Analysis of the Data from Lymphoid Lineage Blood Differentiation

```
clearvars
addpath(genpath('../'))
```

Load the data

```
load data_mpp.mat
data = data';
[N_cell,~] = size(data);
```

Estimation of Cluster Number

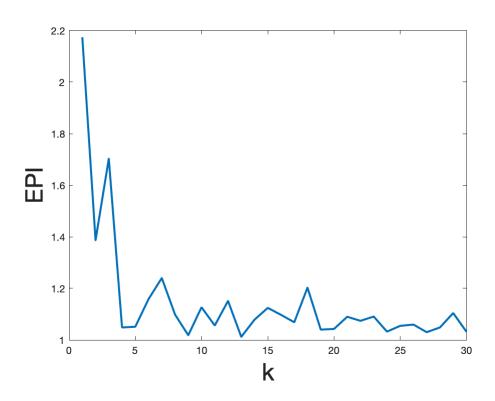
```
par.choice_distance = 'cosine';
out = EstClusterNum(data,par);
```

```
Computed P-values 500 of 2018 datapoint Computed P-values 1000 of 2018 datapoint Computed P-values 1500 of 2018 datapoint Computed P-values 2000 of 2018 datapoint Mean value of sigma: 0.2594 Minimum value of sigma: 0.17169
```

```
plot(out.ratio(1:30),'linewidth',2.0)
```

Maximum value of sigma: 0.43467

```
xlabel('k', 'FontSize', 24);
ylabel('EPI', 'FontSize', 24);
```



Initial visualization by tSNE

```
rng(1)
Dist = squareform(pdist (data, 'cosine')
ydata = tsne_d(Dist);
```

Computed P-values 500 of 2018 datapoint Computed P-values 1000 of 2018 datapoir Computed P-values 1500 of 2018 datapoir Computed P-values 2000 of 2018 datapoir Mean value of sigma: 0.1537

Minimum value of sigma: 0.10088 Maximum value of sigma: 0.27062 Iteration 10: error is 49.8475 Iteration 20: error is 47.0807 Iteration 30: error is 46.0238 Iteration 40: error is 45.9552 Iteration 50: error is 45.7846 Iteration 60: error is 45.7518 Iteration 70: error is 45.8181 Iteration 80: error is 45.7725 Iteration 90: error is 45.6994 Iteration 100: error is 2.9944 Iteration 110: error is 2.3854 Iteration 120: error is 2.0264 error is 1.8718 Iteration 130: Iteration 140: error is 1.7827 Iteration 150: error is 1.7229 Iteration 160: error is 1.6801 Iteration 170: error is 1.6469 Iteration 180: error is 1.6207 error is 1.5994 Iteration 190:

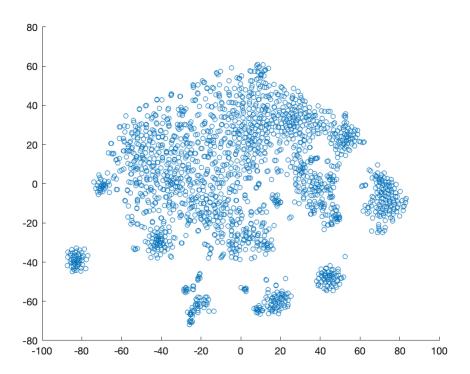
Iteration is 1.5818 200: error Iteration is 1.5667 210: error Iteration 1.5537 is 220: error Iteration 230: error is 1.5423 Iteration 1.5323 240: is error Iteration 1.5234 250: error is Iteration 260: 1.5091 error is Iteration 1.4927 is 270: error Iteration is 1,4794 error 280: Iteration error is 1.4685 290: 1.4594 Iteration 300: is error 1.4518 Iteration 310: error is Iteration 320: error is 1.4454 Iteration 330: error is 1.4398 Iteration 340: 1.435 is error Iteration 350: is error 1.4307 1.4269 Iteration 360: is error Iteration 370: is 1.4236 error Iteration is 1,4206 380: error Iteration is 1.4179 390: error Iteration 400: is 1.4155 error

