'$ whenever the resulting individuals have moved to another location, ℓ' being this location.

		R_1	R_2	R_3	R_4	R_5	R_6	R_7
$R_1:\langle \mathbf{s},\ell,q\rangle$	prob		$\frac{1}{2} \cdot q$	$\frac{1}{2} \cdot q$				
$R_2:\langle \mathbf{s},\ell,q \rangle$	go				$q@(\ell+1)$			
$R_3:\langle \mathbf{s},\ell,q\rangle$	go				$q@(\ell-1)$			
R_4 : $\langle \mathbf{s}, \ell, q \rangle$						q		
$R_5:\langle \mathbf{s},\ell,q \rangle$	prob						$p \cdot q$	$(1-p)\cdot q$
$R_6:\langle \mathbf{s},\ell,q\rangle$		$2 \cdot q$					·	
$R_7:\langle \mathbf{s},\ell,q \rangle$		$3 \cdot q$					·	

3. Let us write $P(t)@\ell$ for the average number of individuals of process R, at time t and location ℓ . This can be computed as follows: $R_i(t)@\ell$ is equal to 2 if $i,t,\ell=1,0,1$, equal to 1 if $i,t,\ell=1,0,2$, and 0, if t=0 and $i\neq 1$ or $\ell \notin \{1,2\}$, whereas if t>0 we have:

$$\begin{array}{lll} R_{1}(t)@\ell & = & 2 \cdot R_{6}(t-1)@\ell + 3 \cdot R_{7}(t-1)@\ell \\ R_{2}(t)@\ell & = & \frac{1}{2} \cdot R_{1}(t-1)@\ell \\ R_{3}(t)@\ell & = & \frac{1}{2} \cdot R_{1}(t-1)@\ell \\ R_{4}(t)@\ell & = & R_{2}(t-1)@(\ell+1) + R_{3}(t-1)@(\ell-1) \\ R_{5}(t)@\ell & = & R_{4}(t-1)@\ell \\ R_{6}(t)@\ell & = & p \cdot R_{5}(t-1)@\ell \\ R_{7}(t)@\ell & = & (1-p) \cdot R_{5}(t-1)@\ell \end{array}$$

By manipulating the equations and restricting attention to how the system evolves between $\sqrt{}$ actions, we obtain:

$$R_1(t)@\ell = 2 \cdot p \cdot R_5(t-2)@\ell + 3 \cdot (1-p) \cdot R_5(t-2)@\ell$$

$$R_5(t)@\ell = \frac{1}{2} \cdot R_1(t-3)@(\ell+1) + \frac{1}{2} \cdot R_1(t-3)@(\ell-1)$$

4 Correctness of the mean-field semantics

In this section, we prove the correctness of our mean-field semantics by establishing the relation between the derived mean-field equations and the S-PALPS semantics. To achieve this, we first define an encoding of the operational semantics of S-PALPS into a *discrete-time Markov chain* (DTMC). Then we show that the recurrence equations obtained from the mean-field semantics of S-PALPS are equivalent to the recurrence equations obtained from DTMC-semantics of S-PALPS. This follows a result of [18], according to which it is possible to derive *ordinary differential equations* (*ODEs*) as an approximation of the average behavior of a DTMC. At the limit, where the DTMC consists of infinitely many agents, the mean of the DTMC is equivalent to the derived ODE's.

Derivation of a DTMC from a S-PALPS system. The semantics of S-PALPS is given operationally via a structural operational semantics [31]. This semantics is given in terms of two transition relations, a non-deterministic transition and a probabilistic transition relation, which give rise to labeled transition systems that present both non-deterministic and probabilistic states. In the context of this work, we present a method for interpreting such transition systems as a DTMC, under an abstract bisimulation.

Essentially, an abstract bisimulation is an equivalence relation that allows us to disregard the structure of the non-deterministic choices and just look at the probabilities of reaching any particular state. This approach to derive a DTMC from a probabilistic process calculus, was proposed first by Tofts for process calculus WSCCS [29].

