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– with a view to biological growth

Eva B. Vedel Jensen, Kristjana Ýr Jónsdóttir,
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Spatio-temporal modelling – with a view to biological growth[1]

Eva B. Vedel Jensen, Kristjana Ýr Jónsdóttir,
Jürgen Schmiegel and Ole E. Barndorff-Nielsen

The T.N. Thiele Centre
Department of Mathematical Sciences
University of Aarhus
Ny Munkegade, DK-8000 Aarhus C
Denmark

1. Introduction

Modelling of biological growth patterns is a field of mathematical biology that has attracted much attention in recent years, see e.g. Chaplain et al. (1999) and Capasso et al. (2002). The biological systems modelled are diverse and comprise growth of plant populations, year rings of tree, capillary networks, bacteria colonies and tumours. This paper deals with spatio-temporal models for such random growing objects. Rather than giving a comprehensive review of the field, we will describe some recent advances in the theory of spatial point processes and the theory of Lévy bases that may renew growth modelling.

The first main group of models to be discussed are based on spatio-temporal point processes and may be characterized as cellular models. We let $Z = \{(t_i, \xi_i)\}$ be a spatio-temporal point process on $S = \mathbb{R}_+ \times \mathcal{X}$ where $\mathcal{X}$ is a bounded subset of $\mathbb{R}^d$ with positive volume $|\mathcal{X}|$. The object at time t is given by

$$Y_t = \cup\{\Xi(\xi_i) : (t_i, \xi_i) \in Z,\ t_i \leq t\},$$

where $\Xi(\xi_i) \subset \mathbb{R}^d$ is a random compact set at position $\xi_i \in \mathcal{X}$. Note that $Y_{t'} \subseteq Y_t$ for $t' \leq t$. The object Y_t depends on Z only via the cumulative spatial point process at time t

$$X_t = \{\xi_i \in \mathcal{X} : (t_i, \xi_i) \in Z,\ t_i \leq t\}.$$

Figure 1 shows an example of a growth pattern that may be modelled using this framework. At six dates, the positions of a particular type of weed plant (Trifolium, clover) are shown. These data are part of a larger data set that has been discussed in Brix and Møller (2001).

We will study extensions of recent models for inhomogeneous spatial point processes to a spatio-temporal framework, cf. Hahn et al. (2003) and references therein. One approach is to identify spatio-temporal point process models for which the cumulative spatial point process has specified properties like a given intensity function. Another approach is to extend inhomogeneous spatial models to a spatio-temporal framework, using conditional intensities, and study the induced models for the cumulative point patterns. It should be noted that many of the inhomogeneous point

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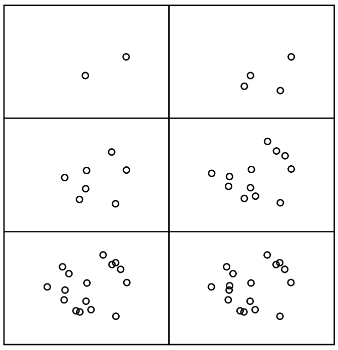

Figure 1: The development of a particular type of weed plant (Trifolium, clover) at six different time points. See Brix and Møller (2001)

patterns analyzed, using purely spatial models, are indeed cumulative point patterns. In the case where Z is a spatio-temporal Poisson point process, the cumulative process X_t is again Poisson and it is easy to control its statistical properties. As we shall see the situation is more complicated in the non-Poisson case.

A second main group of models describes how the boundary of the object expands in time. These models may be characterized as supracellular models. We will mainly discuss growth models based on Lévy bases, cf. Barndorff-Nielsen and Schmiegel (2004), Barndorff-Nielsen et al. (2003) and references therein. A great advantage of these models is the possibility of controlling the correlation structure during the growth process. One example of such a model describes the growth of a star-shaped object, using its radial function. In the planar case, the radial function of Y_t gives the distance $R_t(\phi)$ from a reference point z to the boundary of Y_t in direction $\phi \in [-\pi, \pi)$. For such objects, we study the following model specification

$$R_t(\phi) = \exp\Big(\int_{A_t(\phi)} f_t(\xi, \phi) Z(d\xi)\Big),$$

where Z is a factorizable or a normal Lévy basis, $A_t(\phi)$ is a so-called ambit set and $f_t(\xi, \phi)$ is a deterministic weight function. Figure 2 shows an example of a growth pattern that may be modelled using this framework. At nine time points, the contours of a brain tumour cell island are shown. These data are part of a larger data set that has been discussed in Brú et al. (1998).

In Section 2, models based on spatio-temporal point processes are presented while models based on Lévy bases are dealt with in Section 3. Basic results for spatio-temporal point processes are briefly reviewed in Appendix A.

2. Models based on spatio-temporal point processes

2.1. Set-up

Let $Z = \{(t_i, \xi_i)\}$ be a spatio-temporal point process on $S = \mathbb{R}_+ \times \mathcal{X}$. We assume that the projections of Z on $\mathcal{X}$ and $\mathbb{R}_+$ are both simple point processes (no multiple points). In the following we let

$$Z_t = \{(t_i, \xi_i) \in Z : t_i \leq t\}$$

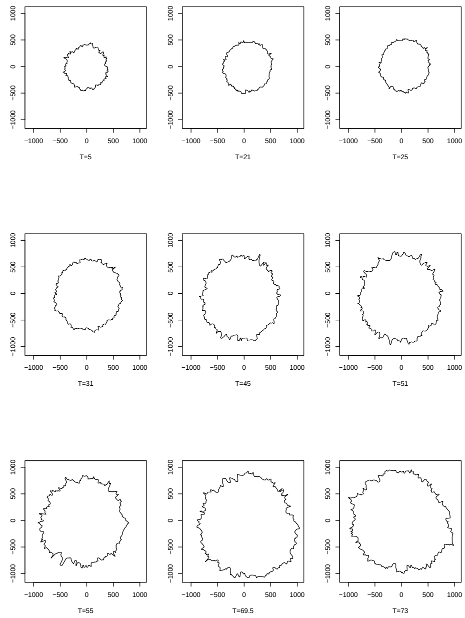

Figure 2: Contours of a brain tumour cell island at nine different time points. See Brú et al. (1998)

be the restriction of Z to $S_t = (0, t] \times \mathcal{X}$. Note that since Z is locally finite and S_t is bounded, Z_t is a finite random subset of S_t. The corresponding cumulative spatial processes are denoted

$$X = \{\xi_i : (t_i, \xi_i) \in Z\}, \quad X_t = \{\xi : (t_i, \xi_i) \in Z_t\}.$$

Note that X and X_t are the projections of Z and Z_t, respectively, on $\mathcal{X}$, see also Figure 3.