Iteration 410: is 1.4132 error 1.4112 Iteration 420: is error Iteration is 1.4094 430: error Iteration error is 1.4076 440: Iteration 450: is 1.406 error Iteration error is 1.4046 460: Iteration 1.4033 470: is error Iteration is 1,402 480: error Iteration is 1,4009 error 490: Iteration 500: error is 1.3998 Iteration 510: 1.3988 error is Iteration 520: error is 1.3978 Iteration 530: 1.3969 error is Iteration 540: error is 1.3961 Iteration 550: 1.3953 is error Iteration 560: error 1.3946 is 1.3939 Iteration 570: is error Iteration 580: is 1.3933 error Iteration 1.3927 590: is error Iteration 600: 1.3921 is error Iteration 610: is 1.3916 error

Iteration 620: is 1.3911 error Iteration 1.3906 630: is error Iteration 1.3901 is 640: error Iteration error is 1.3897 650: Iteration 660: is 1.3892 error Iteration 1.3888 670: is error Iteration 680: 1.3885 is error Iteration 1.3881 is 690: error Iteration is 1.3878 700: error Iteration 1.3874 error is 710: Iteration 720: 1.3871 is error Iteration error is 1.3868 730: Iteration 740: is 1.3865 error Iteration error is 1.3862 750: Iteration 1.386 760: is error Iteration 1.3857 770: error is Iteration 1.3854 780: is error Iteration 790: is 1.3852 error 1.385 Iteration 800: is error Iteration 1.3847 is 810: error Iteration 820: is 1.3845 error

```
Iteration 830:
               error is 1.3843
Iteration 840:
                      is 1.3841
               error
Iteration 850:
               error is 1.3839
Iteration 860:
               error is 1.3837
Iteration
                        1.3836
          870:
               error is
Iteration
               error is 1.3834
          880:
Iteration
          890:
               error is 1.3832
Iteration 900:
               error is 1.3831
Iteration 910:
                      is 1.3829
               error
Iteration 920:
               error is 1.3827
Iteration 930:
               error is 1.3826
Iteration 940:
               error is 1.3824
Iteration 950:
               error is 1.3823
Iteration 960:
               error is 1.3822
Iteration 970:
               error is 1.382
Iteration 980:
               error is 1.3819
Iteration 990:
               error is 1.3818
Iteration 1000:
                error is 1.3816
```

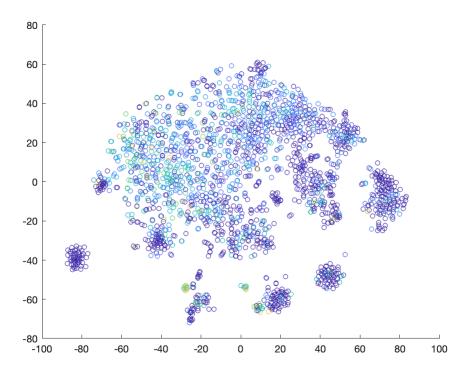
```
score = ydata;
figure;
scatter(score(:,1),score(:,2),22);
```



score_tsne = score;

Show Some Marker Genes

```
genes_plot = 'Ly6a' ;%% pre-B'Igll1'; %
Index = find(contains(genes,genes_plot)
genes_expression = data(:,Index(1));
figure;
scatter(score(:,1),score(:,2),22,genes_
```



%}

MuTrans Dynamical Analysis of the Single-Cell Data

parameter and option settings

```
rng(1)
par.initial = 'other';
par.perplex = 800;
par.K_cluster = 10;
par.trials = 10;
par.score = score_tsne;
```

```
par.init_score = score_tsne;
% Dynamical Analysis and Output
tic;
Output = DynamicalAnalysis (data, par);
Computed P-values 500 of 2018 datapoint
Computed P-values 1000 of 2018 datapoir
Computed P-values 1500 of 2018 datapoir
Computed P-values 2000 of 2018 datapoir
Mean value of sigma: 0.25879
Minimum value of sigma: 0.17126
Maximum value of sigma: 0.43398
J new = 3.9275
J new = 3.9109
J \text{ new} = 3.8908
J \text{ new} = 3.8800
J new = 3.8777
J new = 3.8764
J new = 3.8756
J new = 3.8750
J new = 3.8746
```