To begin with, we define an abstract notion of evolution as follows:

$$P \xrightarrow{\beta[p]} P'$$
 if an only if $P \xrightarrow{p_1}_p P_1 \xrightarrow{p_2}_p \dots \xrightarrow{p_{n-1}}_p P_{n-1} \xrightarrow{p_n}_p P_n \xrightarrow{\beta}_p P'$ where $p = \prod_{1 \le i \le n} p_i$

We lift this notion to evolution into a set of processes as follows, where S is a set of S-PALPS processes:

$$P \xrightarrow{\beta[p]} S$$
 if an only if $p = \sum \{p_i \mid P_i \xrightarrow{\beta[p_i]} P, P \in S\}$

We may now define the notion of abstract bisimulation as follows:

Definition 1. An equivalence relation $\mathscr{R} \subseteq \Pr{\times} \Pr{\text{ is an } abstract } bisimulation \text{ if } (P,Q) \in \mathscr{R} \text{ implies that for all equivalence classes } S \in \Pr{/\mathscr{R}, \text{ actions } \beta, \text{ and for all } p \in [0,1], P \xrightarrow{\beta[p]} S \text{ if and only } Q \xrightarrow{\beta[p]} S.$

We say that two processes are abstract bisimulation equivalent, written $P \sim Q$, if there exists an abstract bisimulation \mathcal{R} such that $(P,Q) \in \mathcal{R}$.

This relation can be used to translate any S-PALPS system into a DTMC: by building an abstract bisimulation on the set of states of the system, we obtain a DTMC whose states are the equivalence classes of the equivalences relation and the transition labels are $\beta[p]$, as defined above.

We now turn to proving the relation between the DTMC semantics and the mean-field semantics of S-PALPS. To do this we refer to [18] where limit theorems were presented relating the mean of Continuous Time Markov Chains and Discrete Time Markov Chains to ordinary differential equations. In particular [18] shows that, at the limit, where a DTMC consists of infinitely many agents, the mean of the Markov chain is equivalent to a derived set of ODEs. An intermediate step of Kurtzs proof produces terms equivalent to those of our mean-field semantics. We use this to show the correctness of our semantics. In particular, we refer to a result of [18] capturing the conditions under which the limit theorem holds and then verify that these conditions apply to S-PALPS models. The theorem states the following:

Theorem 2. Let $X_n(k)$ be a sequence of discrete time Markov processes with measurable state spaces (E_n, \mathcal{B}_n) , $E_n \in \mathcal{B}^k$, the Borel sets in \mathbb{R}^k and one step transition functions denoted by

$$\mu_n(x,\Gamma) = P\{X_n(k+1) \in \Gamma | X_n(k) = x\}$$

Suppose there exist sequences of positive numbers α_n and ε_n

$$\lim_{x\to\infty} \alpha_n = \infty$$
 and $\lim_{x\to\infty} \varepsilon_n = 0$

such that

$$\sup_{n} \sup_{x \in E_n} \alpha_n \int_{E_n} |z - x| \mu_n(x, dz) < \infty$$

and

$$\lim_{x\to\infty} \sup_{x\in E_n} \alpha_n \int_{|z-x|>\varepsilon_n} |z-x|\mu_n(x,dz) = 0$$

Then, for every $\delta > 0$, t > 0

$$\lim_{n\to\infty}\sup_{x\in E_n}P\{\sup_{k\leq\alpha_nt}|X_n(k)-X_n(0)-\sum_{l=0}^k\frac{1}{\alpha_n}F_n(X_n(l))|>\delta \text{ where }X_n(0)=x\}=0$$

where $F_n(x) = \alpha_n \int_{E_n} (z - x) \mu_n(x, dz)$.

Proof of correctness. We recall, from Section 3, that restrictions are as usual when dealing with mean field approximations: the numbers of the agents must be sufficiently large and process constants must be guarded to avoid infinite-sized systems. Essentially, this result proves that, assuming that the various conditions hold, the difference between state changes in the Markov chain and the ones expressed in the relevant ODE are in fact equivalent.