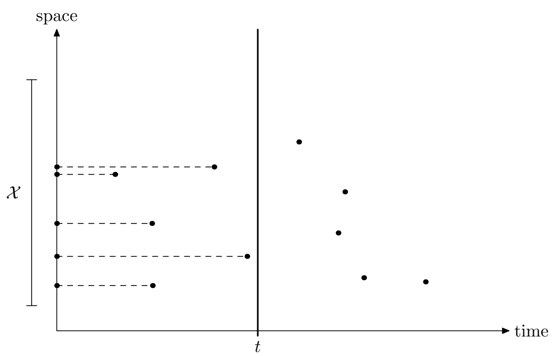

Figure 3: An illustration of the set-up. The points constitute the spatio-temporal point process Z and the dashed lines indicate the projections on $\mathcal{X}$ of points arrived before time t. The points in $\mathcal{X}$ constitute X_t.

Since the projection of Z on $\mathbb{R}_+$ is simple, the temporal part of the process gives a natural ordering of the points that does not exist in general for a spatial point process. This feature will be used at various places in the following. Unless otherwise stated, the numbering of the points of Z is such that

$$t_1 < t_2 < \cdots < t_n < \cdots$$

It will be assumed that Z_t has a density g_{Z_t} with respect to the unit rate Poisson point process on S_t. Because of the natural ordering of the time axis, there are also alternative and perhaps more natural ways of specifying the distribution of Z. Thus, the process can be defined by two families of conditional probability densities

$$\left\{p_n(t \mid t_{(n-1)}, \xi_{(n-1)}) : n \in \mathbb{N}\right\} \tag{1}$$

and

$$\left\{f_n(\xi \mid t_{(n-1)}, \xi_{(n-1)}, t_n) : n \in \mathbb{N}\right\} \tag{2}$$

with respect to the Lebesgue measure on $\mathbb{R}$ and $\mathbb{R}^d$, respectively. Here and in what follows we will use the short notation $t_{(n)}, \xi_{(n)}$ for

$$(t_1, \xi_1), \ldots, (t_n, \xi_n).$$

The density $p_n(\cdot \mid t_{(n-1)}, \xi_{(n-1)})$ describes the distribution of the n-th time point given the history of the whole process up to time t_{n-1}, whereas the density $f_n(\cdot \mid t_{(n-1)}, \xi_{(n-1)}, t_n)$ describes the distribution of the spatial point at time t_n given the history up to time t_{n-1} and the arrival time of the n-th point. The density $p_n(\cdot \mid t_{(n-1)}, \xi_{(n-1)})$ has support (t_{n-1}, ∞) while the density $f_n(\cdot \mid t_{(n-1)}, \xi_{(n-1)}, t_n)$ has support $\mathcal{X}$.

In Appendix A, it is shown for a general spatio-temporal point process how the density of the process Z_t can be expressed in terms of conditional densities. A proof of this well-known result can be found in Daley and Vere-Jones (2002) on conditional intensities and likelihoods for marked point processes. An alternative proof may be found in Appendix A.

An alternative way of specifying a spatio-temporal point process model is in terms of conditional intensities. For a sequence $\{(t_i, \xi_i)\}$ with

$$0 = t_0 < t_1 < \cdots < t_n < \cdots,$$

the conditional intensity is

$$\lambda^\star(t, \xi) = \lambda_g(t) f^\star(\xi \mid t), \quad \text{if } t_{n-1} < t \le t_n,$$

where

$$\lambda_g(t) = \frac{p_n(t \mid t^{(n-1)}, \xi^{(n-1)})}{S_n(t \mid t^{(n-1)}, \xi^{(n-1)})}, \quad \text{if } t_{n-1} < t \le t_n,$$

$$f^\star(\xi \mid t) = f_n(\xi \mid t^{(n-1)}, \xi^{(n-1)}, t), \quad \text{if } t_{n-1} < t \le t_n.$$

It can be shown that the density of Z_t can be written as

$$g_{Z_t}(z) = \exp\Big(-\int_{S_t} [\lambda^\star(s, \xi) - 1] ds d\xi\Big) \prod_{i=1}^{n} \lambda^\star(t_i, \xi_i), \tag{3}$$

where

$$z = \{(t_1, \xi_1), \ldots, (t_n, \xi_n)\}, \quad t_1 < \cdots < t_n.$$

For further details, see Appendix A.

2.2. The Poisson case

If Z is a Poisson point process, the conditional intensity function $\lambda^{\star}$ is equal to the unconditional intensity function λ, say, and the density of Z_t with respect to the unit rate Poisson point process is given by

$$g_{Z_t}(z) = \exp\Big(-\int_{S_t} [\lambda(s,\xi) - 1] d\xi ds\Big) \prod_{i=1}^{n} \lambda(t_i, \xi_i).$$

The distribution of the cumulative spatial process X_t is also Poisson with intensity function

$$\lambda^t(\xi) = \int_0^t \lambda(s,\xi) ds.$$

If the intensity function can be written as $\lambda(t,\xi) = \lambda_1(t)\lambda_2(\xi)$, then

$$\lambda^t(\xi) = a(t)\lambda_2(\xi),$$

where

$$a(t) = \int_0^t \lambda_1(s) ds.$$

Thus, if the intensity function is of product form, the cumulative point pattern at time t is a scaled version of a spatial template Poisson point process with intensity function $\lambda_2(\xi)$.

In the Poisson case, the conditional densities are

$$p_n(t \mid t_{(n-1)}, \xi_{(n-1)}) = \lambda_g(t) \exp\Big(-\int_{t_{n-1}}^{t} \lambda_g(s) ds\Big), \quad t > t_{n-1},$$

and

$$f_n(\xi \mid t_{(n-1)}, \xi_{(n-1)}, t_n) = \frac{\lambda(t_n, \xi)}{\lambda_g(t_n)}, \quad \xi \in \mathcal{X},$$

where

$$\lambda_g(t) = \int_{\mathcal{X}} \lambda(t,\xi) d\xi.$$

Some of the mathematical models for tumour growth specify the development of the intensity of cells in the tumour as a function of spatial position and time, i.e. the cumulative intensity $\lambda^t(\xi)$. An example of a simple model for the concentration of cells at a spatial position ξ at time t is

$$\lambda^t(\xi) = \frac{c}{t} \exp\Big(\rho t - \frac{\| \xi \|^2}{Dt}\Big), \tag{4}$$

where ρ is the net rate of growth of cells, D is a diffusion coefficient and c is a constant determining the size of the initial tumour, cf. e.g. Murray (2003). It is easy to embed such a mathematical model in a Poisson framework. We let Z be a spatio-temporal Poisson point process with cumulative intensity function (4). The tumour at time t is modelled as

$$Y_t = \cup \{B_d(\xi_i, R) : (t_i, \xi_i) \in Z, t_i \leq t\}, \tag{5}$$

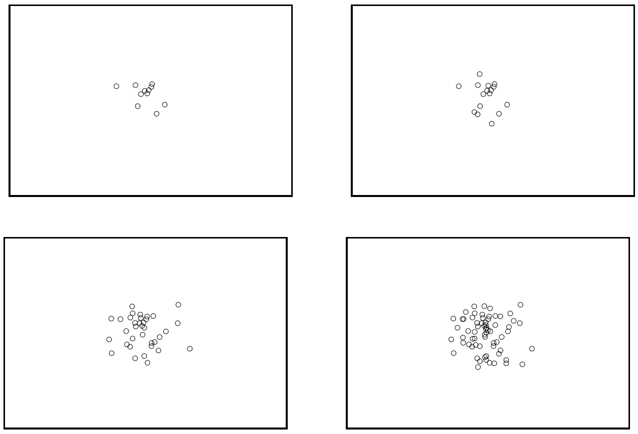

Figure 4: Result of a simulation of the model (5), where X_t is a Poisson process with intensity function (4), for $t = 100, 160, 220, 280$. The parameter values are $\rho = 0.01$, $D = 0.001$, $c = 5 \cdot 10^3$.