- J new = 3.8739
- J new = 3.8736
- $J_{new} = 3.8735$
- J new = 3.8734
- J new = 3.8733
- J new = 3.8734
- $J_{new} = 3.9284$
- J new = 3.9131
- J new = 3.8965
- J new = 3.8814
- J new = 3.8778
- J new = 3.8760
- J new = 3.8754
- J new = 3.8747
- J new = 3.8739
- J new = 3.8736
- J new = 3.8735
- J new = 3.8734
- J new = 3.8733
- J new = 3.8734
- J new = 3.9284

- J new = 3.9133
- J new = 3.8971
- J new = 3.8818
- J new = 3.8784
- J new = 3.8762
- J new = 3.8755
- J new = 3.8748
- J new = 3.8740
- J new = 3.8737
- J new = 3.8736
- J new = 3.8735
- J new = 3.8733
- J new = 3.8732
- J new = 3.8736
- J new = 3.9285
- J new = 3.9128
- $J_{new} = 3.8955$
- J new = 3.8800
- J new = 3.8775
- $J_{new} = 3.8762$
- J new = 3.8753

- J new = 3.8748
- J new = 3.8743
- $J_{new} = 3.8737$
- J new = 3.8736
- J new = 3.8735
- J new = 3.8734
- J new = 3.8733
- J new = 3.8732
- J new = 3.8731
- J new = 3.8728
- J new = 3.8720
- J new = 3.8713
- J new = 3.8707
- J new = 3.8704
- $J_{new} = 3.8703$
- J new = 3.8701
- J new = 3.8701
- J new = 3.8701
- J new = 3.9284
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- J new = 3.8965

- J new = 3.8814
- J new = 3.8778
- $J_{new} = 3.8760$
- J new = 3.8754
- J new = 3.8747
- J new = 3.8739
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- J new = 3.8735
- J new = 3.8734
- J new = 3.8733
- J new = 3.8734
- J new = 3.9491
- J new = 3.9386
- J new = 3.9355
- $J_{new} = 3.9331$
- J new = 3.9304
- $J_{new} = 3.9278$
- J new = 3.9249
- J new = 3.9231
- $J_{new} = 3.9216$
- J new = 3.9204

- $J_{new} = 3.9197$
- J new = 3.9184
- $J_{new} = 3.9174$
- J new = 3.9166
- J new = 3.9161
- J new = 3.9152
- J new = 3.9139
- J new = 3.9127
- J new = 3.9116
- J new = 3.9111
- J new = 3.9101
- J new = 3.9094
- J new = 3.9089
- J new = 3.9088
- J new = 3.9086
- J new = 3.9087
- $J_{new} = 3.9302$
- J new = 3.9140
- J new = 3.8959
- $J_{new} = 3.8809$
- J new = 3.8781

- J new = 3.8764
- J new = 3.8754
- $J_{new} = 3.8748$
- J new = 3.8744
- J new = 3.8737
- J new = 3.8736
- $J_{new} = 3.8735$
- J new = 3.8734
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- J new = 3.8732
- J new = 3.8731
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- J new = 3.8707
- J new = 3.8704
- $J_{new} = 3.8703$
- J new = 3.8701
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- J new = 3.9285

- J new = 3.9128
- J new = 3.8955
- J new = 3.8800
- J new = 3.8775
- J new = 3.8762
- J new = 3.8753
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- $J_{new} = 3.8720$
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- J new = 3.8707
- J new = 3.8704
- J new = 3.8703

- J new = 3.8701
- J new = 3.8701
- $J_{new} = 3.8701$
- J new = 3.9284
- J new = 3.9133
- J new = 3.8971
- J new = 3.8818
- J new = 3.8784
- J new = 3.8762
- J new = 3.8755
- J new = 3.8748
- J new = 3.8740
- J new = 3.8737
- J new = 3.8736
- J new = 3.8735
- J new = 3.8733
- $J_{new} = 3.8732$
- J new = 3.8736
- J new = 3.9284
- $J_{new} = 3.9133$
- J new = 3.8971

