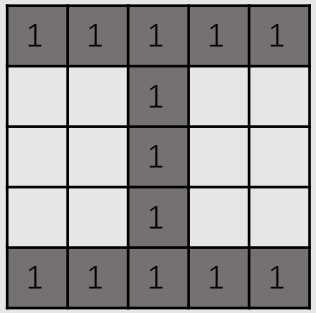
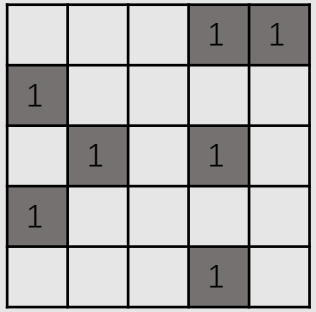
生成空间多组学模拟数据

生成公式-矩阵分解





最终数据 = 底噪 + (空间因子 × 空间权重) + (非空间因子 × 非空间权重)

$$\underset{(N,L_{sp})}{\Lambda} = \underset{0.2}{bkg} + \underset{(N,L_{sp})}{F} \cdot \underset{(L_{sp},J)}{W^T} + \underset{(N,L_{ns})}{U} \cdot \underset{(L_{ns},J)}{V^T}$$

随机指派

$$F = \begin{bmatrix} 1 & 0 \\ 0 & 1 \\ 0 & 1 \end{bmatrix} \begin{matrix} \leftarrow \text{位点}1\text{：只有因子}0 \\ \leftarrow \text{位点}2\text{：只有因子}1 \\ \leftarrow \text{位点}3\text{：只有因子}1 \end{matrix}$$

(3×2)

基因	G1	G2	G3
因子0	1	0	1
因子1	0	1	0

(2×3)

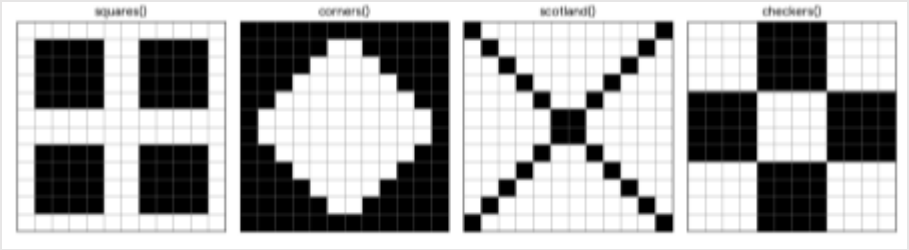
对于矩阵中的每一个元素，程序都会进行一次掷硬币操作：有 20% 的概率生成 1，有 80% 的概率生成 0

nzprob_nsp控制

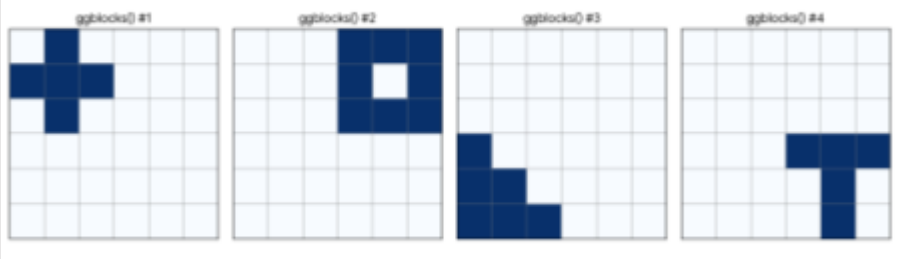
(3×3) (i, j)表示第i个空间点的第j个基因是否表达

空间图生成 - quilt() & ggblocks()