where $B_d(\xi_i, R) \subset \mathbb{R}^d$ is a ball centered at ξ_i with radius $R > 0$. A simulation of Y_t for which Z is Poisson with cumulative intensity function (4) can be seen in Figure 4. A more complicated model is obtained by associating random compact sets to each point.

This cellular growth model can be regarded as a continuous version of the model considered in Cressie and Hulting (1992). Their discrete model, proposed for modelling of tumour growth, can be described as a sequence of Boolean models such that the tumour Y_t at time t is a union of independent random compact sets placed at uniform random positions inside the tumour Y_{t-1} at time $t-1$. Formally this means

$$Y_t = \cup\{\Xi(\xi_i) : \xi_i \in Y_{t-1}\},$$

where $\{\xi_i\}$ is a homogeneous Poisson point process in $\mathcal{X}$ and $\Xi(\xi_i)$ is a random compact set at position ξ_i. A related continuous model has recently been discussed in Deijfen (2003). The object Y_t is here a connected union of randomly sized balls constructed from a spatio-temporal Poisson point process. It is shown that the asymptotic shape of the object is spherical.

An advantage of the Poisson model is that many quantities are analytically known. But Poisson points do not interact. In the following subsections, we will describe models for spatio-temporal point processes with clustering or inhibition between the points.

2.3. Cox processes

A spatio-temporal Cox process on S is a spatio-temporal Poisson point process with a *random* intensity function Λ. Such a process exhibits clustering between the points. The intensity function of a spatio-temporal Cox process is given by $\lambda(t, \xi) = \mathbb{E}\Lambda(t, \xi)$ and the pair correlation function by

$$\rho((t, \xi), (s, \eta)) = \frac{\mathbb{E}(\Lambda(t, \xi)\Lambda(s, \eta))}{\mathbb{E}\Lambda(t, \xi)\mathbb{E}\Lambda(s, \eta)}.$$

It is clear that Z_t is a spatio-temporal Cox process on S_t driven by the restriction Λ_t of Λ to S_t. The cumulative spatial process X_t is a Cox process on $\mathcal{X}$ driven by

$$\Lambda^t(\xi) = \int_0^t \Lambda(s, \xi) ds.$$

The intensity function of X_t is $\lambda^t(\xi) = \mathbb{E}\Lambda^t(\xi)$. It can be shown that for $t' \leq t$, $X_{t'}$ has the same distribution as a process obtained by independent thinning of the points in X_t with retention probability for a point located at $\xi \in \mathcal{X}$ given by

$$p_{t',t}(\xi) = \frac{\lambda^{t'}(\xi)}{\lambda^t(\xi)}.$$

A spatio-temporal Cox process with log-Gaussian intensity function has been used with success in the analysis of weed data of the type shown in Figure 1, see Møller et al. (1998); Brix and Møller (2001).

A particular example of a spatio-temporal Cox process is a spatio-temporal shot noise Cox process Z driven by

$$\Lambda(t, \xi) = \sum_{(u,c,\gamma) \in \Phi} \gamma k((u, c), (t, \xi)),$$

where $k((u, c), \cdot)$ is a kernel (i.e. a probability density on S) and Φ is a Poisson point process on $S \times \mathbb{R}_+$. A comprehensive treatment of the purely spatial case can be found in Møller (2003). The process can be viewed as a cluster process since

$$Z|\Phi \sim \cup_{(u,c,\gamma) \in \Phi} U_{u,c,\gamma},$$

where $U_{u,c,\gamma}$, $(u, c, \gamma) \in \Phi$, are independent spatio-temporal Poisson processes with intensity functions

$$\gamma k((u, c), (t, \xi)).$$

The cumulative spatial process X_t is also a cluster process of Cox-type since

$$X_t|\Phi \sim \cup_{(u,c,\gamma) \in \Phi} V_{u,c,\gamma},$$

where $V_{u,c,\gamma}$, $(u, c, \gamma) \in \Phi$, are independent Poisson point processes on $\mathcal{X}$ with intensity function

$$\gamma \int_0^t k((u, c), (s, \cdot)) ds.$$

The spatio-temporal shot noise Cox processes may be used to model growth patterns where several events occur almost simultaneously in time and space.

2.4. Markov point processes

In recent years, Markov models for inhomogeneous spatial point processes have been studied quite intensively, see Stoyan and Stoyan (1998), Baddeley et al. (2000), Jensen and Nielsen (2000), Hahn et al. (2003) and references therein. The majority of the inhomogeneous models has been constructed by introducing inhomogeneity into a homogeneous Markov point process X, defined on a bounded subset $\mathcal{X}$ of

$\mathbb{R}^d$. In this section, we will discuss extensions of these inhomogeneous point process models to a spatio-temporal framework. In relation to growth, it is interesting to construct spatio-temporal processes $Z = \{(t_i, \xi_i)\}$ with *spatial* inhibition between the points.

We start by giving a short review of recently suggested inhomogeneous spatial Markov point processes.

2.4.1. Inhomogeneous spatial point processes

In principle, any given homogeneous point process can be turned into an inhomogeneous point process by independent thinning with a retention probability $p(\xi)$ that depends on the location $\xi \in \mathcal{X}$. As Baddeley et al. (2000) show, second order functions as Ripley's K-function can be defined for thinned point processes such that they coincide with the corresponding second order functions of the original process. However, thinning changes the interaction structure. Thus, if a very regular point process is subjected to inhomogeneous thinning, regions of low intensity seem to exhibit almost no interaction and look similar to a realization of a Poisson process.

Another method that is applicable on any process is to generate inhomogeneity by a nonlinear transformation of the spatial coordinates. Jensen and Nielsen (2000) prove that the process resulting from transformation of a Markov point process is again Markov. Transformation does in general not preserve (local) isotropy of the template process.