J new = 3.8818J new = 3.8784J new = 3.8762 $J_{new} = 3.8755$ J new = 3.8748J new = 3.8740J new = 3.8737J new = 3.8736J new = 3.8735J new = 3.8733J new = 3.8732J new = 3.8736E best = 0.5804

Iteration	Func-count	f(x)
0	1	3.90558
1	6	3.87904
2	7	3.84528
3	8	3.83661
4	9	3.81351
5	10	3.80266

6	11	3.79805
7	12	3.79168
8	13	3.7867
9	14	3.78246
10	15	3.77999
11	16	3.77696
12	17	3.77317
13	18	3.77204
14	19	3.7683
15	21	3.76099
16	23	3.75698
17	25	3.75365
18	27	3.75209
19	29	3.75055
Iteration	Func-count	f(x)
20	31	3.74851
21	33	3.74725
22	35	3.7462
23	37	3.74485
24	39	3.74371

25	41	3.74253
26	43	3.74162
27	45	3.74047
28	47	3.74004
29	49	3.7385
30	51	3.73766
31	53	3.73651
32	55	3.73568
33	57	3.73502
34	59	3.73437
35	61	3.73374
36	63	3.73329
37	65	3.73263
38	67	3.73182
39	69	3.73122
Iteration	Func-count	f(x)
40	71	3.7309
41	73	3.73054
42	75	3.73026
43	77	3.72983

44	79	3.72911
45	81	3.72881
46	84	3.7284
47	86	3.72801
48	88	3.72748
49	90	3.72713
50	92	3.72681
51	94	3.72656
52	96	3.72618
53	98	3.72594
54	100	3.72558
55	102	3.72535
56	104	3.72503
57	106	3.72481
58	108	3.72468
59	110	3.72449
Iteration	Func-count	f(x)
60	112	3.72437
61	114	3.72425
62	116	3.72412

63	117	3.7238
64	119	3.72367
65	121	3.72347
66	123	3.72332
67	124	3.72319
68	126	3.72296
69	128	3.72269
70	130	3.7225
71	132	3.72242
72	134	3.72232
73	136	3.72227
74	138	3.72221
75	140	3.72214
76	142	3.72209
77	144	3.72203
78	146	3.72195
79	148	3.7219
Iteration	Func-count	f(x)
80	149	3.72184
81	151	3.72184
OT	エ ノエ	J. / LI/ /

82	153	3.72173
83	154	3.7216
84	156	3.72152
85	158	3.72145
86	159	3.72142
87	160	3.72119
88	162	3.72111
89	164	3.721
90	166	3.72095
91	168	3.72088
92	170	3.72085
93	172	3.7208
94	174	3.72076
95	175	3.72063
96	177	3.7206
97	178	3.72058
98	179	3.72055
99	181	3.72045
Iteration	Func-count	f(x)
100	183	3.72038

101	185	3.72035
102	187	3.72032
103	189	3.72029
104	191	3.72022
105	193	3.72018
106	195	3.72007
107	197	3.71998
108	199	3.7199
109	200	3.71987
110	202	3.7198
111	204	3.71974
112	206	3.71972
11 3	208	3.71969
114	210	3.71967
115	211	3.71964
116	213	3.71958
117	214	3.71952
118	216	3.71947
119	217	3.71941

Iteration Func-count f(x)

120	219	3.71933
121	221	3.71929
122	223	3.71923
123	225	3.7192
124	226	3.71919
125	228	3.71917
126	229	3.71916
127	230	3.71915
128	232	3.71913
129	234	3.71912
130	236	3.71911
131	238	3.7191
132	239	3.71908
133	241	3.71902
134	243	3.71901
135	246	3.71888
136	250	3.71887
137	251	3.71878
138	253	3.71871
139	255	3.71865

Iteration	Func-count	f(x)
140	257	3.71862
141	259	3.7186
142	261	3.71858
143	262	3.71857
144	263	3.71856
145	264	3.71855
146	265	3.71854
147	266	3.71851
148	268	3.71846
149	270	3.71844
150	272	3.71842
151	274	3.7184
152	275	3.7184
1 53	276	3.71837
154	278	3.71833
155	280	3.71832
156	281	3.71825
157	283	3.71823
158	285	3.7182
159	286	3.71819

