Università degli Studi di Padova

Modeling Cellular Communication

A System of Communication Channels

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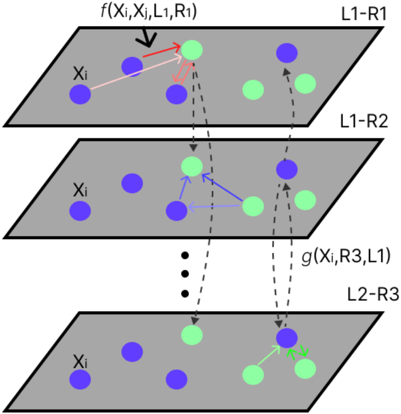
We want to model the cellular communication as a system of different communication channels, where each agent can communicate with others using LR pairs.

Each agent is represented by a cell that has the following status $X_i = [R, x, y]$
Where R is the rna expression counts and x and y are the euclidean spatial coordinates in respect ot a given reference point.



Intralayer links

The links can be thought as pairwise interactions between the cells and modeled by the function: $f(X_i, X_j, L_\alpha, R_\alpha)$ Where L_α is the ligand in layer α and R_α is the receptor in layer α.

Interlayer links

The links can be thought as interactions between the Receptor in layer α and the Ligand in layer β and modeled by the function: $g(X_i, R_\alpha, L_\beta)$ Where the state of the cell X_i is the same for both layers α and β.

Still ongoing, but I did not find any paper that models the cellular communication using multilayer networks. Some ideas may be shared but I don't know.

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Project milestones

1. **Data collection**.
2. **Prior knowledge** interpretation for both definition of comunications channels and relationship between comunication channels.
3. ....

Al momento abbiamo a disposizione 2 dataset MERFISH/MERSCOPE

- **MERFISH - the one we have already seen**: 280'186 x 254 annotated, 2D, brain, from multiple not aligned slices of the MOp. 3 classes and 24 subclasses.
- **MERSCOPE**: 2'846'908 x 1'122 annotated, 3D, brain, from multiple samples. 34 classes and 338 subclasses.
- **Xenium**: .... we might need one. I have some references, but I don't have explored one yet.
- **Visium**: .... we might need one. I have many references, but I don't have explored one yet.

- **NicheCompass**: curated Gene programs
  format: source str -> targets: List[str]
  - GPLR - Ligand receptor pairs from Omnipath
  - GPLRT - Ligand receptor target genes triplets from Nichenet
  - GPES - Enzyme sensor pairs from Mebocost
  - GPTFTG - Transcription factor target genen pairs from Collectri
- **Liana - Mouse consensus**: Ligand-receptor pairs
  Nentries: 3989 format: source str -> target str (93.5+ KB)
- **Nichenet**: Union of ligand-receptor signalings and gene-regulatory pairs:
  Nentries: 8'229'548 format: sourcei (19724) str -> target(22503) str with weight float64 (251+ MB)
- **Omnipath**: Flow activity, general, ligand receptor, enzyme-sensor
  Nentries: 95'855 format: source str -> target str type_source: str type_target: str effect: int64
- **Collectri** Trascription factor target genes pairs:
  Nentries: 43'226 format: source str -> target str weight: float64 and others

Tensor

A tensor is a multilinear function that maps objects defined in a vector space into other objects of the same type. Must be magnitude invariant under a change of basis. More generally, given a vector space $\mathcal{V}$ with algebraic dual space $\mathcal{V}^*$ over the real numbers $\mathbb{R}$.

$$M : \mathcal{V}^* \times \mathcal{V}^* \times \ldots \times \mathcal{V}^* \times \mathcal{V} \times \mathcal{V} \ldots \mathcal{V} \rightarrow \mathbb{R} \tag{1}$$

Formally, we characterize a *rank-mn* tensor $M^{i_1 i_2 \ldots i_n}_{j_1 j_2 \ldots j_m}$ that is *m*-covariant and *n*-contravariant.

Multilayer network

For a graph with N nodes, the canonical covariant vectors $e_i(a) \in \mathbb{R}^N$ are N rank 1 tensors with all entries to 0 except the $a-th$ entry, which is 1. Similarly, for the canonical contravariant vectors. Let the adjacency tensor of a complex network be:

$$W^i_j = \sum_{a,b=1}^{N} w_{ab} e^i(a) e_j(b) = \sum_{a,b=1}^{w} w_{ab} E^i_j(ab) \tag{2}$$

Where w_{ab} is the weight of the edge between nodes a and b. Similarly, let the adjacency tensor of a complex multilayer network be:

$$M^{i\alpha}_{j\beta} = \sum_{a,b=1}^{N} \sum_{p,q=1}^{L} w_{ab}(pq) e^i(a) e_j(b) e^\alpha(p) e_\beta(q) = \sum_{a,b=1}^{N} \sum_{p,q=1}^{L} w_{ab}(pq) E^{i\alpha}_{j\beta}(ab; pq) \tag{3}$$

SNXI decomposition

Different decompositions are possible, however, in multilayer adjacency tensors we can identify four tensors that encode distinct structural information:

$$m^{i\alpha}_{j\beta} = \mathbb{S}_{i\alpha}(M) + \mathbb{N}^{j}_{i\alpha}(M) + \mathbb{X}^{j\beta}_{i\alpha}(M) + \mathbb{I}^{\beta}_{i\alpha}(M) \tag{4}$$

Where:

- $\mathbb{S}_{i\alpha}(M)$: *self-interactions* tensor,interactions from a node to itself.
- $\mathbb{N}^{j}_{i\alpha}(M)$: *endogenous interactions* tensor, interactions between distinct nodes belonging to the same layer.
- $\mathbb{X}^{j\beta}_{i\alpha}(M)$: *exogenous interactions* tensor, interactions between distinct nodes belonging to distinct layers.
- $\mathbb{I}^{\beta}_{i\alpha}(M)$: *intertwining* tensor, interactions from a node to its replicas in other layers.

In our network, we are trying to model an *Interconnected multiplex network*, which is of type *SNI*.

The intralayer links defines the strength of a communication channel between two agens (cells) (spatial locations)

The intralayer links can be modeled by the function:

$$f(X_i, X_j, L_\alpha, R_\alpha) = \frac{X_{il} * X_{jr}}{\sqrt{(x_i - x_j)^2 + (y_i - y_j)^2}} \tag{5}$$

Where X_{il} is the ligand expression of cell i and X_{jr} is the receptor expression of cell j. While, the denominator is the distance between the two cells in the layer. One, could also grid the space and evaluate the possible presence of the ligand l in a specific position by using all cells as sources for the diffusion of such ligand. and other possible modelings that assume saturation of interaction.

Modeling Interlayer links

Interlayer links defines the intracellular signaling pathways within a cell.

The interlayer links needs to be modeled as the influence of a receptor as gene upstream of regulation of other ligands.
We can surely start by looking at the correlation of a receptor that is upstream of regulatory pathways of another ligands as influence score.
Then, we can move to somthing more complex that tries to filter indirect correlations.