Ogata and Tanemura (1986) and Stoyan and Stoyan (1998) suggest to introduce inhomogeneity into Markov or Gibbs models by location dependent first order interactions. As an example, consider a Strauss template X on $\mathcal{X}$ with parameters $\beta > 0$, $\gamma \in [0, 1]$ and $R > 0$, which is defined by a density

$$f_X(x) \propto \beta^{n(x)} \gamma^{s(x)}, \quad s(x) = \sum_{\{\eta,\xi\} \subseteq x} \mathbf{1}_{[0,R]}(\|\eta - \xi\|), \tag{6}$$

with respect to the unit rate Poisson process on $\mathcal{X}$. The resulting inhomogeneous process has density

$$f_X(x) \propto \prod_{\eta \in x} \beta(\eta) \gamma^{s(x)}, \quad s(x) = \sum_{\{\eta,\xi\} \subseteq x} \mathbf{1}_{[0,R]}(\|\eta - \xi\|) \tag{7}$$

with respect to the unit rate Poisson process on $\mathcal{X}$. For such an inhomogeneous process, the degree of regularity in the resulting process depends on the intensity as in the case of thinning, described above.

An approach that preserves locally the geometry of the template model, in particular the degree of regularity and also isotropy, was introduced in Hahn et al. (2003). It can be applied to models that are specified by a density with respect to the unit rate Poisson process. The idea of the approach is that a location dependent scale factor $c(\xi) > 0$ changes the local specification of the model such that in a neighbourhood of any point $\xi \in \mathcal{X}$, the inhomogeneous process behaves like the template process scaled by the factor $c(\xi)$. This is achieved by defining the locally scaled process X_c by a density $f_{X_c}^{(c)}$ with respect to an inhomogeneous Poisson process of rate $c(\xi)^{-d}$. The density $f_{X_c}^{(c)}$ is obtained (up to a normalizing constant) from the template density f_X by replacing all k-dimensional volume measures ν^k, $k = 0, 1, \ldots, d$, that occur in the definition of f_X by their locally scaled counterparts ν_c^k, where $\nu_c^k(A) := \int_A c(u)^{-k} \nu^k(du)$ for all $A \in \mathcal{B}_d$.

A locally scaled version of the Strauss process has thereby the density

$$f_{X_c}^{(c)}(x) \propto \beta^{n(x)} \gamma^{s_c(x)}, \quad s_c(x) = \sum_{\{\eta,\xi\} \subseteq x} \mathbf{1}_{[0,R]}(\nu_c^1([\eta, \xi])), \tag{8}$$

where $\nu_c^1([\eta, \xi]) := \int_{[\eta,\xi]} c(u)^{-1} \nu^1(du)$ is the locally scaled length of the segment $[\eta, \xi]$. This modification applies to all Markov point processes where the higher order interaction is a function of pairwise distances. The resulting inhomogeneous point process is again Markov, now with respect to the neighbour relation

$$\eta \sim \xi \quad \Longleftrightarrow \quad \nu_c^1([\eta, \xi]) \leq R.$$

Since evaluation of the integral in the locally scaled length measure may be computationally expensive in the general case, the scaled distance of two points may be approximated by

$$\nu_c^1([\eta, \xi]) \approx \frac{\|\eta - \xi\|}{(c(\eta) + c(\xi))/2}. \tag{9}$$

Using (9) in (8), and adjusting the first order term in (8), we get the density f_{X_c} of X_c with respect to the unit rate Poisson process as

$$f_{X_c}(x) \propto \beta^{n(x)} \gamma^{s_c(x)} \prod_{\eta \in x} c(\eta)^{-d}, \quad s_c(x) = \sum_{\{\eta,\xi\} \subseteq x} \mathbf{1}_{\left[0, \frac{c(\eta)+c(\xi)}{2} R\right]}(\|\eta - \xi\|). \tag{10}$$

As shown in Hahn et al. (2003), if the scaling function is slowly varying compared to the interaction radius the local intensity in a point ξ of such a locally scaled process is in good approximation proportional to $c(\xi)^{-d}$. Figure 5 shows a realization of a locally scaled Strauss process.

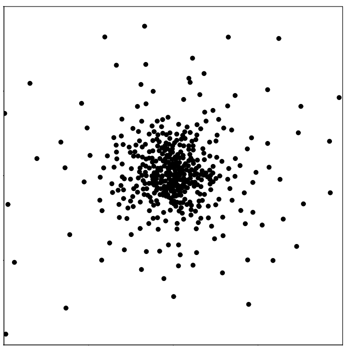

Figure 5: Result of a simulation from a locally scaled Strauss process on $[-1, 1]^2$, with parameters $\beta = 100, \gamma = 0.01$, $R = 0.1$, and scaling function $c(\xi) = 2\|\xi\|^2 + 0.1$.

2.4.2. Spatio-temporal extensions

One possibility is to perform backwards temporal thinning in a spatial Markov point process X with intensity function λ, say. Let the resulting spatio-temporal point process be denoted by

$$Z = \{(t_\xi, \xi) : \xi \in X\}.$$

If, conditionally on X, $\{t_\xi\}$ are independent and t_ξ has density p_ξ, then the cumulative process X_t has intensity function

$$\lambda^t(\xi) = \lambda(\xi) \int_0^t p_\xi(s)ds.$$

Furthermore, for all $t' \leq t$, $X_{t'}$ can be obtained from X_t by independent thinning, with retention probability for a point located at ξ given by

$$p_{t',t}(\xi) = \int_0^{t'} p_\xi(s)ds \bigg/ \int_0^t p_\xi(s)ds.$$

Note that the special $K-$function defined in Baddeley et al. (2000) will be the same for all processes X_t. Note also that the thinning, backwards in time, implies that X_t may look Poisson-like for small t. If the original spatial point process X has the property that any pair of points has a mutual distance of at least R, then any of the cumulative spatial point processes X_t has the same property.

Below, we study thinning of a locally scaled spatial point process.

Example 2.1 *Temporal thinning of a locally scaled Strauss process.* Let $c_1 : \mathbb{R}_+ \to \mathbb{R}$ and $c_2 : \mathbb{R}^d \to \mathbb{R}$ be positive and bounded local scaling functions for time and space, respectively. Let the density of X be a locally scaled Strauss process

$$f_X(x) \propto \beta^{n(x)} \gamma^{s_{c_2}(x)} \prod_{\eta \in x} c_2(\eta)^{-d},$$

where

$$s_{c_2}(x) = \sum_{\{\eta,\xi\} \subseteq x} \mathbf{1}_{[0,R]}(\nu^1_{c_2}([\eta, \xi])).$$

A birth time at ξ is distributed with a density which does not depend on ξ

$$p_\xi(t) \propto c_1(t)^{-1}, \tag{11}$$

if $t \in [0, T]$, and $p_\xi(t) = 0$, otherwise.