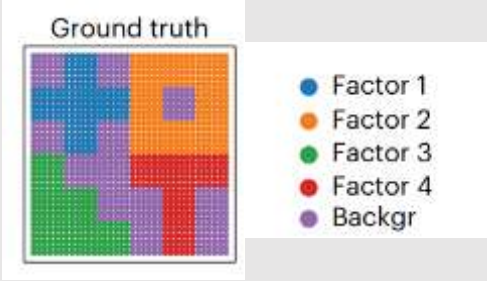
12×12 的网格



6×6 的网格



SpatialGlue



这些图案完全由硬编码写死

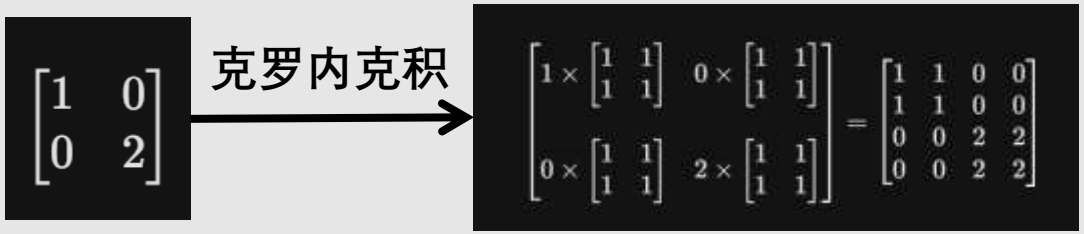
```
def corners():
  B = np.zeros([6,6])
  for i in range(6):
    B[i,i:] = 1
  A = np.flip(B,axis=1)
  AB = np.hstack((A,B))
  CD = np.flip(AB,axis=0)
  return np.vstack((AB,CD))
```

```
def quilt():
  A = np.zeros([4,144])
  A[0,:] = squares().flatten()
  A[1,:] = corners().flatten()
  A[2,:] = scotland().flatten()
  A[3,:] = checkers().flatten()
  return A #basic block size is 12x12
```

```
def ggblocks():
  A = np.zeros( [ 4 , 36 ] )
  A[0, [ 1 , 6 , 7 , 8 , 13 ] ] = 1
  A[1, [ 3 , 4 , 5 , 9 , 11 , 15 , 16 , 17  ] ] = 1
  A[2, [ 18 , 24 , 25 , 30 , 31 , 32 ] ] = 1
  A[3, [ 21 , 22 , 23 , 28 , 34 ] ] = 1
  return A #basic block size is 6x6
```

特性	quilt()	ggblocks()
解析难度	解析复杂的重叠纹理和边缘	识别离散、非连续的空间区域
模拟对象	皮层分层、规则排列的组织结构	淋巴滤泡、肿瘤病灶、免疫浸润点
论文用途	展示算法对几何特征的提取能力	展示算法对局部区域聚类的准确性

空间及基因因子生成



生成空间因子矩阵将上述的小图案，平铺到一个更大的网格上

6×6 / 12×12 → 36×36 (1296)

nside可控

```
(1296, 1000)
(1296, 20)
```

生成基因表达特征决定了基因的行为：$J = J_{sp} + J_{mix} + J_{ns}$

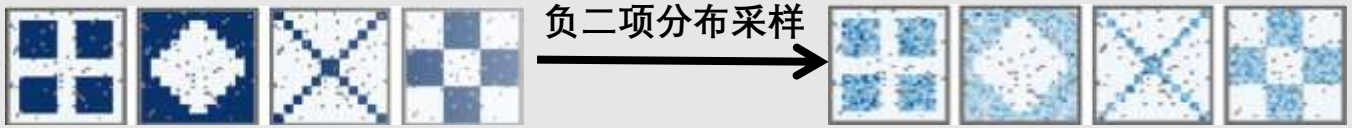
1.J_{sp}纯空间基因，完美遵循空间图案 $\Lambda = F \cdot 20 + U \cdot 0$

