Copulae and networks modeling

Laura Sacerdote*

Collaborators:
. Roberta Sirovich *
. Massimiliano Tamborrino**
. Cristina Zucca*
. Ottavia Telve

* Dept. Mathematics, University of Torino
**Dept. Mathematical Sciences, University of Copenhagen
Summary

• Information transmission: single neuron - networks
• Dependencies measures
• First models using copulas
• Open problems and future work
Information transmission

Single neurons “code” the information through intertimes between spikes

How the information propagates in the network?
Simultaneously recorded spike trains

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Analysis of the pattern

Different view points:

• Statistical
  – Crosscorrelogram
  – Spatio-temporal pattern detection method (Abeles)

• Mathematical Models for large networks
  – Simulation approach
  – Mean field approach, Master equations....
  – Complex system approach

Both view points share the necessity to study dependencies between the point processes describing the spike trains
Models

• We have “good” mathematical models describing single neuron spike activity;
  – they reproduce main observed features of the neuron;
  – they help our understanding of these features (role of noise, effect of periodic stimula...)

• Separately we have network models:
  – Large networks: simulation of oversimplified units with adaptive connections; object oriented networks; multiparticles systems; limit theorems for large systems,...
  – Small networks: jump-diffusion models; Hodkin-Huxley like model neuron network

How to insert single neuron models in network models?
Copulae: mathematical objects catching dependencies

Consider two random variables $X_1$ and $X_2$ their distribution $F(x_1, x_2)$ completely describes their joint behavior:

$$F(x_1, x_2) = P(X_1 < x_1, X_2 < x_2)$$

Let $C(u,v)$ be a function such that:

$$F(x_1, x_2) = C(F(x_1), F(x_2))$$

Where

$$F(x_1)=P(X_1 < x_1)$$ and $$F(x_2)=P(X_2 < x_2)$$

$C(u,v)$ is the copula function: it catches the dependencies between the random variables $X_1$ and $X_2$. Their marginal behavior is considered by the marginal distributions $F(x_1)$ and $F(x_2)$.

Extensions to the n-dimensional case ...
Some important properties

Sklar Theorem
Let $F_1, \ldots, F_n$ be marginal d. of $X_1, \ldots, X_n$ with joint d. $H$. Then exists a copula $C$ such that

$$H(x_1, \ldots, x_n) = P(X_1 < x_1, \ldots, X_n < x_n) = C(F_1(x_1), \ldots, F_n(x_n))$$

If $F_i$ are continuous then $C$ is unique. Vice versa, if $C$ is a copula and $F_i$ are d.f. then the function $H$ is a joint d.f. with marginals $F_{i_1}, i=1,\ldots,n$.

Invariance under strictly increasing trasformation

- Scale free: it’s possible to avoid assumptions on dimensions of the marginals.

Frechet – Höffning bound

$$W(u_1,\ldots,u_n) \leq C(u_1,\ldots,u_n) \leq M(u_1,\ldots,u_n)$$

Counter-monotone $\max(u_1+\ldots+u_n-1,0)$, Comonotone $\min(u_1,\ldots,u_n)$.

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Information measure and copulae

The copula entropy is equivalent to the negative of the mutual information between the two random variables \(X\) and \(Y\), but with the benefit of being computed directly from dependence structure:

\[
H_c[u_1, u_2, \ldots, u_N | \theta] = -\int_{[0,1]^N} c[u_1, u_2, \ldots, u_N | \theta] \log c[u_1, u_2, \ldots, u_N | \theta] du = I(X,Y)
\]

Copulae in neurosciences

Statistical approach - Construction of flexible join distributions (likelihood and mutual information estimates)


Onken, Grunewaelder, Munk and Obermayer *PLOS Computational Biology* 5, 11, e1000577, DOI 10.1371 (2009)

Berkes, Pillow *Advances in Neural Information Processing Systems*, 21 (to appear)

Mathematical models:

1. **Toy models illustrate the use of copulas.**
   
   Sacerdote and Sirovich *J. Physiol. Paris* (to appear)

2. **Spike train modeled through coupled Poisson processes**

3. **Coupling of neurons described through LIF models**
Why copulas for neuron models?