Theorem 3. Given System = $(\Pi_{1 \leq j \leq m} P_1: \langle \mathbf{s}_1, \ell_j, q_{1,j} \rangle | \dots | \Pi_{1 \leq j \leq m} P_n: \langle \mathbf{s}_n, \ell_j, q_{n,j} \rangle) \setminus L$ in S-PALPS, the system of recurrence equations with variables $P_1(t) @ \ell_1 \dots P_1(t) @ \ell_m, \dots, P_n(t) @ \ell_1, \dots P_n(t) @ \ell_m$ represents the average behavior of the system at any discrete-time unit t.

Proof. We show that the recurrence equations obtained from the mean-field semantics of S-PALPS are equivalent to the recurrence equations obtained from the mean-field approximation of the derivation of S-PALPS's operational semantics into a DTMC.

To do this we must confirm that the condition of the theorem above are satisfied.

- 1. According to the theorem, we require a set of DTMC processes $X_n(k)$. Indeed, the states of an S-PALPS system is in \mathbb{N}^k , where k is the number of different processes in the system times the number of locations. This is a consequence of the initial-state matrix defined in Section 3.
- 2. When considering processes over $\{0, 1, ..., n\}$, Kurtz rescales such processes to [0, 1] by dividing each element by n and letting $n \to \infty$. Processes in a system of S-PALPS range over $\{0, 1, ..., n\}$, where n is the number of different processes in the system times the number of locations. They can also be rescaled to match the defined conditions.
- 3. According to the theorem, the one step transition function is represented by $\mu_x(x,\Gamma) = P\{X_n(k+1) \in \Gamma | X_n(k) = x\}$. If we consider the labelled-transition system of S-PALPS under abstract bisimulation, the one step transition function can be extracted as $\mu_n(P, \{P' | P \xrightarrow{\beta[p]} P'\}) = p$.
- 4. Finally, the theorem assumes that there exists sequence of positive numbers α_n and ε_n such that $\lim_{x\to\infty} \alpha_n = \infty$ and $\lim_{x\to\infty} \varepsilon_n = 0$, and

$$\sup_{n} \sup_{x \in E_n} \alpha_n \int_{E_n} |z - x| \mu_n(x, dz) < \infty$$

and

$$\lim_{x\to\infty} \sup_{x\in E_n} \alpha_n \int_{|z-x|>\varepsilon_n} |z-x|\mu_n(x,dz) = 0$$

In terms of S-PALPS, we can think of x and z being state matrices with a component representing each type of process in the system at each location. The term |z-x| denotes the difference between the two states x and z. As $n \to \infty$, the number of states that can be reached in one step becomes very large. Furthermore, there is higher probability of moving to a state with small change from

the previous state when there are lots of components since there are lots of ways to make that change. Similarly, the states for which the change is high are less likely to occur. In addition we have that, since process are rescaled to [0,1], then $0 \le |x-z| \le 1$, and since $\mu(x,z)$ is a probability, we conclude that $0 \le \mu(x,z) \le 1$. Given the relation of probabilities and degree of changes noted above, we conclude that $\int_{E_n} |z-x| \mu_n(x,dz) \to 0$ and that as n and α_n tend to infinity, $\alpha_n \int_{E_n} |z-x| \mu_n(x,dz) \to 0$

 $x|\mu_n(x,dz) < \infty$ as required. Similarly, we may verify the last relation by noting that it captures the states for which $\mu(x,z) = 0$.

Thus, by Theorem 2, for every $\delta > 0$, t > 0, we have

$$\lim_{n\to\infty}\sup_{x\in E_n}P\{\sup_{k\leq\alpha_nt}|X_n(k)-X_n(0)-\sum_{l=0}^k\frac{1}{\alpha_n}F_n(X_n(l))|>\delta \text{ where }X_n(0)=x\}=0$$

where $F_n(x) = \alpha_n \int_{E_n} (z-x) \mu_n(x,dz)$. Applying the above over a single time step we obtain

$$\lim_{n\to\infty} \sup_{x\in E_n} P\{\sup_{k\leq \alpha_n t} |X_n(1)-X_n(0)-\int_{E_n} (z-x)\mu_n(x,dz)| > \delta \text{ where } X_n(0)=x\} = 0.$$

This implies that as $n \to \infty$, the difference $X_n(1) - X_n(0) - \int_{E_n} (z - x) \mu_n(x, dz)$ tends to 0, therefore $X_n(1) = X_n(0) + \int_{E_n} (z - x) \mu_n(x, dz)$, and, since Markov process are memoryless, we conclude that

$$X_n(1) = X_n(0) + \int_{E_n} (z - x) \mu_n(x, dz)$$

So, finally, by noting that $\int_{E_n} (z-x) \mu_n(x,dz)$ is equivalent to the way the mean-field equations of Section 3 are constructed, the result follows.