2.J_{mix}混合基因，既受空间图案影响，也受随机噪音影响 $\Lambda = F \cdot 11 + U \cdot 9$

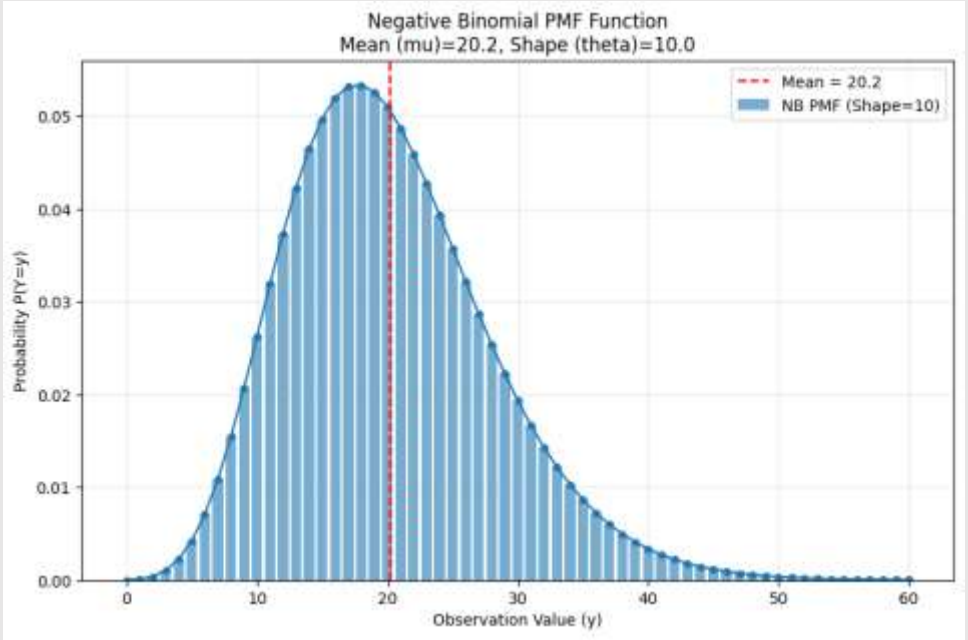
3.J_{ns}纯噪音基因，完全随机，与位置无关 $\Lambda = F \cdot 0 + U \cdot 20$

```
def gen_loadings(Lsp, Lns=3, Jsp=0, Jmix=500, Jns=0, expr_mean=20.0,
                 mix_frac_spat=0.55, seed=101, **kwargs):
```

特征融合



合成最终数据把所有东西拼在一起，拿到空间结构 F 和基因权重 W 和 V，生成随机噪音 U，计算期望表达量 $Lambda$，使用负二项分布模拟真实测序数据中常见的过离散现象。最后把坐标、表达量、真实因子打包成一个 $AnnData$ 对象。



假设没有Jmix情况下：
1.信号区$\lambda = 20.2$在这个区域，基因表达很活跃
2.背景区$\lambda = 0.2$在这个区域，理论上几乎没有表达

$$Y_{ij} \sim NegativeBinomial(\text{mean} = \lambda_{ij}, shape = 10)$$

$$\text{方差 } (Variance) = \text{均值}(\mu) + \frac{\text{均值}(\mu^2)}{Shape}$$ 其中$Shape$取10