Sklar theorem
The 3 functions: 1. marginal respect to $X_1$
2. marginal respect to $X_2$
3. The copula
Uniquely determine the joint distribution

Our knowledge on single neuron ISIs distribution can be used if we determine the correct copula: we know the marginal distributions.

Problem: spike trains are point processes and not simple single random variables.

Scarce literature on copulas and stochastic processes
A toy example
Sacerdote and Sirovich J. Physiol. Paris (to appear)

When A is connected with B and C, B spikes at \( \min(T_A, T_B) \) and C spikes at \( \min(T_A, T_C) \) and \( T_B \) and \( T_C \) are not independent.

When \( T_A, T_B \) and \( T_C \) are exponentially distributed of parameters \( \lambda_1, \lambda_2, \lambda_3 \) we can compute the copula (Marshall Olkin, 1967)

\[
C(u,v) = \min(u^{1-a} v, uv^{1-a})
\]

\[
\alpha = \frac{\lambda_2}{\lambda_1 + \lambda_2}, \quad \beta = \frac{\lambda_3}{\lambda_2 + \lambda_3}
\]

- changing \( \lambda_{12} \) we change the coupling strength
- we could use the same copula with different marginals
Marshal Olkin Copulae

\begin{align*}
C(u,v) & = \min(u^{1-a}v,uv^{1-a}) \\
\alpha & = \frac{\lambda_{12}}{\lambda_1 + \lambda_{12}} \\
\beta & = \frac{\lambda_{12}}{\lambda_2 + \lambda_{12}}
\end{align*}

\lambda_1 = 10 \quad \lambda_2 = 4 \quad \lambda_{12} = 1 \text{ ev/sec}

\lambda_1 = 10 \quad \lambda_2 = 4 \quad \lambda_{12} = 100 \text{ ev/sec}

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From coupled ISIs to time series

• Different copulae with the same marginals give different raster displays
• The same copula with different marginals gives different raster displays

Significant patterns: related to the copula structure
Coupled point processes: FPT of diffusion processes

**Description of the model:**

- Equations
- Marginally: return processes (renewal)
- Gaussian increments coupled through different copulas

\[ T = \inf \{ t : X(t) > S \mid X(0) = X_0 < S \} \]

Point processes as FPT through a boundary:

\[
\begin{align*}
    dX_t &= \left( -\frac{X_t}{\theta} + \mu_1 \right) dt + \sigma_1 dW_1(t); \quad X_{t_0} = 0 \\
    dY_t &= \left( -\frac{Y_t}{\theta} + \mu_2 \right) dt + \sigma_2 dW_2(t); \quad Y_{t_0} = 0.
\end{align*}
\]
How to couple the increments?

\[ h = \frac{T}{k}; \quad t_n = \frac{n}{h}, \]

Euler schema on \((0, T)\):

\[
X_n = X_{n-1} + \left( -\frac{X_n}{\theta} + \mu_1 \right) h + \sigma_1 Z_{n-1}^1; \quad X_{t_0} = 0
\]

\[
Y_n = Y_{n-1} + \left( -\frac{Y_n}{\theta} + \mu_2 \right) h + \sigma_2 Z_{n-1}^2; \quad Y_{t_0} = 0.
\]

where \( Z_{n}^l = W^l(i/h) \sim N(0, h), \ l=1,2; \ n=1,\ldots,k; \)

We couple the increments through suitable copula.
The model
Sacerdote and Tamborrino (submitted)

Coupling of the increments:

\[ F_{Z_{i+1}, Z_{i+m}} (z_1, z_2) = C (\phi (z_1), \phi (z_2)) \quad i = m, m+1, ... \]

\( m \): delay in the dependence of the increments

\( \phi (\cdot) = \text{Erf}(\cdot) \)

- If \( m = 0 \): no delay
- Different criteria to determine the copula:
  - Statistical: from intracellular data
  - Theoretical: from assumption on causes determining the coupling
Differences between spike trains coupled through different copulas (through crosscorrelograms)

Comparison criteria:

1. Wiener versus OU underlying diffusion (with the same coupling copula and coherent diffusion parameters)

2. OU diffusions with different coupling copulas (but the two copulas have the same level of association, measured in terms of $\tau$ of Kendall)