5 Case study: Population dynamics of dengue in Bello, Colombia

An interesting case study where system components can number in millions is the eco-epidemiology of dengue. Dengue is a disease caused by a virus transmitted to humans by the bite of the *Aedes aegypti* mosquito. To date, there is no available treatment nor specific vaccine for this disease. Dengue is a serious public health problem in Colombia. During the last 10 years, there were around 600,000 cases, from which 9% corresponded to aggravated forms of the disease [2]. Unfortunately, current programs to prevent and control dengue in Colombia are insufficient [1]. In the Valley of Aburrá (Department of Antioquia), the city of Bello is one of the most affected by dengue. In Bello, dengue is endemic; the rate oscillated from 11.1 to 427 cases by 100,000 inhabitants, during the years 2002-2009.

Given the endemic status of dengue in Bello, it is important to analyze the factors involved in the eco-epidemiology of the dengue disease. Previous results have shown the influence of environmental variables in the distributions of cases of the disease [4]. Ongoing work carried out by three of the authors, Arboleda, Puerta and Vélez, aims to analyze the macro and micro climatic and population factors to determine cases of dengue in Bello¹. There is a disadvantage with such models: the models are population models based on differential equations; it means, that they analyze the average behavior

¹Research carried out within a project founded by Colombian research agency Colciencias: "Design and Computational Implementation of a Mathematical Model for the Prediction of Occurrences of Dengue"

of the populations, but it is not possible to know how low-level specifications at the individual level will affect the population behavior.

The model we present is an individual-based version of the model presented in [33]. To establish the initial conditions for the model defined with respect to the human population, we adopted a total population size of 403,235, as recorded for the urban area of Bello (Antioquia) in 2010 by the *Colombian administrative department of statistics* ². The size of the susceptible human population at the beginning of the last registered epidemic was estimated based on the risk map developed by Arboleda et al. [5], in which the probability of infection was reported to be 0.3 in 2008 and 2009, with a standard deviation of 0.096; thus, it was determined that the size of the susceptible human population should be between 244,402 and 321,734. The initial condition considered for the infectious human population was the number of cases reported at the beginning of the epidemic. There were six reported cases in Bello during the first week of the epidemic (week 51 in 2009). Because of under-reporting concerns, which can affect up to 75% of the total number of cases [10], we assumed that the initial number of infectious human individuals should lie in the range of 6 to 24. In what follows we explain how we model the mosquitoes and the humans.

Mosquitoes. The aquatic phases of the mosquito's life cycle are described briefly. The egg, larva and pupa states are represented by E, L and P, respectively. Parameters σ_e , σ_l , σ_p are the probabilities to change from egg to larva, from larva to pupa and from pupa to adult. Co-action infect models when a mosquito infects a human. We only consider female mosquitoes in the model. When a mosquito infects a human, it may reproduce and produce 3 offspring; otherwise, it will die in the next time unit. Mosquitoes can migrate from one district to another.

Humans. The dynamics of dengue transmission in human population is described by susceptible (s), exposed (e), infectious (i), recovered (r) and dead (d) individuals. Parameter μ_h represents the probability of an infected human to die from the disease. Action *infect* represents the action of being infected by a mosquito. When a human being is infected by a mosquito, it will remain in the exposed state for 3 time units; afterwards, it will become infectious. For simplicity, we do not consider how humans may infect mosquitoes when the mosquitoes bite on infected humans and we do not consider how humans migrate among districts.

