College of Medicine and he is a member of the Pelotonia Institute for Immuno-Oncology of Ohio State University as a candidate and a member. His research focuses on integrative analysis on synaptic and genomic data with biomedical real data. So welcome back Dongjun Chung.

Thank you Wei, for the kind introduction and it’s so great to come back. Although it’s all virtual. I hope someday we can see in person. So today I will discuss our recent project about the SPRUCE and MAPLE: Bayesian Multivariate Mixture Models for Spatial Transcriptomics Data.

Oh, by the way, can you hear me well? Ah yes, we can hear you. Okay, great.

So, let me start us from some quick introduction about the single cell genomics. In some sense, the last decade was the era of single cell genomic experiments. So it changed science in many ways. And also a great amount of the data has been generated using the single cell genomic technology. Single cell genomic experiments provide high-dimensional data at the cell level.
By doing so, it allows to investigate cellular heterogeneity within each subject or the patient which was not possible previously with the bulk of genomic data. Which means that genomic data collected at the tissue level. So some kind of standard visualization of the single cell genomic data is called a UMAP. And here, this UMAP shows the distribution of the different clusters in the tumor, including the different immune cell type. And in this way, we can interrogate different types of the immune cell composition. And also there, we can look at what kind of general features imaged for each cell cluster. One of the recent (mumbles) is the emergence of the high-throughput spatial transcriptomics or the HST technology. So, with the emergence of the HST technology, we do not only look at the gene expression in the cell level or the close-to-cell level. We can now also notice that there are cross pointing spatial information. The figure at the bottom shows one example. Here it shows the mouse brain tissue, and each cell cone. Here cross pointer to one spot.
which is a group of the smaller…
small number of like two to ten at most.
And color here indicate expression level of different
gene.
So left one cross point to the H pca gene.
Right one cross point to the T tr gene, for example.
And with the HST data,
we can do a lot of interesting science
So for example,
So at the figure at the bottom left shows the UMAP.
And here,
the different color indicates a different cell cluster.
And if you look at the figure on the right,
then you can see that there are a cluster
in a meaningful way on the tissue.
So in this way, we do not look at the different cell types
within a tissue.
But also look at their spatial information at the same
time.
And there’s many exciting applications
of the HST experiment, including the neuroscience.
Including the brain cancer study such as the immuno-
ology
and the developmental biology
which looks at the changes of the cellular composition
across the different stage of the development.
And here I specifically discuss the application in the cancer, especially the tumor microenvironment. And with the spatial information, we can now study their location of the immune cell and the tumor cell in the tumor tissue. We can also interrogate implication of distance on the tissue and their corresponding density. And we can also study the distribution of the immune regulator. And finally, the special spacial patterns such as the tertiary lymphoid structure. Then from the statistical point of view, how the HST data look like. The first observation is in the HST data spatial structure, in the tissue architecture in a meaningful way. So as you discussed earlier, we can see a similar type of the cell cluster often located in the close proximity in the tissue. And even after we exclude such kind of cell competition in the spatial location, we can start to see some spatial pattern in the patient on the tissue. So the figure on the top shows the expression pattern of the three genes, PCP4, MBP and MTC01. After regressing out, with respect to the cell clusters. And as you can see, even after considering the cell cluster patterns, you can start to see some interesting spatial patterns. That the figure at the bottom shows the distribution.
of each gene for each cell cluster.

And you can see that sometimes it’s asymmetric but also often we can see non-symmetry in vascular distribution for each gene.

So these are some of the key features of the HST data we want to consider in the modeling of the HST data.

Gene expression outcomes feature complex correlation such as the spatial correlation, also gene-gene correlation, which mainly effects the biological pathway. Spatial structure can be cellular clustering entity expression patterns.

And gene expression densities, often feature skewness and or heavy tears due to outlier cell spots.

So ideally we seek to provide a model for identifying the tissue architecture while accommodating these challenging features.

So, especially during the last two years, several statistical methods have been proposed to model HST data.

And still many of them are network-based approaches. Partially because the stragglers; the very famous packages for the single cell genomic data analysis.

And network-based approach has been proven to be powerful in this context.