拓展生成多组学数据

SpaMV将这些点划分为 9 个的方形子区域，每个子区域代表一个独特的空间域

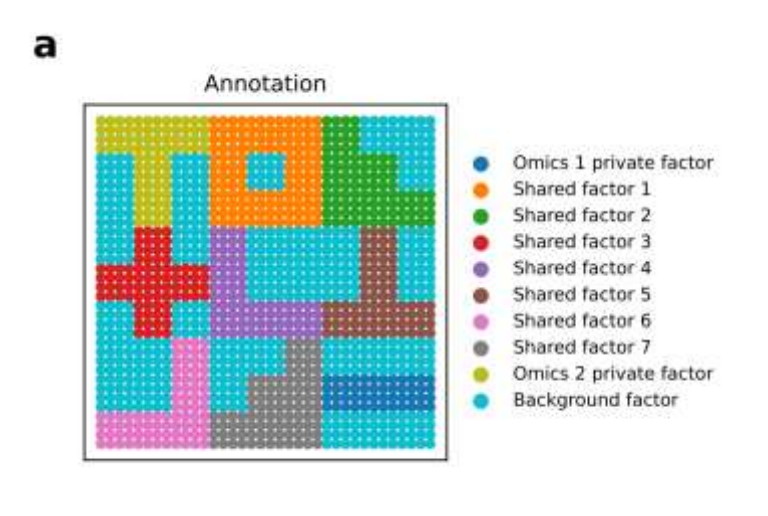
将这些空间域分配给私有因子、共享因子或背景因子

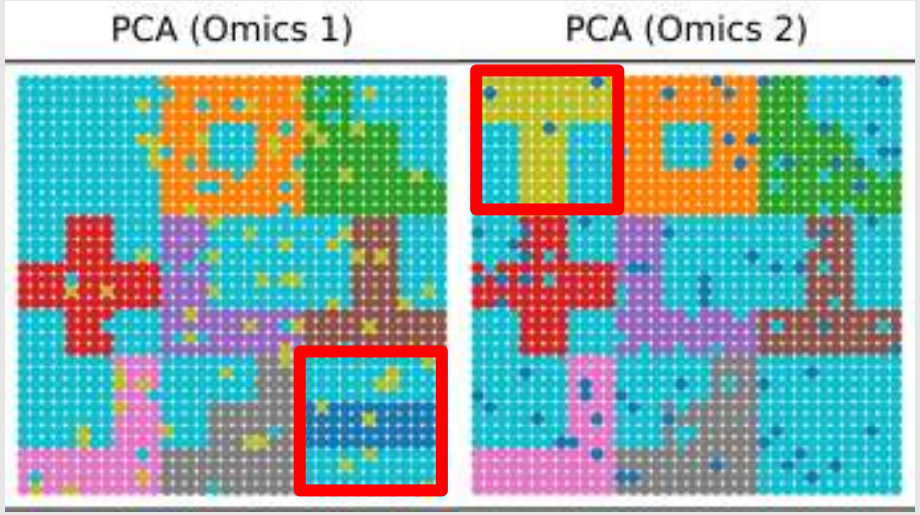
模拟了某些生物学信号是特定组学私有，而另一些是所有组学共享

Omics 1 模拟转录组： 生成 1000 个特征，遵循零膨胀负二项分布

Omics 2 模拟其它组学： 生成 100 个特征，遵循负二项分布

转录组测序数据通常存在drop-out现象，
即很多表达的mRNA没有被捕捉到，
导致检测出来的基因表达量为零或者接近零





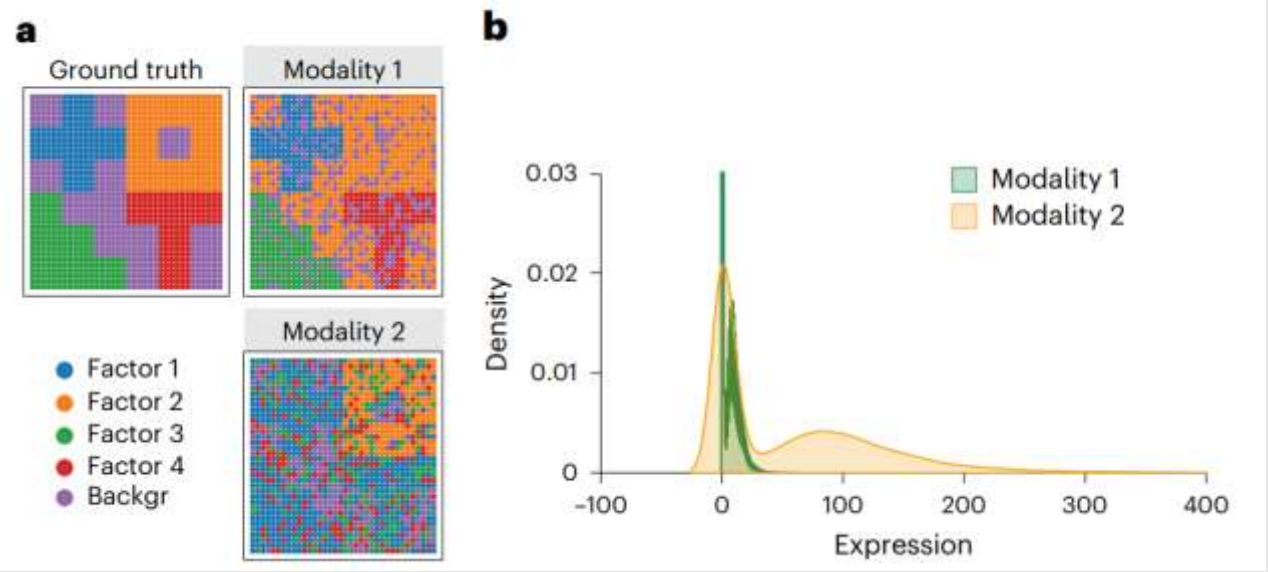
拓展生成多组学数据

SpatialGlue生成的数据包含两类组学，设计了特定的因子来代表解剖结构

因子 1、3、4 由模态 1 决定，而因子 2 仅通过模态 2 识别

模态 1 模拟转录组：遵循零膨胀负二项分布

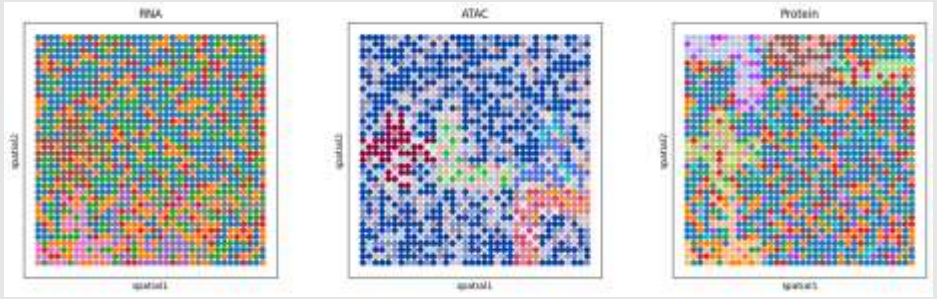
模态 2 模拟蛋白质组：遵循负二项分布