$$E \quad \stackrel{\mathrm{def}}{=} \quad \sigma_e : \sqrt{L} \oplus (1 - \sigma_e) : \sqrt{.W_6} \qquad \qquad s \quad \stackrel{\mathrm{def}}{=} \quad \overline{infect}? (\sqrt{.e}, \sqrt{.s})$$

$$L \quad \stackrel{\mathrm{def}}{=} \quad \sigma_l : \sqrt{.P} \oplus (1 - \sigma_l) : \sqrt{.W_6} \qquad \qquad e \quad \stackrel{\mathrm{def}}{=} \quad \sqrt{.e_1}$$

$$P \quad \stackrel{\mathrm{def}}{=} \quad \sigma_p : \sqrt{.W} \oplus (1 - \sigma_p) : \sqrt{.W_6} \qquad \qquad e_1 \quad \stackrel{\mathrm{def}}{=} \quad \sqrt{.e_2}$$

$$W \quad \stackrel{\mathrm{def}}{=} \quad infect? (W_3, \sqrt{.W_1}) \qquad \qquad e_2 \quad \stackrel{\mathrm{def}}{=} \quad \sqrt{.i}$$

$$W_1 \quad \stackrel{\mathrm{def}}{=} \quad \sum_{\ell \in \mathbf{Nb}(myloc)} \frac{1}{\|\mathbf{Nb}(myloc)\|} : go\ell.W_4 \qquad \qquad i \quad \stackrel{\mathrm{def}}{=} \quad \mu_h : \sqrt{.d} \oplus (1 - \mu_h) : \sqrt{.r}$$

$$W_2 \quad \stackrel{\mathrm{def}}{=} \quad infect? (W_3, \sqrt{.W_5}) \qquad \qquad r \quad \stackrel{\mathrm{def}}{=} \quad \sqrt{.r}$$

$$W_3 \quad \stackrel{\mathrm{def}}{=} \quad \sqrt{.W} |E|E|E \qquad \qquad d \quad \stackrel{\mathrm{def}}{=} \quad \sqrt{.d}$$

$$W_4 \quad \stackrel{\mathrm{def}}{=} \quad \sqrt{.W} 2$$

$$W_5 \quad \stackrel{\mathrm{def}}{=} \quad \mathbf{0}$$

²http://www.dane.gov.co

- 1. The initial state is represented by a 11×16 matrix.
- 2. The state-transition table for the example is given below. Note that in fact this is a 3-dimensional matrix, the third dimension being the location dimension. To capture this in two dimensions we write $@\ell'$ whenever the resulting individuals have moved to another location, ℓ' being this location.

First, we present the state transitions for the mosquitoes.

		E	L	P	W	W_1	W_2	W_3	W_4	W_5
$E:\langle \mathbf{s},\ell,q \rangle$	prob		$\sigma_e \cdot q$							$(1-\sigma_e)\cdot q$
$L:\langle \mathbf{s},\ell,q \rangle$	prob			$\sigma_l \cdot q$						$(1-\sigma_l)\cdot q$
$P:\langle \mathbf{s},\ell,q \rangle$	prob				$\sigma_p \cdot q$					$(1-\sigma_p)\cdot q$
$W:\langle \mathbf{s},\ell,q_W \rangle$	infect					$q_W - m$		m		
$W_1:\langle \mathbf{s},\ell,q\rangle$	prob								Z	
$W_2:\langle \mathbf{s},\ell,q_{W2}\rangle$	infect							n		$q_{W2}-n$
$W_3:\langle \mathbf{s},\ell,q\rangle$		$3 \cdot q$			q					
$W_4:\langle \mathbf{s},\ell,q \rangle$							q			
$W_5:\langle \mathbf{s},\ell,q\rangle$										\overline{q}

Second, we present the state transitions for the humans.

		S	e	e_1	e_2	i	r	d
$s:\langle \mathbf{s},\ell,q_s\rangle$	infect	p	q_s-p					
$e{:}\langle \mathbf{s},\ell,q angle$				q				
e_1 : $\langle \mathbf{s}, \ell, q \rangle$					q			
$e_2{:}\langle \mathbf{s},\ell,q \rangle$						q		
$i:\langle \mathbf{s},\ell,q angle$	prob						$(1-\mu_h)\cdot q$	$\mu_h \cdot q$
$r:\langle \mathbf{s},\ell,q \rangle$							\overline{q}	
$d:\langle \mathbf{s},\ell,q angle$								\overline{q}

where
$$m = min(q_w, \frac{q_s}{q_w + q_{W2}})$$
, $n = min(q_{W2}, \frac{q_s}{q_w + q_{W2}})$, $p = min(q_s, q_W + q_{W2})$ and $z = \sum_{\ell' \in \mathbf{Nb}(\ell)} \frac{1}{\|\mathbf{Nb}(\ell')\|} \cdot q@\ell'$. Variable z represents the mosquito's dispersal.