So based on that multiple network-based approach
have been proposed including the Giotto, Seurat and stLearn.
Because in the statistical model, recently BayesSpace was proposed by the group of the (mumbles) at the Fred Hutchinson.
And essentially, it uses a multivariate-t mixture model to cluster cell spots. It implement spatial smoothing of clusters via a Pott’s model prior on cluster labels. And interestingly, they try to predict sub-spots to increase the resolution. In spite of such interesting features, it has also some number of drawbacks. For example, it assumes the symmetry of the gene expression densities, and it also relies on the approximate inference.
And here our goal is to develop a statistical model that overcome these limitations and also provide the optimal tissue architecture prediction using the HST data which we call SPRUCE or the spatial random effects-based clustering of the single cell data. So this is our SPRUCE model.
So here we use the i as the index for the cell spot and based on the y_i, we also may find a mixture model.
So here we assume the k number of the mixture component or the cell spot clusters. Theta k indicates the set of the parameters specific to mixture component k. Pi k is the probability of the spot i belonging to the component k. We further introduce z1 to zn, which are the latent mixture component indicators for each spot. And zi can have the value between one to k. And as I mentioned earlier, can you see the gene-gene correlation are key features of the HST data? So to account for skewness and gene-gene correlation, we assume a multivariate skew-normal distribution. Where is the parameters? So first one indicates the main vector for spot i, and alpha k indicates gene-specific skewness parameters for mixture component k. And omega k is the gg scale matrix that captures correlation among the gene expression feature in the component k. And we further represent MSN distribution using a convenient conditional representation. We use mu k for the mean of component k, phi i for the spatial effect, and t i and ksi k for the component-specific skewness of each gene. Epsilon i for the multivariate normal error.
And then in order to further accommodate spatial dependence, we used the multivariate intrinsic conditionally autoregressive, or the CAR prior for \( \phi_i \). So essentially, given all the spots except for spot \( i \), we might suggest \( \pi_i \) as the normal distribution with the mean of its neighbors. And with the covariance matrix denoted as the lambda. And as you can see earlier, we see the two different levels of the spatial patterns. One for the spatial pattern of defect clustering. And another one is the spatial pattern of the gene expression. So for the spatial pattern of the cell clusters, we want to allow the probability of \( \pi \) of belonging to each mixture component. of the gene expression. So in order to do so, we extend model I showed previously using the \( \pi_i \) as the normal distribution with the mean of its neighbors. And as you can see earlier, we see the two different levels of the spatial patterns. One for the spatial pattern of defect clustering. And another one is the spatial pattern of the gene expression. So for the spatial pattern of the cell clusters, we want to allow the probability of \( \pi \) of belonging to each mixture component. of the gene expression. So in order to do so, we extend model I showed previously using the \( \pi_i \) as the normal distribution with the mean of its neighbors. And as you can see earlier, we see the two different levels of the spatial patterns. One for the spatial pattern of defect clustering. And another one is the spatial pattern of the gene expression. So for the spatial pattern of the cell clusters, we want to allow the probability of \( \pi \) of belonging to each mixture component. of the gene expression. So in order to do so, we extend model I showed previously using the \( \pi_i \) as the normal distribution with the mean of its neighbors. Of the gene expression. So in order to do so, we extend model I showed previously using the \( \pi_i \) as the normal distribution with the mean of its neighbors. And as you can see earlier, we see the two different levels of the spatial patterns. One for the spatial pattern of defect clustering. And another one is the spatial pattern of the gene expression. So for the spatial pattern of the cell clusters, we want to allow the probability of \( \pi \) of belonging to each mixture component. Of the gene expression. So in order to do so, we extend model I showed previously using the \( \pi_i \) as the normal distribution with the mean of its neighbors. And as you can see earlier, we see the two different levels of the spatial patterns. One for the spatial pattern of defect clustering. And another one is the spatial pattern of the gene expression. So for the spatial pattern of the cell clusters, we want to allow the probability of \( \pi \) of belonging to each mixture component.
to introduce the spatial association into the component membership model, we further assume the univariate intrinsic CAR prior. As you can see here. And here the one computational challenges, if you’re interested, is format. Then it do not allow us to... It do not provide the closed form posterior distribution, which prevent Gibbs sampler. And in order to address this computation challenge, we extended our model using the results from the Polson et al in 2013, Jasa on Polya-Gamma data augmentation to allow for Gibbs sampling of the mixing weight model parameters. And essentially, we could assume that this can be represented as the Polya-Gama Data Augmentation. And by doing so, everything can be implemented as the Gibbs sampler. In the case of the further outliers or heavy-tails, we can even further extend the model to the multivariate skew-t distribution that you can see here. Which can be very easily implemented given the existing model. To complete our model specification, we use the weekly specified prior, and then the quantity of prior. And by using this conjugate prior, we can do everything using the fully Gibbs sampler.
0:16:22.67 –> 0:16:23.84 of the closed form
0:16:23.84 –> 0:16:26.053 which provide the best computation.
0:16:28.72 –> 0:16:31.303 And some additional consideration.
0:16:33.04 –> 0:16:33.95 So here,
0:16:33.95 –> 0:16:38.1 the one question is the optimal number of the k
0:16:38.1 –> 0:16:40.98 worked in number of disparate clusters.
0:16:40.98 –> 0:16:42.47 So for the proposal,
0:16:42.47 –> 0:16:46.13 we use the product of the model selection approaches,
0:16:46.13 –> 0:16:48.95 and specifically we use the WAIC,
0:16:48.95 –> 0:16:51.723 or the widely applicable information criterion.
0:16:54.521 –> 0:16:56.82 In the patient mixture it’s very common
0:16:56.82 –> 0:16:59.95 to observe the label switching program.
0:16:59.95 –> 0:17:03.2 So to protect against the label switching issue
0:17:03.2 –> 0:17:08.2 in the MCMC sampler, we use the canonical projection of
0:17:08.3 –> 0:17:12.58 using the Peng and Cavalho, in 2016.
0:17:12.58 –> 0:17:16.7 And finally for the actual implementation,
0:17:16.7 –> 0:17:18.69 we use the Rccp
0:17:18.69 –> 0:17:21.833 to further improve the computation efficiency.
0:17:27.09 –> 0:17:32.09 We implement the proposed model as on our package
0:17:33.27 –> 0:17:37.28 and it’s currently available from our data page.
0:17:38.366 –> 0:17:39.199 Here.
0:17:40.409 –> 0:17:43.992 And then the figure shows our digital page.
0:17:45.069 –> 0:17:47.652 When we developed our software,
0:17:49.22 –> 0:17:53.081 one of the popular software to pre-processing
0:17:53.081 –> 0:17:55.248 and analyzing the HST data
0:17:56.536 –> 0:17:58.453 is the Seurat workflow.
0:17:59.661 –> 0:18:01.7 So when you develop our software,
0:18:01.7 –> 0:18:05.432 we provide integration with the Seurat workflow
0:18:05.432 –> 0:18:10.326 so that our software can be embedded
0:18:10.326 –> 0:18:12.18 as part of the (mumbles) flow.
So for example, the data can be loaded into our using the Seurat, and then people can apply the pre-processing using the Seurat workflow. And then that objective can be fed into the SPRUCE analysis workflow. And then the output from the SPRUCE can, again, fit into the Seurat workflow for the visualization and downstream analysis.

