Meta-Population Modelling and Simulation of the Dynamic of Malaria Transmission with Influence of Climatic Factors

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Abstract—We model the dynamic of malaria transmission taking into account climatic factors and the migration between Douala and Yaoundé, Yaoundé and Ngaoundéré, three cities of Cameroon country. We show how variations of climatic factors such as temperature and relative humidity affect the malaria spread. We propose a meta-population model of the dynamic transmission of malaria that evolves in space and time and that takes into account temperature and relative humidity and the migration between Douala and Yaoundé, Yaoundé and Ngaoundéré. More, we integrate the variation of environmental factors as events also called mathematical impulsion that can disrupt the model evolution at any time. Our modelling has been done using the Discrete EVents System Specification (DEVS) formalism. Our implementation has been done on Virtual Laboratory Environment (VLE) that uses DEVS formalism and abstract simulators for coupling models by integrating the concept of DEVS.

Index Terms—Modelling, Simulation, Compartmental models, DEVS, Meta-population model, VLE.

I. INTRODUCTION

Malaria is one of the most important issues in almost all countries of the tropical area. Despite the efforts of various cross disciplines involved, malaria continues to be a major problem of public health. In Cameroon, a country located in the red zone climate with maximum suitability for malaria transmission, health statistics reveal that it is responsible for 35-40% of all deaths in health facilities: 50% of morbidity in children under 5 years old, 40 to 45% of medical consultations and 30% of hospitalizations. Malaria is also the cause of 26% of absences in the workplace and 40% of household health expenditure [1]. Developing countries such as Cameroon are reduced to fight against vector through the use of insecticide-treated bed nets, which means if efficient, to limit the parasite load below critical thresholds in host, rapid detection of cases of sick to reduce contact infesting for vectors. The dynamic of transmission and seasonality of malaria remain research preoccupation not solved. If levels of malaria prevalence in urban areas are lower compared to rural areas, the population growth and the spatial heterogeneity of parts are such that the risk of malaria infection and consequences (disease, mortality), differs among epidemiological status and periods of the year. Considering spatial and climatic heterogeneity of the world in general and Cameroon specifically, take into account spatial and temporal variations is important for vector-borne diseases, where the underlying factors of epidemiology observed can be confused by some large heterogeneities in the host and vector densities across space and time, as in the case of malaria. In this context,
we will focus on the modeling of dynamic of malaria including spatial and temporal consideration between respectively Douala and Yaoundé (respectively Yaoundé and Ngaoundéré) cities and the influence of climatic factors (temperature influences the life cycle of the mosquito, relative humidity plays a role in the life of the mosquito and malaria transmission) on the spread of that disease.

II. Survey

Knowledge of what we want to model is essential for an effective modelling. Modelling in epidemiology depends heavily on knowledge of biology. Malaria is transmitted by the female anophels mosquito genus. In humans, the causative agent of malaria is a single-celled parasite called plasmodium. The understanding of mosquito transmission mechanism to the human has been highlighted in 1897 by Ronald Ross. Many years before the beginning of the nineteenth century, the medical com- munity has long focused on treating patients, not on mosquitoes. The assumption being that it was impossible to completely eradicate mosquitoes in a given area, so there will be always mosquitoes. Ross proposed a model in which he calculated the number of new infections per month as a product of factors; he deduced that there is a critical density of mosquitoes. In 1952, George MacDonald, based on the work of Ross, introduced the concept of reproduction. The basic reproductive number (R0) of malaria is defined as the number of infection distributed in a community resulting from the presence within it of a single primary infected.

In epidemiology, models predict the dynamics of the epidemic inside populations from knowledge at the individual level between epidemiological factors, the long-term behaviour of the dynamic early invasion, or the impact of vaccination on the spread of infection [3]. [4] consider the world as a network where individuals are nodes with sensor. They proposed a Susceptible-Exposed-Infectious-Quarantine-Recovered-Susceptible with Vaccination (SEIRS-V) model that describes the spatial and temporal dynamic of worm spread. The spread of an infectious agent within a population is a dynamic phenomenon: the numbers of healthy and diseased individuals change over time, depending on the contacts during which the agent passes from an infected individual to a healthy individual immunized, infecting turn. This kind of phenomenon can be studied by modelling by differential equations and determining their behaviour through numerical solution of these equations [3], we call them compartmental models. Heterogeneities and structure of the space where a disease evolves is very important in understanding how epidemics spread [5]. Humans and mosquitoes here are organized in well-defined units such as families, villages, cities, countries or regions that constitute what we call patches. Based on the model of Ross-MacDonald, Tsanou [6] provides a meta-population model of many patches, and shows that there is a threshold below which the disease disappears and above which the disease remains within the meta-population. In the Tsanou model, demography is neglected (populations sizes are assumed constant), epidemiological parameters are the same for all patches. More, Tsanou does not take into account climatic factors while Lourenco [7], through a study on the dengue disease, shows that spatial-temporal variations are sufficient to destabilize the balance of a system. Almost all insects have a moisture tolerance and temperature beyond which it becomes impossible for them to survive. Mosquitoes do not escape this rule. [8] compared to a given temperature, the survival of female anopholes pharoensis at 20, 26, 30°C and a slight difference in terms of longevity in conditions of relative humidity taken between 50% and 90%. Whereas the probability of survival was independent of age, [9] measured the longevity of Anopheles gambiae s.s by considering the relative humidity at 40%, 60%, 80% and 100%, and a temperature between 5°C and 40°C. There is a slight difference in survival with a relative humidity between 60% and 100%. Furthermore, molecular biology techniques applied to Anopholes gambiae s.s tested with relative humidity at 42% [10] and 30% [11] have shown that mosquitoes held without food or water survived an average of 15.6 hours at 30% relative humidity compared to 26.2 hours at 70% relative humidity [11]. [12] with a study in sub-saharian Africa region, show that mortality of mosquitoes, especially Anophele gambia s.s., depends on temperature and the mosquito age at different stages (Egg, Larvae, Pupa, Adult). [13] through a study in Eastern Africa, have showed that there is a strong and significant cross-coherence between malaria cases and average rainfall and vegetation. Recent studies on desiccation mosquitoes showed an extremely low relative humidity (<10%) is fatal to mosquitoes who spend a few hours [14]. Several studies show that the Anopholes gambiae s.s and Anopholes arabiensis female survive a whole day for a relative humidity below 10% [15] or less than 20% [16]. Only a few mosquitoes survive beyond 30 hours at a relative humidity below 10%. It thus appears that a relative humidity greater than 60%, Anopholes gambiae is not significantly affected, but a relative humidity below 10% is fatal to the Anopholes gambiae [14]. There are, however, very little information for a relative humidity between 10% and 40%. The commonly used survival equation is the equation of Martens [17] defined by \( p(T) = \exp(-4.4 + 1.31T - 0.03T^2) \), where \( T \) is the mean daily temperature in Celsius degrees. This function provides maximum durability for a temperature between 20-25°C and severe mortality for temperatures below 10°C and above 35°C [18].