Figure 6 shows a result of a simulation of a temporal thinning of such a locally scaled Strauss process on $[-1, 1]^2$ with $\beta = 100$, $\gamma = 0.01$, $R = 0.1$ and local scaling function $c_2(\xi) = 0.2 + 4\|\xi\|^2$. The birth times have density given in (11) with $c_1(t) = 0.2 + 0.05t$ and $T = 12$. The figure shows the corresponding cumulative point patterns $X_{t'}$ for $t' = 2, 4, 8, 12$.

Another possibility is specification of a spatio-temporal point process model in terms of conditional intensities, see e.g. Hawkes (1971); Schoenberg et al. (2002) and references therein. Here, the form of the conditional intensity may be motivated by the form of the Papangelou conditional intensity for a purely spatial point process. A local scaling example is given below.

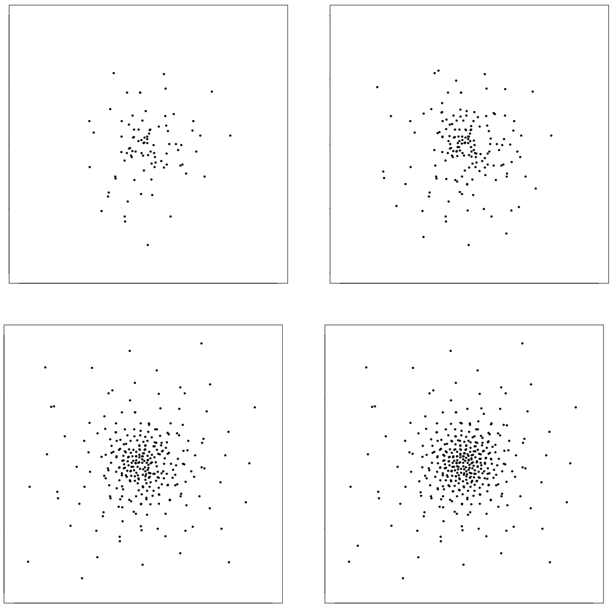

Figure 6: Result of a simulation of a backwards thinning of a locally scaled Strauss process on $[-1,1]^2$. For details, see the text.

Example 2.2 Let $c_1 : \mathbb{R}_+ \to \mathbb{R}$ and $c_2 : \mathbb{R}^d \to \mathbb{R}$ be positive and bounded scaling functions for time and space, respectively. We define the spatio-temporal point process Z by its conditional intensities,

$$\lambda^\star(t,\xi) = \frac{\beta\gamma^{s_{c_2}(\xi|\xi_{(n-1)})}}{c_1(t)c_2(\xi)^d}, \quad t_{n-1} < t \le t_n, \ \ \xi \in \mathcal{X},$$

where

$$s_{c_2}(\xi \mid \xi_{(n-1)}) = \sum_{i=1}^{n-1} \mathbf{1}_{[0,R]}(\nu^1_{c_2}([\xi,\xi_i])).$$

In this case, the density of Z_t is of the following form

$$\begin{aligned} g_{Z_t}(z) &= \exp\Big(-\sum_{i=1}^n \int_{t_{i-1}}^{t_i} \int_{\mathcal{X}} \Big(\frac{\beta\gamma^{s_{c_2}(\xi|\xi_{(i-1)})}}{c_1(t)c_2(\xi)^d} - 1 \Big) dt d\xi \Big) \prod_{i=1}^n \frac{\beta\gamma^{s_{c_2}(\xi_i|\xi_{(i-1)})}}{c_1(t_i)c_2(\xi_i)^d} \\ &= \exp\Big(-\sum_{i=1}^n \int_{t_{i-1}}^{t_i} \int_{\mathcal{X}} \Big(\frac{\beta\gamma^{s_{c_2}(\xi|\xi_{(i-1)})}}{c_1(t)c_2(\xi)^d} - 1 \Big) dt d\xi \Big) \beta^{n(z)} \gamma^{\sum_{i=1}^n s_{c_2}(\xi_i|\xi_{(i-1)})} \\ &\qquad \times \prod_{i=1}^n \frac{1}{c_1(t_i)c_2(\xi_i)^d}. \end{aligned}$$

3. Lévy based growth models

In this section, we will discuss an alternative approach to modelling of growth for a random star-shaped object. We will concentrate on the planar case. The model describes how the boundary of the growing object expands in time. The basic notion of this approach is Lévy bases.

3.1. Set-up

This subsection provides a very brief overview of the theory of Lévy bases, in particular, the theory of integration with respect to a Lévy basis. We will use the following notation for the logarithm of the characteristic function of a random variable X,

$$C\{\lambda \ddagger X\} = \log \mathbb{E}(e^{i\lambda X})$$

and we will refer to it as the cumulant function.

Let $(\mathcal{R}, \mathcal{A})$ be a measurable space. Let $Z = \{Z(A) : A \in \mathcal{A}\}$ be an *independently scattered random measure*, i.e for every sequence $\{A_n\}$ of disjoint sets in $\mathcal{A}$, the random variables $Z(A_n)$ are independent and $Z(\bigcup A_n) = \sum Z(A_n)$ a.s. If $Z(A)$ is *infinitely divisable* for all $A \in \mathcal{A}$, Z is called a *Lévy basis*.

When Z is a Lévy basis, the cumulant function of $Z(A)$ can be written as

$$C\{\lambda \ddagger Z(A)\} = i\lambda a(A) - \frac{1}{2}\lambda^2 b(A) + \int_{\mathbb{R}} (e^{i\lambda x} - 1 - i\lambda \mathbf{1}_{[-1,1]}(x)) U(\mathrm{d}x, A), \quad (12)$$

where a is a signed measure on $\mathcal{A}$, b is a positive measure on $\mathcal{A}$, $U(\mathrm{d}x, A)$ is a Lévy measure on $\mathbb{R}$ for fixed $A \in \mathcal{A}$ and a measure on $\mathcal{A}$ for fixed $\mathrm{d}x$. The Lévy basis is said to have characteristics (a, b, U) and the measure U is referred to as the generalised Lévy measure. The cumulant function (12) can also be expressed in an infinitesimal form

$$C\{\lambda \ddagger Z(\mathrm{d}\xi)\} = i\lambda a(\mathrm{d}\xi) - \frac{1}{2}\lambda^2 b(\mathrm{d}\xi) + \int_{\mathbb{R}} (e^{i\lambda x} - 1 - i\lambda \mathbf{1}_{[-1,1]}(x)) U(\mathrm{d}x, \mathrm{d}\xi).$$

Without loss of generality we will assume that the measure U factorizes as

$$U(\mathrm{d}x, \mathrm{d}\xi) = V(\mathrm{d}x, \xi)\mu(\mathrm{d}\xi),$$

where μ is some measure on $\mathcal{R}$ and $V(\mathrm{d}x, \xi)$ is a Lévy measure for fixed ξ. A Lévy basis is called *factorizable*, if the Lévy measure $V(\cdot; \xi)$ does not depend on ξ. If a Lévy basis is factorizable, then one can write

$$C\{\lambda \ddagger Z(\mathrm{d}\xi)\} = i\lambda a(\mathrm{d}\xi) - \frac{1}{2}\lambda^2 b(d\xi) + C\{\lambda \ddagger Z'\}\mu(\mathrm{d}\xi),$$

where Z' is an infinitely divisible random variable with cumulant function

$$C\{\lambda \ddagger Z'\} = \int_{\mathbb{R}} (e^{i\lambda x} - 1 - i\lambda \mathbf{1}_{[-1,1]}(x)) V(\mathrm{d}x).$$

If, moreover, μ is the Lebesgue measure, then Z is called *homogeneous*.