3. Let us write $P(t)@\ell$ for the average number of individuals of process P, at time t and location ℓ . In what follows, we describe $s(t)@\ell$, $e(t)@\ell$... $W_2(t)@\ell$, for t>0, which represents the mean-field equations for the behavior of the mosquitoes and humans, respectively. Note that, for each process of interest, we have 11 equations, one for each location that represents each district in Bello. A detailed explanation on how we computed the mean-field semantics of the case study is in [30].

By manipulating the equations and restricting attention to how the system evolves between $\sqrt{}$ actions and the processes of interest, we obtain:

$$W(t)@\ell = \sigma_{P} \cdot \sigma_{L} \cdot \sigma_{E} \cdot 3 \cdot \left(\min \left(W(t-4)@\ell, \frac{W(t-4)@\ell \cdot s(t-4)@\ell}{W(t-4)@\ell + W_{2}(t-4)@\ell} \right) + \min \left(W_{2}(t-4)@\ell, \frac{W_{2}(t-4)@\ell \cdot s(t-4)@\ell}{W(t-4)@\ell + W_{2}(t-4)@\ell} \right) \right)$$

$$W_{2}(t)@\ell = \frac{1}{\|\mathbf{Nb}(\ell')\|} \cdot \left(W_{1}(t-3)@\ell' - \frac{W(t-3)@\ell' \cdot s(t-3)@\ell'}{W(t-3)@\ell' + W_{2}(t-3)@\ell'} \right) \right)$$

$$s(t)@\ell = \min(s(t-1)@\ell, W(t-1)@\ell + W_{2}(t-1)@\ell$$

$$e(t)@\ell = e(t-1)@\ell - \min(s(t-1)@\ell, W(t-1)@\ell + W_{2}(t-1)@\ell$$

$$i(t)@\ell = e(t-3)@\ell$$

$$r(t)@\ell = r(t-1)@\ell + (1-\mu_{h}) \cdot i(t-1)@\ell$$

where $\ell' \in \mathbf{Nb}(\ell)$

Up to our knowledge, this is the first system of recurrence equations developed for dengue. We leave as future work the validation of the model with real data.

6 Conclusions

In this paper we presented a mean-field semantics for S-PALPS. Up to our knowledge, S-PALPS is the first spatially-explicit probabilistic process calculus to be extended with mean-field semantics. Using this semantics we can analyze deterministically the average behavior of a spatially-explicit ecological model even for large populations. The advantages of this new semantics is that it allows us to translate from an individual-based model to the underlying population dynamics and that it is possible to do this efficiently without computing the complete state space of the model. In particular, we showed how this is applicable for epidemiological models by our case study on the transmission of dengue.

As future work, we want to further study the spatial distribution of dengue on the lines of Otero et al. [21]. In fact, there is demographic and epidemiological information about the reported cases in each district of Bello (Antioquia), Colombia. It is of vital importance for public health to determine which districts have more risk by determining the migration patterns of mosquitoes from district to district. This is of importance to define vaccination and fumigation schemes to prevent epidemics.

References

- [1] Guía de Atención Clínica Integral del Paciente con Dengue. Available at http://calisaludable.cali.gov.co/saludPublica/2010_Dengue/protocolos_guias_del_INS_y_del_MPS/Guia Dengue 2010.pdf.
- [2] Number of Reported Cases of Dengue and Dengue Hemorrhagic Fever (DHF) in the Americas, by Country. Available at http://new.paho.org/hq/index.php?option=com_content&task=blogcategory&id=1221&Itemid=2481.
- [3] Online PRISM documentation. Available at http://www.prismmodelchecker.org/doc/.