For taking into account climatic factors, some models have been developed. [18] proposed a SIRS-type model using a deterministic approach. Their model was built on the MacDonald equations, specifying states for infected-not-contagious and contagious children. Human part of the cycle was modelled by SIGRS, where S is defined
as the proportion of susceptible children, the state $I$ represents the proportion of infected but not contagious children, $G$ is the production of contagious children and $R$ is the proportion of children resistant to infection. The transition from state $S$ to state $I$ depends on vectorial and climatic factors. Vectorial part was modelled with a two-state model: the state of Susceptible anophelines ($S$) and the state of Contagious anophelines ($I$). They showed that the transmission increases (respectively decreases) when the vegetation index increases (respectively decreases). Nevertheless, [18] has neglected the natality and mortality rates. In their model, climatic factors involve at the infection level (contact Human-Vector), not at the complete mosquito life cycle with/without contact between Human and Vector. More, they don’t take into account migration; their model is not meta-population.

A. Plasmodium species and malaria vector in Cameroon

The surveys published in recent years by the Cameroon National Program against Malaria presented the Plasmodium falciparum parasite species as the most common in Cameroon, followed by Plasmodium malariae and Plasmodium ovale. In Cameroon, a country with one of the richest faunas anophelines in Africa, and it houses 48 species of Anophelles from the work of [19]. Among these, the sporozoites of Plasmodium have been identified in 13 of them. These are Anopheles gambiae ss, the anopholes funes- tus ss, the mouceti Anopheles, Anopheles arabinensis, Anopheles nili, Anopheles hancocki, the paludis Anopheles, Anopheles marshallli, Anopheles coustani, the Anopheles ovgensis, Anopheles pharonensis, wellcomei Anopheles, Anopheles ziemani. Anopheles gambiae ss and Anopheles arabinensis are the main infected species found in Cameroon. The more one leaves the forest for the savannah and the Sahel, the more effective Anopheles gambiae s.s decreases and that of arabinensis increases and vice versa.

Table 1. Spatial distribution of anophelines in the complex ecological facies of Cameroon [20].

<table>
<thead>
<tr>
<th>Facies</th>
<th>Anophele gambiae s.s</th>
<th>Anophele arabinensis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forest</td>
<td>796 (99,7%)</td>
<td>2 (0,3%)</td>
<td>798</td>
</tr>
<tr>
<td>Savannah</td>
<td>146 (25,0%)</td>
<td>439 (75,0%)</td>
<td>585</td>
</tr>
<tr>
<td>Sahel</td>
<td>14 (4,5%)</td>
<td>299 (95,5%)</td>
<td>313</td>
</tr>
<tr>
<td>Total</td>
<td>956 (56,4%)</td>
<td>740 (43,6%)</td>
<td>1696</td>
</tr>
</tbody>
</table>

As we note, the mosquito density varies with region (Forest, Savannah and Sahel) in Cameroon. These three identified geographical areas with different weather and climatic conditions, point to the fact that rainfall, temperature and/or humidity influence the mosquito type and density.

B. Influence of Climatic factors

We focus here on Douala and Yaoundé, two cities located in the Forest area of Cameroon, but with some different climatic variables. Fig. 1 and Fig. 2 show average temperature, rainfall and humidity of Douala and Yaoundé cities.

![Fig. 1. Temperature, rainfall and relative humidity of Douala city. Source: www.climatemps.com](image1)

![Fig. 2. Temperature, rainfall and relative humidity of Yaoundé city. Source: www.climatemps.com](image2)

Table 2 shows the quantities of anophelines breeding sites in Douala and Yaoundé cities depending the seasons (rainy and dry). This is the result of a study conducted from October 2009 to December 2010 by [21]. We mark that Douala and Yaoundé cities, although belonging to the same ecological facies (Forest), demonstrate a significant difference in term of number of breeding sites during the rainy season October to November (416 for Douala and 201 for Yaoundé) and reproduction of sites with Anophelles (102 for Douala against 58 for Yaoundé) during the same period. This difference can be explained by the high humidity in Douala during that period (about 85) compared to Yaoundé (about 70), while temperatures of the two cities is approximately similar over that period, as presented in Fig. 1 and Fig. 2.
Concerning Ngaoundéré, the city is located in the transition area between Forest and Savannah area of Cameroon and the vegetation is of the sudano-guinea type [22].