We will now give two examples of Lévy bases. These are the Poisson basis and the normal Lévy basis. We assume that $\mathcal{R} = \mathbb{R}^n$ and $\mathcal{A} = \mathcal{B}(\mathbb{R}^n)$.

Example 3.1 If Z is a Lévy basis on $\mathcal{R}$, such that $Z(A) \sim \mathrm{Pois}(\Lambda(A))$ for all $A \in \mathcal{A}$ (A bounded), Λ the Lebesgue measure on $\mathcal{R}$, we call Z a Poisson basis. The Poisson basis has characteristics $(\Lambda, 0, U)$, where $U(dx, d\xi) = \delta_1(dx)\Lambda(\xi)$, so Z is factorizable. Clearly the cumulant function of $Z(A)$ is

$$C\{\lambda \ddagger Z(A)\} = (e^{i\lambda} - 1)\Lambda(A),$$

and the cumulant function of the random variable Z' is

$$C\{\lambda \ddagger Z'\} = (e^{i\lambda} - 1 - i\lambda).$$

Example 3.2 If Z is a Lévy basis on $\mathcal{R}$, such that $Z(A) \sim N(\mu\Lambda(A), \sigma^2\Lambda(A))$, we call Z a normal Lévy basis. The normal Lévy basis has characteristics $(\mu\Lambda, \sigma^2\Lambda, 0)$ and the cumulant function is

$$C\{\lambda \ddagger Z(A)\} = i\lambda\mu\Lambda(A) - \frac{1}{2}\lambda^2\sigma^2\Lambda(A).$$

The usefulness of the definitions above becomes clear in connection with the integration of measurable functions f with respect to a Lévy basis Z. We consider the integral of a measurable function f on $\mathcal{R}$ with respect to a factorizable Lévy basis Z. For simplicity we denote this integral by $f \bullet Z$. For the theory of integration with respect to independently scattered random measures, see Kallenberg (1989) and Kwapien and Woyczynski (1992). A key result for many calculations is (subject to minor regularity conditions)

$$C\{\lambda \ddagger f \bullet Z\} = i\lambda(f \bullet a) - \frac{1}{2}\lambda^2(f^2 \bullet b) + \int C\{\lambda f(\xi) \ddagger Z'\}\mu(\mathrm{d}\xi). \qquad (13)$$

A similar result holds for the logarithm of the Laplace transform of $f \bullet Z$,

$$K\{\lambda \ddagger f \bullet Z\} = C\{-i\lambda \ddagger f \bullet Z\} < \infty.$$

We have

$$K\{\lambda \ddagger f \bullet Z\} = \lambda(f \bullet a) + \frac{1}{2}\lambda^2(f^2 \bullet b) + \int K\{\lambda f(\xi) \ddagger Z'\}\mu(d\xi). \qquad (14)$$

If Z is a normal Lévy basis, $Z(A) \sim N(\mu\Lambda(A), \sigma^2\Lambda(A))$, one also has the following equations

$$C\{\lambda \ddagger f \bullet Z\} = \int C\{\lambda f(\xi) \ddagger Z'\}\Lambda(d\xi), \quad K\{\lambda \ddagger f \bullet Z\} = \int K\{\lambda f(\xi) \ddagger Z'\}\Lambda(d\xi), \qquad (15)$$

where Z' is a normal random variable with mean μ and variance σ^2.

3.2. An exponential Lévy growth model for star-shaped planar objects

Let us consider a planar compact object with size and shape changing over time, where the object at time t is denoted by $Y_t \subset \mathbb{R}^2$. In the following we will assume that Y_t is star-shaped with respect to a point $z \in \mathbb{R}^2$ for all t. Then the boundary of the object Y_t can be determined by its radial function $R_t = \{R_t(\phi) : \phi \in [-\pi, \pi)\}$, where

$$R_t(\phi) = \max\{r : z + r(\cos\phi, \sin\phi) \in Y_t\}, \quad \phi \in [-\pi, \pi).$$

The models we will consider here are based on the theory of Lévy bases and integration with respect to those. In the following we will let $\mathcal{R} = \mathbb{R} \times \mathcal{S}$, where $\mathcal{S} = [-\pi, \pi)$ and $\mathcal{A}$ be the Borel σ-algebra of $\mathcal{R}$. The idea behind the following definitions is based on the intuitive picture of an ambit set $A_t(\phi)$, associated to each point (t, ϕ), which defines the causal correlation cone. The radius process $R_t(\phi)$ is defined as the exponential of an integral of some weight function over the attached ambit set, with respect to a factorizable or a normal Lévy basis.

Definition 3.3 Let Z be a factorizable or normal Lévy basis. The field of radius vector functions $R = \{R_t(\phi)\}$ follows an *exponential Lévy growth model* if

$$R_t(\phi) = \exp\Big(\int_{A_t(\phi)} f_t(\xi;\phi) Z(\mathrm{d}\xi)\Big).$$

The ambit set $A_t(\phi) \in \mathcal{A}$ and the deterministic weight function $f_s(a;\phi)$ must be defined cyclically such that $R_t(\phi)$ is cyclic.

There are many interesting problems to study within this model framework. Basically, it is the Lévy basis Z, the ambit sets $A_t(\phi)$ and the weight functions $f_t(a;\phi)$, which determine the growth dynamics. These three ingredients can be chosen arbitrarily and independently which results in a great variety of different growth dynamics.