So first for the simulation, the first for the simulation is about the... Has the two purposes. So first one is to assess the validity of the parameter estimation algorithm. And second is to quantify the effect of ignoring skewness and spatial information. So in order to make our simulation more realistic, we use the sagittal mouse brain data as the tissue shape. And we simulated the full clusters from the multivariate skew-normal distribution with the 16 genes. We considered the 26... 2696 spots. And then we considered three models, including the multivariate normal, multivariate skew-normal, and with no skew-normal with no spatial. So first one shows the implication of inadequate study of skewness and spatial.
Second shows the implication of ignoring the spatial structure. And the final was our proposed model. And here the top left figure, shows the true cluster labels. And top of right shows the UMAP reduction of the gene expression pattern. And as you can see, we can make the orange and the green, which is far away from each other, similar in the gene expression, so that it can be more challenging in the prediction. And we really test the performance of each model using the ARI where the very close one indicates the better performance. And as you can see here, when we ignore the skewness and the spatial pattern, there is the big loss of the ARI. And by considering the skewness, we gain some but still that there is being lost. And by further considering the spatial pattern, we can improve the high level of the ARI. And for the real data application, we consider the two applications. So, to compare the performance of the SPRUCE to existing tools, we used the 10X Visium human brain data from the Maynard et al., 2021, Nature Neuroscience. Here at the rehab we have about the 3000 spots. And one of the good aspect of this data is it’s very well annotated.
So, the author, using his expert knowledge, they annotated the 3000 spots into the 5 brain layers. Including the white matter and the frontal cortex layers.