3. OU diffusions with the same copula but with different levels of association (measured in terms of $\tau$ of Kendall)

4. OU with different coupling delays

\[
\tau = 4 \int_0^1 \int_0^1 C(u,v)dC(u,v) - 1 = 4\mathbb{E}(C(U,V)) - 1
\]
OU versus Wiener model

Wiener

Ornstein_Uhlenbeck

\( \tau = -0.5 \)

\[ \mu = 1 \]

\[ \mu = 2 \]

\( \tau = 0.96 \)

\[ \mu = 1 \]

\[ \mu = 2 \]

• Both Wiener and OU: Bumps around 0 → simultaneous inhibition

• Both Wiener and OU: Peaks around 0 → simultaneous excitation
  - Bumps around 0 when \( \mu \) increases
Bumps around zero?

\[ \tau = 0.96 \]

**Suprathreshold regime:** \( \mu \theta > S \)

In the suprathreshold regime the bumps are determined by the **marginal behavior of the two neurons**

**Subthreshold regime:** \( \mu \theta < S \)

In the subthreshold regime the bumps are determined by the **strong positive dependency of the two neurons** (only for OU)

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Different copulae but with the same $\tau$

$\tau = 0.8$

No significant differences arise when we use two different families of copulas with the same $\tau$!
Different values of $\tau$

Underthreshold behavior

Autocorrelograms  Crosscorrelograms

- Increasing the positive dependency the peak around zero increases
- Negative dependencies determine inhibition
- Inhibition phenomena around synchronism arise when $\tau$ is large enough

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Different delays

\[ \tau = 0.8 \quad \mu = 0.7 \]

**Panel A**

- \( X = 0.75 \)
- \( m = 10 \)

**Panel B**

- \( X = 3 \)
- \( m = 30 \)

The delay in the coupling determines a shift of the peak
Model conclusion

- The model can reproduce synchronization and mutual inhibition, also with delays, between the 2 modelled neurons.
- Increasing positive/negative dependencies determine higher peaks/depressions in the crosscorrelograms.
- With $\tau \leq 1$ bumps appear in the crosscorrelograms:
  - Suprathreshold regime: bumps are explained from the autocorrelograms
  - Underthreshold regime: bumps are related with the introduced dependency between neurons
- Changes of the copula family does not affect the results
- The results may be influenced by the method of analysis (but we have not alternatives...)

Crosscorrelograms lacks:
- capture global properties of spike trains loosing local dependencies;
- do not detect all possible association behaviors (they are means);
- give scarce help in mathematical modelling;
- merge single neuron and coupled neurons behaviors;
- Their shape is influenced by the choice of the bin
Lack of differences with the change of the copula

Possible motivations:
1. The crosscorrelograms smooth the differences: they exist but are not detected
2. The coupling between the two processes at the time of boundary crossing is the same because a large number of increments has been added:

\[ X_n = n\mu_1 h + \sigma_1 \sum_{i=1}^{n-1} Z_i^1 \]
\[ Y_n = n\mu_2 h + \sigma_2 \sum_{i=1}^{n-1} Z_i^2 \]

The copula between these two points “determines” the coupling between the spikes
Coupling of the sum of the increments

Theorem

Consider a couple of discretized Wiener processes, characterized by increments \((Z_{i1}, Z_{i2})\) coupled through the copula \(C_\theta:\)

\[
X_n = n\mu_1 h + \sigma_1 \sum_{i=1}^{n-1} Z_i^1,
\]
\[
Y_n = n\mu_2 h + \sigma_2 \sum_{i=1}^{n-1} Z_i^2.
\]

For each \(C_\theta\), when \(n \to \infty\) one has \(C_{XY} \to C_{\Sigma}\), where

\[
\Sigma = \begin{bmatrix} nh & n\sigma_{12} \\
\sigma_{12} & nh \end{bmatrix}^{n \times n}
\]
Example