In the following we will assume that we have a homogeneous factorizable Lévy basis with $a \equiv 0$ and $b \equiv 0$ or a normal Lévy basis. Equations (13), (14) and (15) allows us to calculate arbitrary n-point correlations. Here n-point correlations $c_n(t_1, \phi_1; \ldots; t_n, \phi_n)$ for arbitrary times $t_1, \ldots, t_n$ and angles $\phi_1, \ldots, \phi_n$ are defined as

$$c_n(t_1, \phi_1; \ldots; t_n, \phi_n) \equiv \mathbb{E}(R_{t_1}(\phi_1) \cdot \ldots \cdot R_{t_n}(\phi_n)).$$

If we assume the correlations are finite, i.e. $\mathrm{E}\{R_{t_1}(\phi_1) \cdot \ldots \cdot R_{t_n}(\phi_n)\} < \infty$, we get from (14) and (15) the expression

$$c_n(t_1, \phi_1; \ldots; t_n, \phi_n) = \exp\Bigg\{\int_{\mathcal{R}} \mathrm{K}\Bigg[\sum_{j=1}^{n} f_{t_j}(\xi, \phi_j) \mathbf{1}_{A_{t_j}(\phi_j)}(\xi) \ddagger y\Bigg] \mu(\mathrm{d}\xi)\Bigg\}. \tag{16}$$

This is the basic relation for modelling a prescribed correlation structure in terms of n-point correlations $c_n(t_1, \phi_1; \ldots; t_n, \phi_n)$. Modelling of a given correlation structure reduces to solving the above equation for the weight-function f and the shape and size of the ambit sets $A_t(\phi)$. In practice this might be a complicated task, but for special applications it is possible. Equation (16) also provides some useful geometric interpretation of the correlation structure. This can most easily be seen for the simple case of a constant weight-function $f_t(\xi, \phi) \equiv f$ for all $\xi, (t, \phi) \in \mathcal{R}$. In this case (16) reduces in second order $n = 2$ to

$$\frac{\mathbb{E}(R_t(\phi) R_{t'}(\phi'))}{\mathbb{E}(R_t(\phi))\mathbb{E}(R_{t'}(\phi'))} = \exp(\overline{\mathrm{K}}\, \mu(A_t(\phi) \cap A_{t'}(\phi'))) \tag{17}$$

where $\overline{\mathrm{K}} = \mathrm{K}[2f \ddagger y] - 2\mathrm{K}[f \ddagger y]$. For a constant weight function the modelling of spatio-temporal two-point correlations reduces to the problem of finding ambit sets $A_t(\phi)$ whose measure of the overlap $\mu(A_t(\phi) \cap A_{t'}(\phi'))$ fulfills (17) (see Figure 7 for an illustration). Note that only the measure of the overlap is involved and not the shape of the overlap. Similar relations also hold for higher order correlations under the assumption of a constant weight function f. All finite n-point correlations can be expressed in terms of various overlaps of ambit sets.

Figure 8a shows a simulation from an exponential Lévy growth model with

$$A_t(\phi) = \{(s, \theta) : t - T(t) \leq s \leq t,\ |\theta - \phi| \leq \Theta(t)\},$$

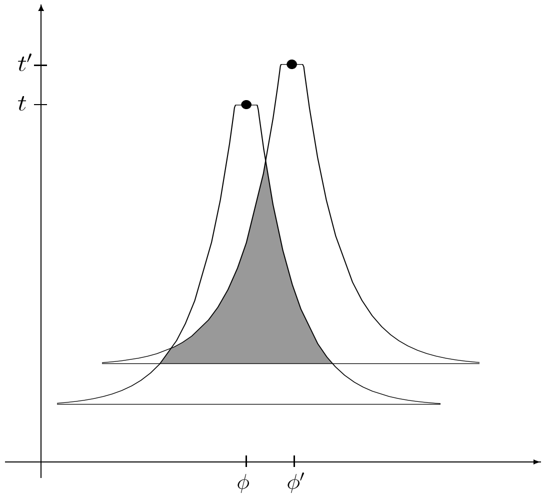

Figure 7: Illustration of the overlap (shaded area) of two ambit sets located at (t, ϕ) and (t', ϕ'), respectively.

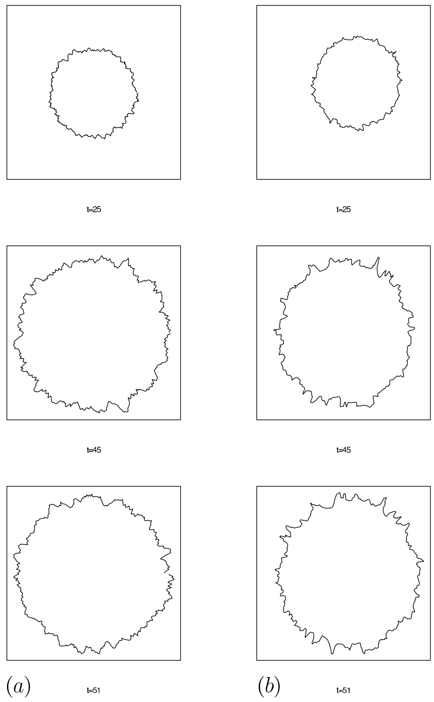

Figure 8: Comparison of a simulation of a log-normal model (a) with in vitro tumour growth (b) at times $t = 25, 45, 51$ (arbitrary units). Parameters of the simulation are $\mu = 0.11$, $\sigma = 0.01$, $T(t) = t/20$, $\Theta(\phi) = \pi/90$ and $f_t(\phi) = 1$. For details, see the text.

$(t, \phi) \in \mathcal{R}$, $f_t(\xi; \phi) = f$ and Z a normal Lévy basis. The similarities between the simulation and the observed in vitro growth pattern in Figure 8b are striking.

A similar type of field of stochastic processes has been used to model the statistics of the energy dissipation in fully developed turbulence (Barndorff-Nielsen and Schmiegel (2004), Barndorff-Nielsen et al. (2003), Schmiegel (2002), Schmiegel et al. (2004)). Barndorff-Nielsen and Schmiegel (2004) also discusses the field of processes

X_t in more detail.

3.3. Other Lévy based growth models

For a factorizable *positive* Lévy basis Z on $\mathcal{R}$ we may also consider a *linear Lévy growth model* given by

$$R_t(\phi) = \int_{A_t(\phi)} f_t(\xi;\phi) Z(\mathrm{d}\xi).$$

The ambit set $A_t(\phi) \in \mathcal{A}$ and the positive deterministic weight function $f_t(\xi;\phi)$, which is assumed to be suitable for the integral to exist, must be defined cyclically such that $R_t(\phi)$ is cyclic. One may also consider the following type of model

$$R_t(\phi) = r_0(\phi) + \int_0^t \int_{A_s(\phi)} f_s(\xi;\phi) Z(\mathrm{d}\xi)\mathrm{d}s. \tag{18}$$

Note that under the model (18), we have that the time derivative of $R_t(\phi)$ is given by

$$R'_t(\phi) = \int_{A_t(\phi)} f_t(\xi;\phi) Z(\mathrm{d}\xi). \tag{19}$$

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Appendix A: Conditional densities and conditional intensities

Let Π be the unit rate Poisson point process on S and Π_t the restriction of Π to S_t. We let Ω be the set of all locally finite subsets of S and Ω_t the set of finite subsets of S_t. On Ω_t, we use the $\sigma-$algebra $\mathcal{A}_t$ generated by

$$\{z \in \Omega_t : n(z \cap B) = k\}, \quad k \in \mathbb{N}_0, B \in \mathcal{B}_t,$$

where $\mathcal{B}_t$ is the Borel σ-algebra on S_t.

We will first state the following basic result for the Poisson point process.