And as I mentioned earlier, we use the standard Seurat pre-processing pipeline, including the normalization of using the sc transform and also selection of the most variable genes using the existing pipeline. We consider the top 16 most variable genes. And we also consider the three other existing algorithms including BayesSpace, stLearn, Seurat and Giotto as the computing algorithms. And we use the default parameters for each of them.

Here it shows the regions and top left figure shows the manual annotation provided by the author in the paper. And you can see the nice, five spatial clusters from inside out. And also there you can see that there is one, narrow cell cluster corresponding to the number four. Here we showed the real data for the SPRUCE, BayesSpace, stLearn, Seurat and the Giotto. And in this case, the network-based approaches, including the stLearn, Seurat and the Giotto, all showed a lower performance compared to those algorithms.

The BayesSpace showed relatively higher performance about the ARI of 0.55. SPRUCE further improved the performance.
0:23:49.24 –> 0:23:51.57 compared to the BayesSpace.
0:23:51.57 –> 0:23:54.83 And one thing I noted here is the...
0:23:57.796 –> 0:24:00.13 The narrowed cell cluster,
0:24:00.13 –> 0:24:02.633 could it be identified by the SPRUCE?
0:24:04.015 –> 0:24:05.003 Which is interesting.
0:24:06.09 –> 0:24:08.333 And as the second example.
0:24:09.557 –> 0:24:12.62 So first one is the more labeled data.
0:24:12.62 –> 0:24:17.25 We can compare our prediction to the existing annotation.
0:24:17.25 –> 0:24:21.17 And to further demonstrate the application of the SPRUCE
0:24:22.174 –> 0:24:26.29 to unlabeled data, we analyze the publicly available
0:24:26.29 –> 0:24:30.89 human invasive ductal carcinoma breast tissue.
0:24:30.89 –> 0:24:33.633 Again using the 10 X Visium platform.
0:24:35.9 –> 0:24:38.42 And we essentially followed the similar workflow
0:24:38.42 –> 0:24:43.42 and we identify the top 16 most spatially variable genes.
0:24:44.544 –> 0:24:49.544 And those included several tumor associated antigens,
0:24:49.65 –> 0:24:53.847 TAA, in creating the GFRA1 and CXCL14.
0:24:56.47 –> 0:25:00.25 And also that there is the tumor suppressive gene,
0:25:00.25 –> 0:25:02.823 like MALAT1.
0:25:04.43 –> 0:25:09.43 And we use the SPRUCE to identify the 5 sub regions
0:25:09.6 –> 0:25:11.493 using these 16 features.
0:25:12.479 –> 0:25:16.37 This shows the 16 most variable genes.
0:25:16.37 –> 0:25:21.37 And you can see that there are very clear spatial patterns.
0:25:22.43 –> 0:25:27.43 For example the CXCL14 and GFRA1,
0:25:27.84 –> 0:25:30.35 expel on the right bottom side.
0:25:30.35 –> 0:25:35.35 While the MALAT1 express higher in the top left side.
0:25:38.4 –> 0:25:41.54 And this is the cluster prediction
0:25:41.54 –> 0:25:43.883 made by the SPRUCE algorithm.
0:25:45.67 –> 0:25:47.76 And you can see that it identified
the cluster too, which it highly coincide with the CLCX14
and GFRA1 with a study on.

What the cell cluster 1,
Is the MALAT1
which is more tumor suppressor.

So here we can see that the SPRUCE can identify
the different group of the tissue architecture,
such as the tumor suppressor and then tumor related
spruce can identify the different group of the tissue architecture,
such as the tumor suppressor and then tumor related
the different group of the tissue architecture,
such as the tumor suppressor and then tumor related

And we can also easily look at there,
within cluster expression pattern
and gene-gene correlation.
As you could see earlier,
on cell cluster 2 which equals 0.2 to the right
higher than the GFRA1 and CXCL14.
One, which is the cross point here is the high-end MALAT1
and so on.

And also, in the case of cell cluster 2,
there’s a very strong gene-gene correlation pattern.
So we just support the proposed model that considered
spatial pattern and also gene-gene correlation
simultaneously.
So,
so far I discussed the method
for our SPRUCE and its application.
And that we essentially expanded our work a little bit more
to the MAPLE,
Which is the multi-sample spatial transcriptomics model

Why we care about the multi-sample analysis of HST data?