### III. OUR MODELLING

Inspired by the model developed by [23] who work on diseases with direct transmission between individuals of the same nature, we model malaria where transmission between humans is done via a vector (mosquito). Moreover, our model considers meta-population between respectively Douala and Yaoundé (Yaoundé and Ngaoundéré) cities that evolves different epidemiological faces in the city (SEIR model for Douala, SEIRS model for Yaoundé and SEIS for Ngaoundéré). Moreover, we consider births and also take into account the climatic and meteorological factors using the survival function proposed by [24] (inspired by the Martens equation presented above) defined as:

\[
p(T, RH) = e^{-\frac{1}{T^2 \beta_2 + T \beta_1 + \beta_0}},
\]

where \(\beta_0 = 0.00113 \cdot RH^2 - 0.158 \cdot RH - 6.61\)
\(\beta_1 = -2.32 \cdot 10^{-4} \cdot RH^2 + 0.0515 \cdot RH + 6.61\)
\(\beta_2 = 4 \cdot 10^{-6} \cdot RH^2 - 1.09 \cdot 10^{-3} \cdot RH - 0.0255\)

\(p\) is the probability of survival and the mortality rate is giving by \(-\ln(p(T, RH))\) [25].

We assume that there is no cross-infection and that infectious humans do not travel (they are quarantined). We also assume that only humans move between patches (voluntary moving of mosquitoes in space is limited over the patches considered are remote) and the mortality rate of these travellers in a city is the same as that of the residents of the host city.

Let \(N_i\) (respectively \(N_V\)) be the total human population (respectively vectors) patch \(i\). We also denote by \(\phi_i S_i\) the Susceptible residents of patch \(i\) that are travelling in the patch. \(\phi_i E_i\) is the infected residents of patch \(i\) who are travelling in the patch \(j\). \(\phi_i R_i\) the Recovered and Immunized residents of patch \(i\) that are moving in the patch \(j\). \(S_{ij}\) represents the Susceptible mosquitoes residents in the patch, \(E_{ij}\) the Infected mosquitoes residents in the patch, and \(I_{ij}\) Infectious mosquitoes residents in the patch.

<table>
<thead>
<tr>
<th>Douala and Yaoundé seasons</th>
<th>Number of breeding sites</th>
<th>Breeding site housing the Anopheles</th>
<th>Breeding site housing the Anopheles and Cules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Douala - Rainy season (October-November 2009)</td>
<td>416</td>
<td>102 (24.5%)</td>
<td>12 (3%)</td>
</tr>
<tr>
<td>Douala - Dry season (February-March 2010)</td>
<td>100</td>
<td>29 (29%)</td>
<td>24 (24%)</td>
</tr>
<tr>
<td>Douala - Rainy season (May-June 2010)</td>
<td>126</td>
<td>79 (63%)</td>
<td>28 (22.2%)</td>
</tr>
<tr>
<td>Douala - Dry season (August-September 2010)</td>
<td>146</td>
<td>95 (65%)</td>
<td>27 (18.5%)</td>
</tr>
<tr>
<td>Douala - Dry season (December 2010)</td>
<td>68</td>
<td>33 (48.5%)</td>
<td>18 (47.4%)</td>
</tr>
<tr>
<td>Yaoundé - Rainy season (October-November 2009)</td>
<td>201</td>
<td>58 (28.9%)</td>
<td>18 (9%)</td>
</tr>
<tr>
<td>Yaoundé - Dry season (February-March 2010)</td>
<td>115</td>
<td>40 (34.8%)</td>
<td>34 (29.6%)</td>
</tr>
<tr>
<td>Yaoundé - Rainy season (May-June 2010)</td>
<td>173</td>
<td>81 (46.8%)</td>
<td>26 (15%)</td>
</tr>
<tr>
<td>Yaoundé - Dry season (August-September 2010)</td>
<td>117</td>
<td>40 (34%)</td>
<td>13 (11.1%)</td>
</tr>
<tr>
<td>Yaoundé - Dry season (December 2010)</td>
<td>84</td>
<td>38 (45.2%)</td>
<td>14 (42.4%)</td>
</tr>
</tbody>
</table>
Table 3. Parameters and description.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>number of patches</td>
</tr>
<tr>
<td>$\phi_{ij} \geq 0$</td>
<td>proportion of migration of humans from the patch $i$ to the patch $j$</td>
</tr>
<tr>
<td>$d_{H_i}$</td>
<td>natural mortality rate of humans of the patch $i$</td>
</tr>
<tr>
<td>$d_{V_i}$</td>
<td>natural mortality rate of mosquitoes of the patch $i$</td>
</tr>
<tr>
<td>$\beta_{ij}$</td>
<td>Proportion of contact inside the patch $i$ between susceptible humans and infectious mosquitoes. $k_i$ is the average number of such contacts. $b_i = k_i \beta_{ij}$</td>
</tr>
<tr>
<td>$\omega_{ij}$</td>
<td>Proportion of contact inside the patch $i$ between infectious humans and susceptible mosquitoes. $f_i$ is the average number of such contacts</td>
</tr>
<tr>
<td>$\delta_{H_i}$</td>
<td>rate of infected humans that become infectious inside the patch $i$</td>
</tr>
<tr>
<td>$\rho_{H_i}$</td>
<td>rate of infectious humans that become susceptible inside the patch $i$</td>
</tr>
<tr>
<td>$\sigma_{V_i}$</td>
<td>rate of infected mosquitoes that become infectious inside the patch $i$</td>
</tr>
<tr>
<td>$\alpha_{H_i}$</td>
<td>recovery rate of infectious humans inside the patch $i$</td>
</tr>
<tr>
<td>$\alpha_{V_i}$</td>
<td>mosquito birth rate in the patch $i$</td>
</tr>
<tr>
<td>$\nu_{H_i}$</td>
<td>human birth rate in the patch $i$</td>
</tr>
<tr>
<td>$\nu_{V_i}$</td>
<td>mosquito birth rate in the patch $i$</td>
</tr>
<tr>
<td>$p((T, RH))$</td>
<td>recovery rate of recovered humans (eventually immunised) become susceptible later</td>
</tr>
<tr>
<td>$p((T, RH))$</td>
<td>survival probability for a mosquito inside the patch $i$ with a temperature $T$ and a relative humidity $RH$</td>
</tr>
</tbody>
</table>