- [4] S. Arboleda, O.N. Jaramillo & A.T. Peterson (2012): Spatial and temporal dynamics of Aedes aegypti breeding sites in Bello, Colombia. Journal of Vector Ecology 37(1), pp. 37–48, doi:10.1111/j.1948-7134.2012.00198.x.
- [5] Sair Arboleda, Nicolas Jaramillo O. & A. Townsend Peterson (2009): *Mapping Environmental Dimensions of Dengue Fever Transmission Risk in the Aburrá Valley, Colombia.* International Journal of Environmental Research and Public Health 6(12), p. 3040, doi:10.3390/ijerph6123040.
- [6] R. Barbuti, A. Maggiolo-Schettini, P. Milazzo & G. Pardini (2011): *Spatial Calculus of Looping Sequences*. *Theoretical Computer Science* 412(43), pp. 5976–6001, doi:10.1016/j.tcs.2011.01.020.
- [7] Roberto Barbuti, Andrea Maggiolo-Schettini, Paolo Milazzo & Angelo Troina (2006): A Calculus of Looping Sequences for Modelling Microbiological Systems. Fundamenta Informaticae 72(1-3), pp. 21–35.
- [8] Thomas Anung Basuki, Antonio Cerone, Roberto Barbuti, Andrea Maggiolo-Schettini, Paolo Milazzo & Elisabetta Rossi (2010): *Modelling the Dynamics of an Aedes albopictus Population*. In: *Proceedings of AMCA-POP'10, EPTCS* 33, pp. 18–36, doi:10.4204/EPTCS.33.2.
- [9] D. Besozzi, P. Cazzaniga, D. Pescini & G. Mauri (2008): *Modelling metapopulations with stochastic membrane systems*. *BioSystems* 91(3), pp. 499–514, doi:10.1016/j.biosystems.2006.12.011.
- [10] S. Bratt, P. W. Gething, O. J. Brady, J. P. Messina, A. W. Farlow, C. L. Moyes, J. M. Drake, J. S. Brownstein, A. G. Hoen, Osman Sankoh, Monica F. Myers, Dylan B. George, Thomas Jaenisch, G. R. William Wint, Cameron P. Simmons, Thomas W. Scott, Jeremy J. Farrar & Simon I. Hay (2013): *The global distribution and burden of dengue*. Nature 496, pp. 504–507, doi:10.1038/nature12060.
- [11] Qiuwen Chen, Fei Ye & Weifeng Li (2009): *Cellular-automata-based ecological and ecohydraulics modelling*. *Journal of Hydroinformatics* 11(3/4), pp. 252–272, doi:10.2166/hydro.2009.026.
- [12] Frédéric Didier, Thomas A. Henzinger, Maria Mateescu & Verena Wolf (2010): *SABRE: A Tool for Stochastic Analysis of Biochemical Reaction Networks*. *CoRR* abs/1005.2819, doi:10.1109/QEST.2010.33.
- [13] Peter Drábik, Andrea Maggiolo-Schettini & Paolo Milazzo (2011): Modular Verification of Interactive Systems with an Application to Biology. Scientific Annals of Computer Science 21(1), pp. 39–72, doi:10.1016/j.entcs.2010.12.006.
- [14] S. C. Fu & G. Milne (2004): *A Flexible Automata Model for Disease Simulation*. In: *Proceedings of ACRI'04*, LNCS 3305, Springer, pp. 642–649, doi:10.1007/978-3-540-30479-1_66.
- [15] Ronald L. Graham, Donald E. Knuth & Oren Patashnik (1994): Concrete Mathematics: A Foundation for Computer Science, 2nd edition. Addison-Wesley Longman Publishing Co., Inc., Boston, MA, USA, doi:10. 1063/1.4822863.
- [16] Jane Hillston, Mirco Tribastone & Stephen Gilmore (2012): Stochastic Process Algebras: From Individuals to Populations. Computing Journal 55(7), pp. 866–881, doi:10.1093/comjnl/bxr094.
- [17] Jetty Kleijn, Maciej Koutny & Grzegorz Rozenberg (2011): *Petri Nets for Biologically Motivated Computing*. *Scientific Annals of Computer Science* 21(2), pp. 199–225.
- [18] Thomas Kurtz (1970): Solutions of Ordinary Differential Equations as Limits of Pure Jump Markov Processes. Journal of Applied Probability 7(1), doi:10.2307/3212147.
- [19] C. McCaig, R. Norman & C. Shankland (2008): *Process Algebra Models of Population Dynamics*. In: *Proceedings of AB'08*, LNCS 5147, Springer, pp. 139–155, doi:10.1007/978-3-540-85101-1_11.
- [20] Chris McCaig, Rachel Norman & Carron Shankland (2011): From individuals to populations: A mean field semantics for process algebra. Theoretical Computer Science 412(17), pp. 1557–1580, doi:10.1016/j.tcs.2010.09.024.
- [21] M. Solari H.G. Otero (2010): Stochastic eco-epidemiological model of dengue disease transmission by Aedes aegypti mosquito. Mathematical Biosciences 223(1), pp. 32–46, doi:10.1016/j.mbs.2009.10.005.
- [22] Jorge Pérez & Camilo Rueda (2008): *Non-determinism and Probabilities in Timed Concurrent Constraint Programming*. In: *Proceedings of ICLP'08*, *LNCS* 5366, pp. 677–681, doi:10.1007/978-3-540-89982-2_56.
- [23] Anna Philippou & Mauricio Toro (2013): *Process Ordering in a Process Calculus for Spatially-Explicit Ecological Models*. In: *Proceedings of MOKMASD'13*, LNCS 8368, Springer, pp. 345–361, doi:10.1007/978-3-319-05032-4_25.
- [24] Anna Philippou, Mauricio Toro & Margarita Antonaki (2013): Simulation and Verification for a Process Calculus for Spatially-Explicit Ecological Models. Scientific Annals of Computer Science 23(1), pp. 119–