So currently most algorithms are designed in a way that it can more focus on a single sample.

But even intuitively, joint analysis of the multiple HST data can potentially boost the signal by sharing the information amongst samples.

And also the joint analysis of the different samples can allow the differentiation analysis of the HST data.

So very often, each tissue is not our main interest. But we also want to compare tissue architecture between the different samples.

For example, between the disease group versus the controls, responders versus the non responders to 13 treatments, such as the cancer immuno-therapy.

So to offset this limitation, we proposed MAPLE. And actually our existing SPRUCE framework already allows this one naturally.

So, simply what it can do is instead of now analyzing each sample individually, we can jointly analyze all the samples together.

And then by doing so, we can share information about the modeling of each cell spot cluster, and also their spatial pattern.

But by introducing the sample-level covariate exp xi in the cell type composition, we can see the impact.
0:29:28.79 → 0:29:31.817 of the different sample-level covariate.
0:29:33.32 → 0:29:36.823 Which I show more in detail in the coming slides.
0:29:41.46 → 0:29:44.97 So the first application is the same mouse brain data,
0:29:44.97 → 0:29:47.23 the human brain data...
0:29:47.23 → 0:29:49.31 Sorry this should be the mouse brain,
0:29:49.31 → 0:29:53.033 and here we see the two anterior parts,
0:29:53.9 → 0:29:55.6 which look very similar.
0:29:55.6 → 0:29:57.4 And then as you can see here,
0:29:57.4 → 0:30:00.807 when we jointly analyze the two sample
0:30:00.807 → 0:30:04.38 cross pointing to the same part of the brain.
0:30:04.38 → 0:30:08.21 It nicely identifies the cross pointing part
0:30:08.21 → 0:30:09.83 between the two sample.
0:30:09.83 → 0:30:13.682 Like one in the end, three on the top,
0:30:13.682 → 0:30:15.853 five at the bottom and so on.
0:30:17.12 → 0:30:20.95 And because this is the Bayesag framework,
0:30:20.95 → 0:30:24.64 it can also provide uncertainty measures
0:30:24.64 → 0:30:27.51 about our clustering prediction.
0:30:27.51 → 0:30:30.94 And as you can see usually there is more uncertain
0:30:30.94 → 0:30:34.52 about the clustering prediction
0:30:34.52 → 0:30:37.85 around the boundary between different cell clusters.
0:30:37.85 → 0:30:40.07 Which kind of makes sense,
0:30:40.07 → 0:30:43.19 because we expect that maybe cell type
0:30:43.19 → 0:30:47.51 might be more mixed together in the same cell spot.
0:30:47.51 → 0:30:50.19 Also, there are some cell clusters
0:30:50.19 → 0:30:52.89 with the higher level of the uncertainty
0:30:52.89 → 0:30:55.64 of which we are still trying to understand more
0:30:55.64 → 0:30:56.493 at this point.
0:30:58.18 → 0:31:01.45 And this kind of the figure is the...
0:31:01.45 → 0:31:04.673 what utility of this kind of joint analysis.
0:31:05.51 → 0:31:08.84 So, for the identifier with T,
0:31:08.84 → 0:31:13.65 we set the first cell cluster as the reference.
And then here we see the two (mumbles) The top one shows the intercept, and then we can interpret this one as the relative size of each cell cluster. So then compared to the one, we can say three and the six are larger. So the three and the six are larger, compared to the one. Why the four is the smaller, well just smaller compared to the one. So this is what it can see by eye from the tissue prediction region. But good thing is that this model allows us to quantify, what you see by eye. And what is more interesting is the second one. So this one, is about the difference between the two sample. So this one, is about the difference between the two sample. So again, so basically if it’s higher, then it means that certain tissue spot cluster getting bigger in the second sample. And if it’s lower immune state is a kind of smaller in the second sample and so on. So in this way, we can quantify the change of the tissue architecture between different cell clusters. Another interesting example is this one. So here, the image of 2D to anterior samples, we now also look at the posterior sample as well. So because this is two parts of the brain anterior and the posterior,
the issue is kind of continuous between two.

And as you can see here,

Cell cluster three is connected to the posterior side here.

Cell cluster one is connected to here and so on.

And then this kind of pattern is not clear

if you analyze each data independently.

And our MAPLE framework nicely captures

such kind of sharing pattern.