A. SEIR model: Case of Douala

Malaria transmission there is continuous throughout the year [20], we model Douala city by a SEIR model. We distinguish three cases: Model without climatic factors, Model taking into account climatic factors only during human-mosquito contact, Model taking into account climatic factors throughout all the mosquito evolution cycle ($S \rightarrow E \rightarrow I$). With the notation presented earlier, our modelling of humans present in Douala ($i$ denotes Douala and $j$ Yaoundé) model is as follows:

A.1 Model without climatic factors

\[ \begin{align*}
    S_H &= \mu_H N_H - \sum_{j=i}^{a} \phi_{ij} S_H - \sum_{j=i}^{a} \phi_{ji} S_H + k_i \beta_{ij} \frac{S_H}{N_H} I_V - d_H S_H \\
    E_H &= \sum_{j=i}^{a} \phi_{ji} E_H - \sum_{j=i}^{a} \phi_{ij} E_H + k_i \beta_{ij} \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H \\
    I_H &= \delta_H E_H - \alpha_H I_H - \gamma_H I_H - d_H I_H \\
    R_H &= \sum_{j=i}^{a} \phi_{ji} R_H + \alpha_H I_H - \sum_{j=i}^{a} \phi_{ij} R_H - d_H R_H \\
    S_V &= \mu_V N_V - f_i \omega_i \frac{S_V}{N_H} I_H - d_V S_V \\
    E_V &= f_i \omega_i \frac{S_V}{N_H} I_H - \delta_i E_V - d_V E_V \\
    I_V &= \delta_i E_V - d_i I_V
\end{align*} \]  

(1)

A.2 Model taking into account climatic factors only during human-mosquito contact

\[ \begin{align*}
    S_H &= \mu_H N_H - \sum_{j=i}^{a} \phi_{ij} S_H - \sum_{j=i}^{a} \phi_{ji} S_H + k_i \beta_{ij} \frac{S_H}{N_H} I_V - d_H S_H \\
    E_H &= \sum_{j=i}^{a} \phi_{ji} E_H - \sum_{j=i}^{a} \phi_{ij} E_H + p(T, RH) k_i \beta_{ij} \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H \\
    I_H &= \delta_H E_H - \alpha_H I_H - \gamma_H I_H - d_H I_H \\
    R_H &= \sum_{j=i}^{a} \phi_{ji} R_H + \alpha_H I_H - \sum_{j=i}^{a} \phi_{ij} R_H - d_H R_H \\
    S_V &= \mu_V N_V - f_i \omega_i \frac{S_V}{N_H} I_H - d_V S_V \\
    E_V &= f_i \omega_i \frac{S_V}{N_H} I_H - \delta_i E_V - d_V E_V \\
    I_V &= \delta_i E_V - d_i I_V
\end{align*} \]

(2)

A.3 Model taking into account climatic factors throughout all the mosquito life cycle
Remark III.1 An immunized human in his home-city can lose his immunity in the city that hosts him. So, if we consider a migration from a city A (modelled by SEIR) to another city B (modelled by SEIRS), individual R coming from A may lose his immunity in B and become S.

B. SEIRS model: Case of Yaoundé

Malaria transmission is continuous [20].

B.1 model without climatic factors

\[
\begin{align*}
\dot{S}_H &= \mu_H N_H + \sum_{j=1}^{n} \phi_j S_H - \sum_{j=1}^{n} \phi_j S_H - k_i \beta_i \frac{S_H}{N_H} I_V - d_H S_H, \\
\dot{E}_H &= \sum_{j=1}^{n} \phi_j E_H - \sum_{j=1}^{n} \phi_j E_H + k_i \beta_i \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H, \\
I_H &= \delta_H E_H - \alpha_H I_H - \gamma_H I_H - d_H I_H, \\
R_H &= \sum_{j=1}^{n} \phi_j R_H + \alpha_H I_H - \gamma_H I_H - d_H R_H, \\
\dot{S}_V &= \mu_c N_v - f_o \alpha_s \frac{S_v}{N_v} I_V + \ln(p_I(T, RH))^* S_V, \\
\dot{E}_V &= f_o \alpha_s \frac{S_v}{N_v} I_V - \delta_V E_V + \ln(p_I(T, RH))^* E_V, \\
I_V &= \delta_V E_V + \ln(p_I(T, RH))^* I_V
\end{align*}
\]