- 167, doi:10.7561/SACS.2013.1.119.
- [25] G. Michele Pinna & Andrea Saba (2008): An Event Based Semantics of P Systems. Scientific Annals of Computer Science 18, pp. 99–127.
- [26] Martin L. Puterman (1994): *Markov Decision Processes: Discrete Stochastic Dynamic Programming*, 1st edition. John Wiley & Sons, Inc., New York, NY, USA, doi:10.1002/9780470316887.
- [27] Neda Saeedloei & Gopal Gupta (2014): *Timed PI Calculus*. In Martn Abadi & Alberto Lluch Lafuente, editors: *Trustworthy Global Computing*, *Lecture Notes in Computer Science* 8358, Springer International Publishing, pp. 119–135, doi:10.1007/978-3-319-05119-2_8.
- [28] D. J. T. Sumpter, G. B. Blanchard & D. S. Broomhear (2001): Ants and Agents: a Process Algebra Approach to Modelling Ant Colony Behaviour. Bulletin of Mathematical Biology 63, pp. 951–980, doi:10.1006/bulm.2001.0252.
- [29] Chris Tofts (1994): *Processes with probabilities, priority and time. Formal Aspects of Computing* 6(5), p. 536564, doi:10.1007/BF01211867.
- [30] Mauricio Toro, Anna Philippou, Sair Arboleda, Carlos Vélez & María Puerta (2015): *Mean-field semantics for a Process Calculus for Spatially-Explicit Ecological Models*. Technical Report, Department of Informatics and Systems, Universidad Eafit. Available at http://blogs.eafit.edu.co/giditic-software/2015/10/01/mean-field/.
- [31] Mauricio Toro, Anna Philippou, Christina Kassara & Spyros Sfenthourakis (2014): *Synchronous Parallel Composition in a Process Calculus for Ecological Models*. In: *Proceedings of ICTAC'14*, pp. 424–441, doi:10.1007/978-3-319-10882-7 25.
- [32] Mirco Tribastone, Stephen Gilmore & Jane Hillston (2012): Scalable Differential Analysis of Process Algebra Models. IEEE Transactions on Software Engineering 38(1), pp. 205–219, doi:10.1109/TSE.2010.82.
- [33] Hyun Mo Yang & Cláudia Pio Ferreira (2008): Assessing the efects of vector control on dengue transmission. Applied Mathematics and Computation 198, pp. 401–413, doi:10.1016/j.amc.2007.08.046.