Lemma A.1 Let π_t be the distribution of Π_t and $g_t : (\Omega_t, \mathcal{A}_t) \to (\mathbb{R}, \mathcal{B}(\mathbb{R}))$ be a Borel function. Then

$$\begin{aligned} &\int_{\Omega_t} g_t(z)\pi_t(dz) \qquad (20)\\ &= \sum_{n=0}^{\infty} \exp(-t|\mathcal{X}|) \int_{\mathcal{X}} \cdots \int_{\mathcal{X}} \int_0^t \int_{t_1}^t \cdots \int_{t_{n-1}}^t g_t(\{(t_1,\xi_1),\ldots,(t_n,\xi_n)\}) \\ &\qquad \times dt_n \cdots dt_1 d\xi_n \cdots d\xi_1, \end{aligned}$$

where $|\cdot|$ denotes the Lebesgue measure on $\mathbb{R}^d$.

Proof of Lemma A.1. For the restriction Π_t of the unit rate Poisson point process to S_t, the number N of points (t_i, ξ_i) in S_t is Poisson distributed with parameter $t|\mathcal{X}|$ and conditionally on $N = n$, Π_t is distributed as

$$\{(t_1, \xi_1), \ldots, (t_n, \xi_n)\}$$

where $(t_i, \xi_i), i = 1, \ldots, n$, are independent and uniform in S_t. It follows that

$$\begin{aligned}
&\int_{\Omega_t} g_t(z)\pi_t(dz) \\
&= \sum_{n=0}^{\infty} \exp(-t|\mathcal{X}|)\frac{(t|\mathcal{X}|)^n}{n!} \int_{\mathcal{X}} \cdots \int_{\mathcal{X}} \int_0^t \cdots \int_0^t g(\{(t_1, \xi_1), \ldots, (t_n, \xi_n)\}) \\
&\qquad\qquad\qquad\qquad \times \frac{1}{(t|\mathcal{X}|)^n} dt_n \cdots dt_1 d\xi_n \cdots d\xi_1 \\
&= \sum_{n=0}^{\infty} \exp(-t|\mathcal{X}|) \int_{\mathcal{X}} \cdots \int_{\mathcal{X}} \int_0^t \int_{t_1}^t \cdots \int_{t_{n-1}}^t g(\{(t_1, \xi_1), \ldots, (t_n, \xi_n)\}) \\
&\qquad\qquad\qquad\qquad dt_n \cdots dt_1 d\xi_n \cdots d\xi_1.
\end{aligned}$$

□

If Z_t has density

$$g_{Z_t}(z), \quad z \in \Omega_t$$

with respect to the unit rate Poisson point process Π_t on S_t, then for $A \in \mathcal{A}_t$,

$$\mathrm{P}(Z_t \in A) = \int_A g_{Z_t}(z)\pi_t(dz) = \int_{\Omega_t} \mathbf{1}[z \in A] g_{Z_t}(z)\pi_t(dz)$$

and Lemma A.1 can be used to calculate the integral.

The density of Z_t can be expressed in terms of the two families of conditional densities (1) and (2), as shown in the proposition below.

Proposition A.2 Let

$$g_n(t_{(n)}, \xi_{(n)}) = \prod_{i=1}^{n} p_i(t_i \mid t_{(i-1)}, \xi_{(i-1)}) f_i(\xi_i \mid t_{(i-1)}, \xi_{(i-1)}, t_i)$$

be the density of the first n points of Z. Then, the density of Z_t with respect to Π_t is

$$g_{Z_t}(z) = \exp(t|\mathcal{X}|) g_n(t_{(n)}, \xi_{(n)}) S_{n+1}(t \mid t_{(n)}, \xi_{(n)}), \tag{21}$$

if $z \in \Omega_t$ is of the form

$$z = \{(t_1, \xi_1), \ldots, (t_n, \xi_n)\}, \quad t_1 < \cdots < t_n.$$

Here

$$S_{n+1}(t \mid t_{(n)}, \xi_{(n)}) = \int_t^{\infty} p_{n+1}(u \mid t_{(n)}, \xi_{(n)}) du, \quad t > t_n,$$

is the survival function of $p_{n+1}(\cdot \mid t_{(n)}, \xi_{(n)})$.

Proof of Proposition A.2. Let $N = n(Z_t)$. Then, for $A \in \mathcal{A}_t$,

$$\begin{aligned}
&\mathrm{P}(Z_t \in A)\\
&= \sum_{n=0}^{\infty} \mathrm{P}(Z_t \in A, n(Z_t) = n)\\
&= \sum_{n=0}^{\infty} \int_{\mathbb{R}_+ \times \mathcal{X}} \cdots \int_{\mathbb{R}_+ \times \mathcal{X}} \mathbf{1}[\{(t_1, \xi_1), \ldots, (t_n, \xi_n)\} \in A] 1[t_{n+1} > t]\\
&\qquad\qquad g_{n+1}(t_{(n+1)}, \xi_{(n+1)}) dt_{n+1} d\xi_{n+1} \cdots dt_1 d\xi_1\\
&= \sum_{n=0}^{\infty} \int_{\mathcal{X}} \cdots \int_{\mathcal{X}} \int_0^t \int_{t_1}^t \cdots \int_{t_{n-1}}^t \mathbf{1}[\{(t_1, \xi_1), \ldots, (t_n, \xi_n)\} \in A] g_n(t_{(n)}, \xi_{(n)})\\
&\qquad\qquad S_{n+1}(t \mid t_{(n)}, \xi_{(n)}) dt_n \cdots dt_1 d\xi_n \cdots d\xi_1.
\end{aligned}$$

Now Lemma A.1 implies the result. □

Another possibility is specification of the model in terms of the conditional intensities. For an increasing sequence

$$(t_1, \xi_1), \ldots, (t_n, \xi_n), \ldots, \quad t_1 < \cdots < t_n < \cdots, \tag{22}$$

we define the conditional intensity at (t, ξ) by

$$h_n(t, \xi \mid t_{(n-1)}, \xi_{(n-1)}) = \frac{p_n(t \mid t_{(n-1)}, \xi_{(n-1)}) f_n(\xi \mid t_{(n-1)}, \xi_{(n-1)}, t)}{S_n(t \mid t_{(n-1)}, \xi_{(n-1)})}, \tag{23}$$

for $t_{n-1} < t \leq t_n$ $(t_0 = 0)$. If a realization of Z is represented as in (22), then

$$h_n(t, \xi \mid t_{(n-1)}, \xi_{(n-1)}) dt d\xi$$

can be interpreted as the conditional probability of observing a point at (t, ξ) given the previous history of the process and a waiting time for the n-th point at least uptil t. Note that the conditional intensity h_n is the product of the hazard function for the n-th time point given the history $(t^{(n-1)}, \xi^{(n-1)})$ and the density of the n-th spatial point given the history $(t^{(n-1)}, \xi^{(n-1)})$ and the n-th time point.

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