(3)

B.2 Model taking into account climatic factors only during human-mosquito contact

\[
\begin{align*}
\dot{S}_H &= \mu_H N_H + \epsilon_H R_H + \sum_{j=1}^{n} \phi_j S_H - \sum_{j=1}^{n} \phi_j S_H - k_i \beta_i \frac{S_H}{N_H} I_V - d_H S_H, \\
\dot{E}_H &= \sum_{j=1}^{n} \phi_j E_H - \sum_{j=1}^{n} \phi_j E_H + k_i \beta_i \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H, \\
I_H &= \delta_H E_H - \alpha_H I_H - \gamma_H I_H - d_H I_H, \\
R_H &= \sum_{j=1}^{n} \phi_j R_H + \alpha_H I_H - \gamma_H I_H - d_H R_H, \\
\dot{S}_V &= \mu_c N_v - f_o \alpha_s \frac{S_v}{N_v} I_V + \ln(p_I(T, RH))^* S_V, \\
\dot{E}_V &= f_o \alpha_s \frac{S_v}{N_v} I_V - \delta_V E_V + \ln(p_I(T, RH))^* E_V, \\
I_V &= \delta_V E_V + \ln(p_I(T, RH))^* I_V
\end{align*}
\]

(5)

B.3 Model taking into account climatic factor throughout all the mosquito life cycle

\[
\begin{align*}
\dot{S}_H &= \mu_H N_H + \epsilon_H R_H + \sum_{j=1}^{n} \phi_j S_H - \sum_{j=1}^{n} \phi_j S_H - k_i \beta_i \frac{S_H}{N_H} I_V - d_H S_H, \\
\dot{E}_H &= \sum_{j=1}^{n} \phi_j E_H - \sum_{j=1}^{n} \phi_j E_H + k_i \beta_i \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H, \\
I_H &= \delta_H E_H - \alpha_H I_H - \gamma_H I_H - d_H I_H, \\
R_H &= \sum_{j=1}^{n} \phi_j R_H + \alpha_H I_H - \gamma_H I_H - d_H R_H, \\
\dot{S}_V &= \mu_c N_v - f_o \alpha_s \frac{S_v}{N_v} I_V + \ln(p_I(T, RH))^* S_V, \\
\dot{E}_V &= f_o \alpha_s \frac{S_v}{N_v} I_V - \delta_V E_V + \ln(p_I(T, RH))^* E_V, \\
I_V &= \delta_V E_V + \ln(p_I(T, RH))^* I_V
\end{align*}
\]

(6)

C. SEIS model: Case of Ngaoundéré

Malaria is seasonal, about 6 months per year [20], we model the transmission in Ngaoundéré by a SEIS model.

C.1 model without climatic factors
\[
S_H = \mu_H N_H + \rho_H I_H + \sum_{j=1}^{N_H} \phi_j S_H - \sum_{j=1}^{N_H} \phi_j I_H - k_\beta S_H \frac{S_H}{N_H} I_V - d_H S_H
\]
\[
E_H = \sum_{j=1}^{N_H} \phi_j E_H + k_B \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H
\]
\[
I_H = \delta_H E_H - \gamma_H I_H - d_H I_H - \rho_H I_H
\]
\[
S_V = \mu_N N_V - f_s \frac{S_V}{N_V} I_H - d_V S_V
\]
\[
E_V = f_s \frac{S_V}{N_V} I_H - \delta_V E_V - d_V E_V
\]
\[
I_V = \delta_V E_V - d_V I_V
\]

(7)

C.2 Model taking into account climatic factors only during human-mosquito contact

\[
S_H = \mu_H N_H + \rho_H I_H + \sum_{j=1}^{N_H} \phi_j S_H - \sum_{j=1}^{N_H} \phi_j I_H - p_i(T, RH) k_B \frac{S_H}{N_H} I_V - d_H S_H
\]
\[
E_H = \sum_{j=1}^{N_H} \phi_j E_H + \sum_{j=1}^{N_H} \phi_j E_H + p_i(T, RH) k_B \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H
\]
\[
I_H = \delta_H E_H - \gamma_H I_H - d_H I_H - \rho_H I_H
\]
\[
S_V = \mu_N N_V - f_s \frac{S_V}{N_V} I_H - d_V S_V
\]
\[
E_V = f_s \frac{S_V}{N_V} I_H - \delta_V E_V - d_V E_V
\]
\[
I_V = \delta_V E_V - d_V I_V
\]

(8)

C.3 Model taking into account climatic factor throughout all the mosquito life cycle

\[
S_H = \mu_H N_H + \rho_H I_H + \sum_{j=1}^{N_H} \phi_j S_H - \sum_{j=1}^{N_H} \phi_j I_H - k_\beta S_H \frac{S_H}{N_H} I_V - d_H S_H
\]
\[
E_H = \sum_{j=1}^{N_H} \phi_j E_H + \sum_{j=1}^{N_H} \phi_j E_H + k_B \frac{S_H}{N_H} I_V - \delta_H E_H - d_H E_H
\]
\[
I_H = \delta_H E_H - \gamma_H I_H - d_H I_H - \rho_H I_H
\]
\[
S_V = \mu_N N_V - f_s \frac{S_V}{N_V} I_H + \ln(p_i(T, RH)) S_V
\]
\[
E_V = f_s \frac{S_V}{N_V} I_H - \delta_V E_V + \ln(p_i(T, RH)) E_V
\]
\[
I_V = \delta_V E_V + \ln(p_i(T, RH)) I_V
\]