Iteration	Func-count	f(x)
160	287	3.71814
161	289	3.7181
162	291	3.71808
163	293	3.71807
164	294	3.71807
165	295	3.71806
166	297	3.71803
167	299	3.71803
168	300	3.71801
169	301	3.71801
170	302	3.718
171	303	3.71799
172	305	3.71792
173	308	3.71792
174	309	3.7179
175	311	3.71789
176	313	3.71787
177	315	3.71786
178	316	3.71785

Iteration	Func-count	f(x)
180	319	3.71782
181	321	3.7178
182	323	3.71777
183	325	3.71776
184	326	3.71773
185	328	3.71769
186	331	3.71767
187	333	3.71764
188	335	3.71762
189	337	3.71757
190	339	3.71756
191	341	3.71756
192	343	3.71755
193	344	3.71755
194	345	3.71755
195	346	3.71754
196	348	3.71753
197	350	3.7175

198	353	3.71749
199	355	3.71747
Iteration	Func-count	f(x)
200	356	3.71744
201	357	3.71743
202	358	3.71742
203	359	3.71742
204	360	3.71741
205	361	3.71741
206	362	3.7174
207	363	3.7174
208	364	3.71739
209	365	3.71739
210	366	3.71738
211	368	3.71737
212	370	3.71737
213	371	3.71737
214	372	3.71737
215	373	3.71736
216	374	3.71735

377	3.71731
379	3.7173
380	3.71728
Func-count	f(x)
381	3.71726
382	3.71726
383	3.71724
384	3.71723
385	3.71722
386	3.71722
387	3.71722
388	3.71721
390	3.71721
392	3.7172
393	3.7172
394	3.7172
395	3.7172
397	3.71719
399	3.71719
400	3.71719
	379 380 Func-count 381 382 383 384 385 386 387 388 390 392 393 394 395 397 399

236	401	3.71719
237	402	3.71719
238	403	3.71718
239	404	3.71718
Iteration	Func-count	f(x)
240	406	3.71717
241	408	3.71716
242	409	3.71716
243	410	3.71715
244	412	3.71714
245	414	3.71713
246	416	3.71713
247	417	3.71713
248	418	3.71713
249	419	3.71713
250	420	3.71711
251	424	3.71706
252	427	3.71705
253	428	3.71699
254	429	3.7169

255	431	3.71687
256	433	3.71685
257	435	3.71684
258	436	3.71683
259	437	3.71682
Iteration	Func-count	f(x)
260	438	3.71681
261	439	3.7168
262	440	3.7168
263	441	3.71679
264	443	3.71678
265	445	3.71678
266	446	3.71677
267	448	3.71677
268	449	3.71677
269	450	3.71676
270	451	3.71676
271	453	3.71675
272	454	3.71675
273	455	3.71674

457	3.71673
459	3.71673
460	3.71673
462	3.71672
463	3.71672
464	3.71672
Func-count	f(x)
469	3.71659
473	3.71659
474	3.71656
475	3.71652
477	3.7165
478	3.71649
479	3.71648
481	3.71646
482	3.71645
484	3.71643
486	3.71643
487	3.71642
489	3.71642
	459 460 462 463 464 Func-count 469 473 474 475 477 478 479 481 482 484 486 486 487

293	490	3.71642
294	491	3.71641
295	492	3.71641
296	493	3.71641
297	494	3.71641
298	495	3.71641
299	496	3.7164
Iteration	Func-count	f(x)
300	497	3.7164
301	498	3.7164
302	499	3.7164
303	501	3.7164
304	502	3.7164
305	503	3.7164
306	504	3.7164
307	505	3.7164
308	507	3.71639
309	510	3.71639
310	511	3.71639
311	512	3.71639

312	51 3	3.71638
313	514	3.71638
314	516	3.71638
315	517	3.71637
316	518	3.71637
317	519	3.71636
318	521	3.71636
319	523	3.71636
Iteration	Func-count	f(x)
320	524	3.71636
321	525	3.71636
322	526	3.71636
323	527	3.71636
324	528	3.71636
325	529	3.71636
326	534	3.71635
327	536	3.71635
328	537	3.71635
329	538	3.71634
330	540	3.71633