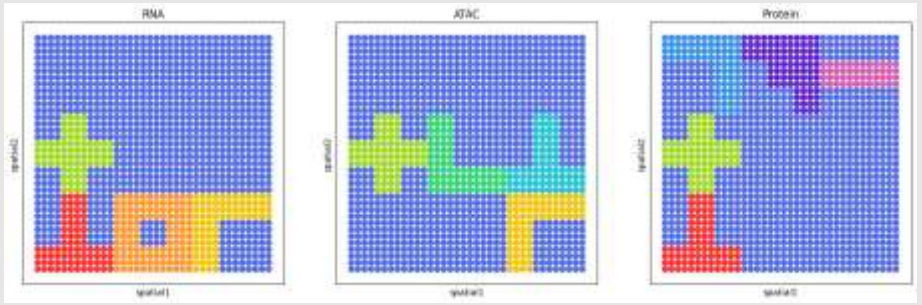
拓展生成多组学数据

可指定组学个数和
每个组学影响的因子

```
{
    "name": "RNA",
    "params": {
        "Jsp": 200, "Jmix": 200, "Jns": 200,
        "expr_mean": 20.0,
        "nb_shape": 10.0,
        "dropout_rate": 0.5
    },
    "active_factors": [0, 1]
},
```

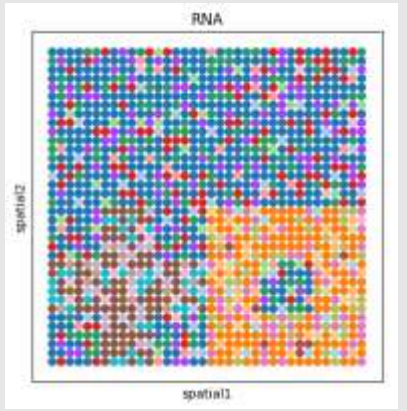


最后输出的leiden聚类结果

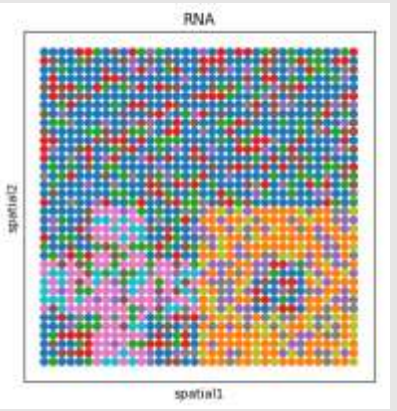


空间因子

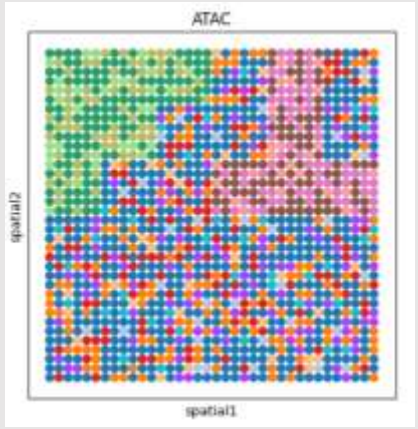
参数差异



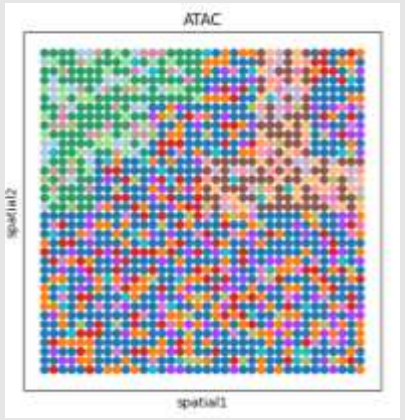
dropout_rate=0.0



dropout_rate=0.5



Jsp=700,Jmix=500,Jns=300



Jsp=500,Jmix=500,Jns=500