(9)

D. DEVS formalism

The meta-population models of previous works that we have presented do not take into account the spatial and temporal heterogeneity of patches considered. Nevertheless, consideration of this important factor for modelling the dynamic transmission can lead to different models depending on the city considered. This would imply that there could be in a city, several migrations that come from several cities with different modelling. In this case, it would be important to make what we call the model coupling, which is far ignored by previous works on modelling the dynamic of malaria transmission. The geographical areas in which people live may be considered remote and scattered from each other (case of Douala and Yaoundé cities, which are not border), the space is the considered to be discreet. To take into account the models coupling, space discretization, and also integrate the variation of environmental factors (call events) that can disrupt the model evolution at any time, we rely on DEVS (Discrete Event System Specification) formalism, developed by [26]. There are two layers DEVS formalism: atomic DEVS and coupled DEVS.

The structure of an atomic DEVS model is:

\[
\text{DEVS atomic}= \{X, Y, S, \delta_{ext}, \delta_{int}, \delta_{conf}, \lambda, t_a\}
\]

where

- \(X\) is the set of ports and input values
- \(Y\) the set of ports and output values
- \(S\) the set of system states
- \(\delta_{ext}\) the external transition function
- \(\delta_{int}\) the internal transition function
- \(\delta_{conf}\) the conflict transition function
- \(\lambda\) the output function
- \(t_a\) the advance time function

Fig.3. Representation of Douala (at the right) and Yaoundé (at the middle) and Ngaoundéré (at the left) compartments.
A coupled model is defined as:

\[ \text{DEV} \text{S coupled} = \{X, Y, C, EIC, EOC, IC\} \]

where:

- \( X \) is the set of input ports
- \( Y \) is the set of output ports
- \( C \) is the list of models that comprise the coupled model
- \( EIC \) is the set of input links that connect the coupled model
- \( EOC \) is the set of output links that connect components of the coupled model
- \( IC \) is the set of links that connect components together

**Fig. 4.** Representation of atomic model by DEVS.

**Fig. 5.** Representation of coupled model by DEVS.

The external transition represents the system responses to external events and the internal transition, the autonomous developments. The advance time is the time during which the model is in state \( S \) (not disruption by external events).

### E. VLE Framework

VLE is the framework that we used to implement and simulate our model. VLE is based on DEVS concept and can integrate most different programming languages into one single multi-model. So, VLE is oriented towards the integration of heterogeneous formalisms. It is written in C++ programming language. The VLE architecture is defined as follow:

**Fig. 6.** Representation of the VLE framework Application Programming Interface (API). Clear grey boxes are plug-in or components developed by users to extends VLE API (simulations plug-in, etc.) and white boxes are external libraries coming from the open sources projects to increase the portability (glibmm, boost, etc.) or extends VLE [27].

GVLE is a graphical user interface. It provides tools to visually construct a hierarchy of coupled models. A modelling plug-in can be used to define and to modify the behaviour of atomic models displaying a text editor where DEVS functions can be coded. Moreover, GVLE enables the definition of experimental frames.

EOV, the Eyes Of VLE, is a graphical application which displays the values of states during simulation. EOV is a set of visualization plug-ins. A particular plug-in defines the type of visualization like coloured gridded surfaces or curves for instance.

VLE is the core of the environment. The four other applications depend on VLE (that is why the name of this application is the same as the general framework). VLE implements the DEVS abstracts simulators and the extensions cited in the previous section. To perform simulations, VLE records the experimental frame generated by GVLE and then dynamically loads simulation and visualization components of EOV and finally connect them to the DEVS-Bus. The Simulation plugins simulates the behaviours of the DEVS atomic models and VLE coordinates the simulation.

AVLE (Analysis for VLE) is a graphical interface binding the experimental frame defined by GVLE and the R statistical tool [28].

RVLE (R for VLE) is a R-Package to build experimental frames, to launch the simulation and to get the results of the simulation within the R environment.
VLE has two particular types of port in addition to input and output ports in DEVS models: the initialization and state ports. Initialization ports receive initial values of parameters. State ports are connected to one or several measure objects which receive the state values under observation. After that, the measure object sent values to a specialized component [27]. VLE implements the abstract simulators of DEVS extensions. All atomic models inherit the Dynamics class to build simulation component. Dynamic’s functions that can be overloaded by the user are:

```cpp
Time init();
void internalTransition(const Time& time); //represents the internal transition function defined by DEVS formalism
void externalTransition(const ExternalEventList& events); //represents the external transition function defined by DEVS
Time timeAdvance() const; //this is the advance time defined by DEVS
void output(const Time& time, EventList& out) const; //this is the output function defined by DEVS
void finish();
```

We also have confluent transition defined as:

```cpp
type confluentTransitions(const Time& time, const ExternalEventList& e) const;
```

That last one is called when events occur at the same time. It can be defined to choose the order of treatment for events between internal and external event. Is the conflict function defined by DEVS formalism.

F. Perturbation of the model by unforeseen weather (events)

Considering weather changes that may occur over time, we introduce in our model what we call events, which can be considered as weather disturbances during the year. So at time $t$, we can introduce a disturbance that corresponds to the values of temperature and relative humidity at the time $t$. The architecture of our new model becomes as shown in Fig. 7.