331	541	3.71633
332	542	3.71633
333	543	3.71633
334	544	3.71633
335	546	3.71633
336	547	3.71633
337	548	3.71633
338	549	3.71633
339	550	3.71633
Iteration	Func-count	f(x)
340	551	3.71633
341	552	3.71632
342	553	3.71632
343	554	3.71632
344	555	3.71632
345	556	3.71632
346	557	3.71632
347	558	3.71632
348	559	3.71632
349	561	3.71632

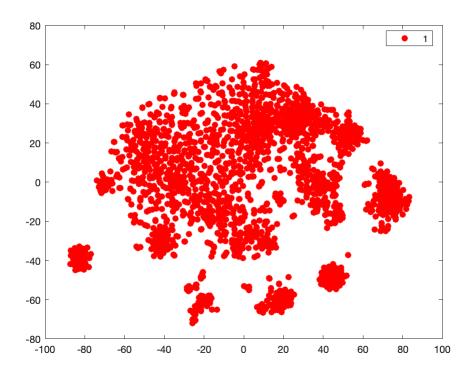
350	564	3.71632
351	565	3.71631
352	566	3.71631
353	567	3.71631
354	568	3.7163
355	569	3.7163
356	570	3.7163
357	571	3.7163
358	572	3.71629
359	573	3.71629
Iteration	Func-count	f(x)
360	574	3.71627
361	577	3.71626
362	580	3.71625
363	582	3.71623
364	583	3.7162
365	585	3.71618
366	587	3.71616
367	589	3.71614
368		

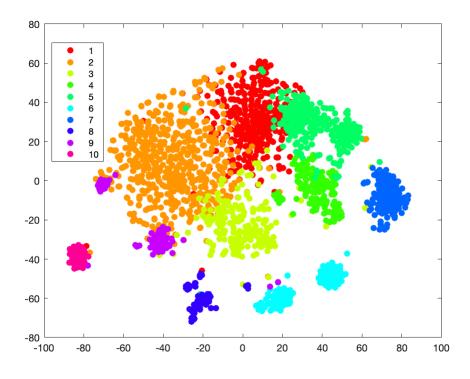
369	591	3.71613
370	592	3.71613
371	593	3.71612
372	594	3.71612
373	595	3.71612
374	596	3.71612
375	597	3.71612
376	598	3.71611
377	600	3.71611
378	601	3.71611
379	602	3.71611
Iteration	Func-count	f(x)
380	604	3.71611
381	605	3.71611
382	606	3.71611
383	607	3.71611
384	608	3.71611
385	609	3.71611
386	610	3.7161
387	611	3.7161

388	614	3.7161
389	617	3.7161
390	618	3.71609
391	619	3.71609
392	620	3.71608
393	621	3.71608
394	622	3.71608
395	624	3.71607
396	626	3.71607
397	628	3.71606
398	630	3.71606
399	631	3.71606
Iteration	Func-count	f(x)
400	632	3.71606
401	633	3.71606
402	634	3.71606

Optimization completed: The first-order than options.OptimalityTolerance = 1.00

Elapsed time is 10879.987367 seconds.





toc;

Elapsed time is 10889.274322 seconds.

```
class_order = Output.class_order;
data_perm = Output.data_perm;
k = par.K_cluster;
perm_class = Output.perm_class;
```

Cell-fate Landscape

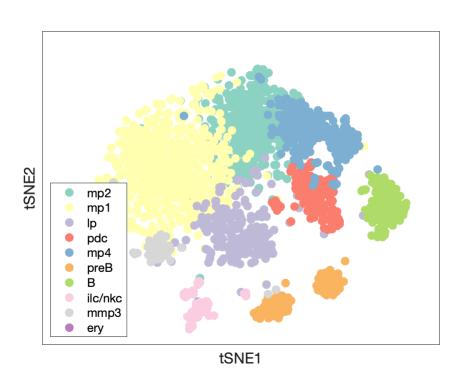
embeddings and centers

```
name_cluster = {'mp2','mp1','lp','pdc',
colors_cluster = brewermap(k,'set3');
labs_perm = Output.labs_perm;

Output.embedding_2d = score_tsne(perm_c)
score_2d = score_tsne(perm_class,:);

figure;
gscatter(score_2d(:,1),score_2d(:,2),c)
legend(name_cluster,'Fontsize',12,'Locate)
set(gca,'xtick',[],'ytick',[]);
```

```
xlabel('tSNE1','Fontsize',15)
ylabel('tSNE2','Fontsize',15)
```