And also the difference pattern

between the different samples, interestingly.

So at this point,

we are working on more simulation study

and the real data analysis

to further show the performance

and understand the properties of the MAPLE at this point.

So then I can’t summarize my presentation today.

So the high throughput spatial transcriptomics, or HST,

provides unprecedented opportunities

to investigate novel biological hypotheses,

such as the tumor microenvironment and certain structure

about the human brain and Alzheimer,

and so on.

And here we propose SPRUCE,

a Bayesian multivariate mixture model

for HST data analysis.

SPRUCE has multiple strengths

including the novel combination

of the skewed normal density,
Polya-Gamma data augmentation, and spatial random effect. Altogether, it allows to precisely infer spatially correlated mixture component membership probabilities. In our simulation study and real data analysis, we could see that SPRUCE outperforms the existing method, in the tissue architecture identification. And finally our recent extension of the MAPLE allows the joint clustering and differential analysis of multiple HST data. So at this point SPRUCE is on the review in, (mumbles) in the biometrics. Cross pointing manuscript is available in the bio archive. And there are multiple ongoing work regarding the HST data modeling in our lab. So we are actually currently working on further improving the SPRUCE and the MAPLE by incorporating other characteristics of the HST data, such as the relationships among cells. For example, we know that there are some likened and receptor, which we expect that they interact with each other in their cell structure. And then by incorporating different prior information, we can further improve the SPRUCE and MAPLE.
We are also working on the other statistical models for somewhat relevant, but different tasks. For example, currently we are also working on the streamlining framework, especially the graph neural network, which is called RESEPT. And then using the gene framework, we tried to come up with good embedding of the HST gene expression pattern. Our current results show that such a combination can provide nice prediction performance. For this proposal, we developed a framework called RESEPT and cross pointing bio archive is also available publicly. And then cross pointing paper is now under revision in the nature communications. Regarding cell-cell communications, using network-based approaches has some benefit because the cell-cell communication can be nicely and naturally modeled using AGR network. So we have the parallel work called the the Banyan to identify the cell-cell communication and tissue architecture using the network-based approaches. And finally, there are the multiple effort experimentally to generate the spatial multimodal data. For example, the effect to seek such as the single cell genomics, proteomics and the T-cell receptor at the same time.
And very soon, everything are expected to be combined as the spatial transcriptomic structure. We are working on the direction to develop the statistical model for integration of the HST data with other matched data. So I would like to acknowledge my research team at OSU. Carter Allen is the main driver this project, and also my pitch assistant Qin Ma and Yuzhou Chang is my close collaborator for the HST data modeling project. And Zihai Li, who is the director of the Immuno-Oncology Institute and also the expert in cancer, Won Chang at the University of Cincinnati who are the spatial statistics expert, and MUSC collaborator Brian Neelon and my grant support. So, and this is the end of my presentation, if you have any questions and comment, please let me know by email at chung.911@osu.edu. Thank you for your attention.
Yes, mm-hm.

Right, Dongjun welcome back.

Great work, it’s a nice presentation.

I’m just wondering, like,

when you do this from your own experience

on the cell clustering,

how much the spatial information contributes

to the clustering.

Sure.

So,

If you’re here,

so if you look at the Seurat workflow,

you can see there’s a still lot of the, kind of,

local boundary between different cell spot clusters.

And when you analyze the same data using the SPRUCE,

you can see much cleaner boundary.

And often it will coincide with the

expert analogy annotation.

So given that there is the significant contribution,

course even the gene expression,

we still get some big picture, as you can see here.

But spatial information provide much cleaner prediction

about the tissue architecture in general.

I see.

And also the skewness.

Do you estimate that or that’s like your heart

was persuaded by the skewness?

You mean which one?

On k model.