Using VLE environment, our dynamics functions used for disturbing our model are defined as:

```cpp
Time init(const vd::Time&)  
/ mstate = BEFORE PERTURBATION;  
return sendTime; 
Time timeAdvance() const  
/ switch(mstate)/  
//case BEFORE PERTURBATION: return sendTime; break; case DURING PERTURBATION: return 0; break;  
//case AFTER PERTURBATION: return vd::infinity; break; default: return 0; / 
void internalTransition(const vd::Time& t) / switch(mstate)/  
//case BEFORE PERTURBATION: / if(nbBags == 0) / mstate = AFTER PERTURBATION; /  
else / mstate = DURING PERTURBATION; / break; /  
//case DURING PERTURBATION: /  
currentBag++;  
if(currentBag == bBags) / mstate = AFTER PERTURBATION; /  
else / mstate = AFTER PERTURBATION; / break; /  
void output(const vd::Time&, vd::ExternalEventList& out) const  
/ switch(mstate)/  
//case BEFORE PERTURBATION: /  
if(nbBags == 0)/  
vle::ExternalEvent* ee = new vle::ExternalEvent("p");  
ee->putAttributes(message); output.push_back(ee); / break;/  
//case DURING PERTURBATION: /  
if(currentBag == nbBags)/  
vle::ExternalEvent* ee = new vle::ExternalEvent("p");  
ee->putAttributes(message); output.push_back(ee); / break;/  
//case AFTER PERTURBATION: / break; /  
void externalTransition(const vd::ExternalEventList& e) const  
/ throw vu::ArgError(vle::fmt("[\%1\%] Model that does not handle external events ") % getModelName()); /  
```
message represents the value of temperature or relative humidity to send; sendTime is the time to send the message and nbBags (default = 0) is the number of bags to wait at sendTime before sending the message.

IV. SIMULATION

As mosquitoes are usually active at night, we consider minimum daily temperatures and maximum daily relative humidity for the years 2013 and 2014; we summarize the monthly averages in Table 4.

Table 4. Annual temperatures (minimum) and relative humidities (maximum) for Douala, Yaoundé and Ngaoundéré for the years 2013 and 2014.

<table>
<thead>
<tr>
<th>Climatic factors</th>
<th>January</th>
<th>February</th>
<th>March</th>
<th>April</th>
<th>May</th>
<th>June</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Climatic factors</th>
<th>July</th>
<th>August</th>
<th>September</th>
<th>October</th>
<th>November</th>
<th>December</th>
</tr>
</thead>
</table>

A. Migration between Douala and Yaoundé, Yaoundé and Ngaoundéré

According to the report on the General Census of Population and Housing in Cameroon, published in 2010 [29], N_{H_dia} = 1,907,479, N_{H_nda} = 1,817,524 and N_{H_ndere} = 262,747. We consider data of rail “intercity” trains between Douala and Yaoundé for the year 2014. Data collected after a survey we conducted in the Cameroon railways (Camrail) have reported an average of 496 passengers per day from Yaoundé to Douala, and an average of 519 passengers per day from Douala to Yaoundé. Concerning the trip between Yaoundé and Ngaoundéré, we have an average of 788 passengers per day from Yaoundé to Ngaoundéré and an average of 860 passengers per day from Ngaoundéré to Yaoundé. We also collected data from travel agencies by bus (Touristique voyage, Garanti Express, Buca voyage, Finexs voyage) and they show an average of 2,800 passengers per day from Douala to Yaoundé and an average of 2,700 passengers per day from Yaoundé to Douala.

So, \( \phi_{dya} = \frac{496 + 788}{N_{H_{dia}}} = \frac{1284}{1907479} = 0.0007 \), 0.18% ;
\( \phi_{nda} = \frac{519 + 860}{N_{H_{ndere}}} = \frac{1379}{262747} = 0.0052 \), 0.17% ;
\( \phi_{nda} = \frac{788}{N_{H_{nda}}} = \frac{788}{1817524} = 0.0004 \), 0.043% ;
and \( \phi_{nda} = \frac{860}{N_{H_{nda}}} = \frac{860}{262747} = 0.0033 \), 0.33% .
B. Analysis

We firstly compare evolution of infected and infectious Humans with the consideration of climatic factors only during Human-Mosquito contact against the consideration of climatic factors throughout the mosquito life cycle.

As we can mark (Fig. 8, Fig. 9, Fig. 10, Fig. 11, Fig. 12 and Fig. 13), there is a difference when we take into account climatic factors (temperature and relative humidity) only during human-mosquito contact to a consideration of these climatic factors throughout the mosquito life cycle. Specifically, for Douala city, when we take into account climatic factors (temperature and relative humidity) only during human-mosquito contact, the number of infected humans passed under 10 000 after 96 days and stabilizes at 0 (zero) after about 574 days and the number of infectious humans passed under 10 000 after 99 days and stabilizes at 0 (zero) after about 571 days. However, when we take into account climatic factors throughout the mosquito life cycle, we find that the number of people stabilizes around 65 000 after 321 days and the number of infectious humans stabilizes under 522 000 after 333 days.

Concerning Yaoundé city, the consideration of climatic factors (temperature and relative humidity) throughout the mosquito life cycle highlights a number of humans infected under 20 000 after 63 days and stabilizes around 13 000 after 117 days, while the number of infectious human passed under 20,000 after 64 days and stabilizes around 10 000 after 363 days. However, take into account climatic factors only during human-mosquito contact shows a number of infected humans passed under 10 000 after 41 days and stabilizes at 0 after 347 days, while the number of infectious humans passed under 10 000 after 55 days and stabilizes at 0 after 348 days.