<table>
<thead>
<tr>
<th>(\tau)</th>
<th>(n_{\text{clayton}})</th>
<th>(\mu = 2)</th>
<th>(\mu = 1.5)</th>
<th>(\mu = 0.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n_{T_1})</td>
<td>(n_{T_2})</td>
<td>(n_{T_1})</td>
<td>(n_{T_2})</td>
</tr>
<tr>
<td>0.5</td>
<td>25</td>
<td>63</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>0.8</td>
<td>200</td>
<td>53</td>
<td>50</td>
<td>81</td>
</tr>
<tr>
<td>0.96</td>
<td>100</td>
<td>52</td>
<td>52</td>
<td>80</td>
</tr>
<tr>
<td>-0.5</td>
<td>100</td>
<td>48</td>
<td>63</td>
<td>55</td>
</tr>
<tr>
<td>-0.96</td>
<td>400</td>
<td>48</td>
<td>64</td>
<td>57</td>
</tr>
</tbody>
</table>

\(n_{\text{clayton}}\): number of terms necessary to the convergence of \(C_{XY}\) to \(C_{\Sigma}\)

\(n_{T_1}, n_{T_2}\): number of iterations till the boundary crossing for the neurons 1 and 2

\(\tau\): Kendall’s tau  \(\mu\): Drift

Similar results also for Frank and Gumbel copulas but these families tend to anticipate the convergence to the normal copula with respect to the Clayton one.
Simplified model

Analysis of the spike trains is difficult. We use Crosscorrelograms but...

To use a mathematical approach we switch to simpler problems:

1. Coupling of FPTs: \( T', T'' \)
   - Theoretical study of the dependence between FPTs.
   - Statistical/simulative study to hypothesize a possible copula for \( (T', T'') \)

2. Backward and forward times \( T_{-1} - T_1 \)
   - Theoretical study the dependence between these times.
   - Statistical/simulative study to hypothesize a possible copula for \( (T_1, T_{-1}) \).
Scatterplots between interspikes times

Clayton $\tau=0.8$

Wiener
$\mu_x=\mu_y=0.7$

Wiener
$\mu_x=1 \mu_y=0.5$

OU
$\mu_x=\mu_y=0.7$

OU
$\mu_x=1 \mu_y=0.5$

The scatterplot merges marginal and joint behavior: it is difficult to interpret

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Copulas

Clayton Copula between increments

Frank Copula between increments

Copulas between times

Wiener O.U. Wiener O.U.

μₓ=μᵧ=0.7 μₓ=μᵧ=0.7

The copulas look very similar (also looking the values of τ)!
Can we prove theoretically their properties?

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Determine the copula between $T_1$ and $T_2$, exit times from a strip

Remark: for the Wiener process without drift the copula does not depend upon the noise intensity

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A first result

For any diffusion process the copula density between $T_1$ and $T_2$ can be expressed as the ratio of first passage time probability densities through suitable boundaries.
Coupled point processes: Poisson processes

**Farlie – Gumbel – Morgenstern (FGM) Copula**

\[ C(u,v) = uv + \theta (1-u)(1-v) \quad \tau = \frac{2}{9} \theta , \quad \theta \in [-1,1] \]

Independent processes

\[ \theta = 0 \quad \tau_{\text{FGM}} = 0 \]

\[ \theta = -0.9 \quad \tau_{\text{FGM}} = -0.2 \]

\[ \theta = -0.2 \quad \tau_{\text{FGM}} = -0.04 \]

\[ \theta = 0.3 \quad \tau_{\text{FGM}} = 0.06 \]

\[ \theta = 0.8 \quad \tau_{\text{FGM}} = 0.17 \]

Poisson Processes “look” independent!!

The dependence of the component processes is limited to the somewhat arbitrary base interval.

If we choose a time T large enough, the process will be asymptotically independent, a.s. as \( T \to \infty \). *Bauerle and Grubel, 2005*
Open problems....and some ideas

• We need the copula between \( T', T'' \), FPT of the two coupled processes.
  – A first step may consider the special case of two Wiener processes. For the special case of two Wiener processes one can use a result by Iyenegar (1985): he gives the joint distribution of the FPTs of two Wiener processes ....But we prefer an alternative approach (in progress)
  – The dependence of the copula from some parameters may be obtained using suitable monotone transformations

• How to switch from coupled FPTs to coupled point processes?
  Starting ideas:
  – use \( T^{-1} , T^1 \) ....
  – Get suggestions from statistical models
Thank you!!