Your model to specify, the k model you have there.
0:41:19.12 –> 0:41:20.44 I missed that part.
0:41:20.44 –> 0:41:22.863 Like, do you need to specify the skewness?
0:41:24.396 –> 0:41:26.44 Or learn from data.
0:41:26.44 –> 0:41:27.273 Oh, I see.
0:41:27.273 –> 0:41:28.87 But from the data, how skew?
0:41:28.87 –> 0:41:30.6 I mean, just in terms of how stable
0:41:30.6 –> 0:41:32.573 that alpha k can be estimated.
0:41:35.79 –> 0:41:38.24 So maybe I can answer it in two different ways.
0:41:39.72 –> 0:41:42.663 So if there is this skewness in the data, I think yes.
0:41:43.655 –> 0:41:47.65 So we’ll say it depends on how processed the data as well.
0:41:48.878 –> 0:41:50.91 So usually there’s three different approaches
0:41:50.91 –> 0:41:55.91 to model the HST data in closed spatial embedding gene.
0:41:56.83 –> 0:41:58.103 And so you can see here,
0:41:58.103 –> 0:42:00.853 who are the people using the principle components?
0:42:01.854 –> 0:42:04.596 Who are the people use the team learning
0:42:04.596 –> 0:42:05.953 as the embedding step?
0:42:08.179 –> 0:42:12.04 If you use the team learning or the PCA
0:42:12.04 –> 0:42:15.58 it’s more likely symmetry in the real data.
0:42:15.58 –> 0:42:19.94 If you consider the spatial embedding gene,
0:42:19.94 –> 0:42:23.123 we often hope to have the skewness, as you can see here.
0:42:24.41 –> 0:42:29.41 And then regarding your question, overall it works well.
0:42:30.434 –> 0:42:32.993 I don’t have the exact quantification, but it works well.
0:42:34.22 –> 0:42:36.83 Especially stably in most cases.
0:42:36.83 –> 0:42:38.77 Yeah, I read the spatial Bayes paper.
0:42:38.77 –> 0:42:41.16 They seem to be working on the principle components, right?
0:42:41.16 –> 0:42:42.94 They do not work on individual genes, right?.
0:42:42.94 –> 0:42:43.773 No, yeah.
0:42:43.773 –> 0:42:45.5 They base this on the PCA.
Yeah, that’s why it’s completely puzzling me while you’re doing that.

But anyway, yeah.

Thank you.

Yeah so, so...

(mumbles)

so they mainly target the PCA.

So they only can start the multivariate distribution.

And also because of the same reason,

their equivalence metrics means less density.

I see.

Thank you.

Thank you.

Do we have any questions from students in the classroom?

Wait, can I ask another question?

So, towards the end,

you mentioned you tried to look at the cell-cell communication.

That part.

I’m very interested in that

From our experience on the single cell spatial data are...

Are you talking about you’re learning from the single cell,

or the spatial single cell?

So, regarding the cell-cell communication

it’s still very ongoing research at this point.

I mean, not just our side but in general.

Because most of the cell-cell communication prediction

based on the database.

So based on data, like on the receptor,
pairing the database and checking their cross point on the expression in cross point spot of the cell. And then by checking that the cross pointing pair of the expression pattern between the like and the receptor. They want to model cell-cell communication. It’s not perfect, as you know, because it’s like a computer. If you look at the chip, it’s almost like but more like motive analysis. So there’s some limitation, but it’s a more likely general limitation at this point. Yeah, I’m asking because we’ve been looking at some of the spatial single cell data that were too noisy for the like and receptor gene expression levels. Just couldn’t make it too far. Yeah, three already. I mean, probably there’ll be more that, like... Yeah, three already. I mean, so if you go to high-resolution, it’s a very noisy, so very often we need to do some simplification. Like looking at multi-modal or the cell cluster, rather than the cell. It’s still very multiple experimental limitation, at this point.
On the data from multiple samples, so, if we have samples from...

Oh yeah, that’s a very good question. So, actually we can answer in the two different ways. In some sense, good pre-processing is still important because it still depends on the expression patterns. But still regarding the differences between the different tissues. If there is a big difference, it can still detect the difference between the different sample. So, it can detect spots. But still like a main goal is more for the similar type of tissue. If it’s too different, maybe it’s different research project. So, for example, here our targets is more about, for example, like same breast tissue, but with a different responders and non-responders group. For example. Or like a cell-cell long tissue, but the tumor but not tumor and so on. If you like a human and mouse,
then it might be somewhat different story,
which might need much more work.
Do we have any more questions here?
Okay, can we have all the questions
from the audience on zoom?
Okay, so it looks like we don’t have any more questions.
So Dr. Chung, thank you again for your nice presentation.
Look forward to meeting in person sometime soon.
And then thank you again Wei and Hongyou
for the invitation
and it’s a great come back, although virtually.
And I hope to see you again.
We’ll come by in person.
Hopefully someday soon.
Okay, thank you.