For Ngaoundéré city, the consideration of climatic factors (temperature and relative humidity) throughout the mosquito life cycle highlights a number of humans infected Oscillating between the values under 36,000 after 5 days with minima of 9 840 (respectively 9,709) at the 58th day (respectively 403th day) and maxima of 35 089 (respectively 32 959) at 279th day (respectively 6528th day). The number of humans infectious Oscillates between the values under 115 000 with minima of 39 326 (respectively 41 299) at the 100th day (respectively 438th day) and maxima of 59 711 (respectively 114 986 and 106,866) at the 29th day (respectively 291th day and 668th day). However, take into account climatic factors only during human-mosquito contact shows a number of infected humans passed under 5 000 after 24 days and stabilizes at 0 after 247 days, while the number of infectious humans passed under 5 000 after 100 days and stabilizes at 0 after 400 days.

The second point of our analysis is to compare the impact of climatic factors (temperature and relative humidity) in the context of human’s migration. We have two cases: without taking into account climatic factors and taking into account climatic factors throughout the mosquito life cycle.

![Fig.8. Comparison of evolution of infected Humans in Douala with the consideration of climatic factors only during Human-Mosquito contact against the consideration of climatic factors throughout the mosquito life cycle.](image)
Fig. 9. Comparison of evolution of infectious Humans in Douala with the consideration of climatic factors only during Human-Mosquito contact against the consideration of climatic factors throughout the mosquito life cycle.

Fig. 10. Comparison of evolution of infectious Humans in Yaoundé with the consideration of climatic factors only during Human-Mosquito contact against the consideration of climatic factors throughout the mosquito life cycle.

Fig. 11. Comparison of evolution of infectious Humans in Yaoundé with the consideration of climatic factors only during Human-Mosquito contact against the consideration of climatic factors throughout the mosquito life cycle.

Fig. 12. Comparison of evolution of infected Humans in Ngaoundéré with the consideration of climatic factors only during Human-Mosquito contact against the consideration of climatic factors throughout the mosquito life cycle.

Fig. 13. Comparison of evolution of infectious Humans in Ngaoundéré with the consideration of climatic factors only during Human-Mosquito contact against the consideration of climatic factors throughout the mosquito life cycle.

Fig. 14. Comparison of evolution of infected Humans in Douala without taking into account climatic factors and taking into account climatic factors throughout the mosquito life cycle.
We can observe (Fig. 15, Fig. 13, Fig. 16, Fig. 17, Fig. 18 and Fig. 19) that the non-consideration of climatic factors in Douala city shows that the number of infected humans passed under 20 000 after 74 days and stabilizes at 0 (zero) after about 605 days and the number of infectious humans passed under 20 000 after 78 days and stabilizes at 0 (zero) after about 601 days. The inclusion of that climatic factors in Douala city shows a number of infected humans stabilizes around 65 000 after 321 days and the number of infectious humans stabilizes under 522 000 after 333 days.

Concerning Yaoundé city, the non-consideration of climatic factors in Douala city shows that the number of infected humans passed under 10 000 after 41 days and stabilizes at 0 after 368 days, while the number of infectious humans passed under 10 000 after 55 days and stabilizes at 0 after 366 days. The inclusion of that climatic factors shows a number of infected humans under 20 000 after 63 days and stabilizes around 13 000 after 117 days, while the number of infectious human passed under 20 000 after 64 days and stabilizes around 10 000 after 363 days.
For Ngaoundéré city, the inclusion of that climatic factors highlights a number of humans infected Oscillating between the values under 36,000 after 5 days with minima of 9,840 (respectively 9,709) at the 58th day (respectively 403rd day) and maxima of 35,089 (respectively 32,959) at 279th day (respectively 652th day). The number of humans infected Oscillates between the values under 115,000 with minima of 39,326 (respectively 41,299) at the 100th day (respectively 438th day) and maxima of 59,711 (respectively 114,986 and 106,866) at the 29th day (respectively 291th day and 668th day). The non-consideration of climatic factors shows that the number of infected humans passed under 5,000 after 24 days and stabilizes at 0 after 249 days, while the number of infectious humans passed under 5,000 after 100 days and stabilizes at 0 after 401 days.

V. CONCLUSION

We have analysed the impact of climatic factors in malaria transmission taking into account migration between Douala, Yaoundé and Ngaoundéré, three cities of Cameroon country. We showed how variations of climatic factors such as temperature and relative humidity affect the malaria spread by proposing and implementing a meta-population model of malaria that evolves in space and time and that takes into account climatic factors and the humans migration between Douala and Yaoundé, Yaoundé and Ngaoundéré. Our model incorporates the dynamic of the malaria spread inside a population between sick and healthy individuals. Results show difference between human evolution when we consider in the context of migration, climatic factors or not. More, there is a difference of results, specifically inside infected and infectious humans with the consideration of climatic factors throughout the mosquito life cycle and during only the contact Human-Mosquito. We plan to perform by coupling our model with a model where average number of contacts between susceptible humans and infectious mosquitoes \((b)\) and average number of contacts between susceptible mosquitoes and infectious humans \((f\cdot\alpha)\) will be both dynamic (evaluate by simulation) and evolve with each step of time.

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