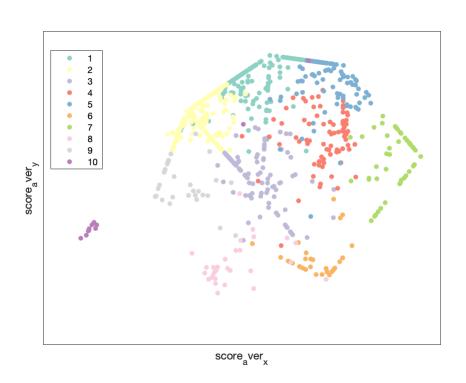
```
Output.embedding_2d = score_2d;

% construct landscape
par.thresh_calc_center = 0.9;
par.thresh_calc_cov = 0.2;
par.N_mesh = 1000;
par.mksize = 15;
par.scaleaxis = 1.1;
```

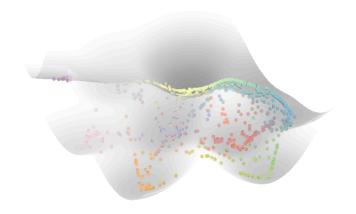
```
par.scalevalue = 1.0;
par.fontsize = 30;
par.alpha = 0.4;

par.plot_label = class_order;
par.legend_text = name_cluster;
par.colors = colors_cluster;
par.color_mixing = true;

land = ConstructLandscape (Output, par)
```



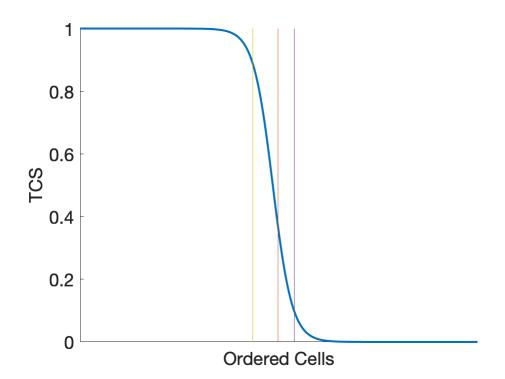
view([49 77])



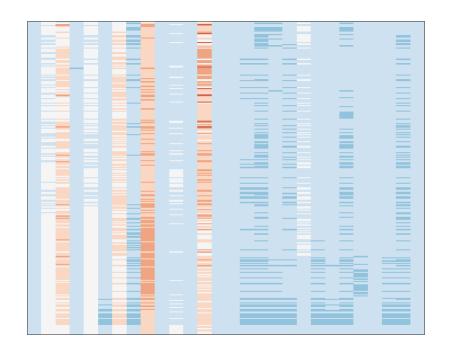
Transcendental transition cell and gene analysis

```
par.genes = genes;
par.true_labs = labs_perm;
par.thresh_otherkeep = 0.3;
par.thresh_de_pvalues = 5e-3;
par.thresh_ms_pvalues = 1e-2;
par.thresh_tcs = 0.4;
par.thresh_td_genes = 0.4;
par.colors = colors_cluster;
par.L_select_top_genes = 5;
```

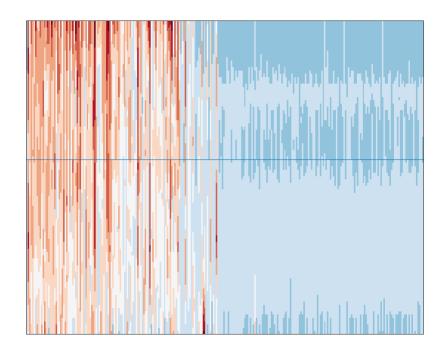
```
par.flip = false;
par.display_genes_label = false;
par.output_heatmap = true;
% check the state id before preceeding
% clustering id. Results unchanged.
out = GeneAnalysis(7, 6, Output,par);
```



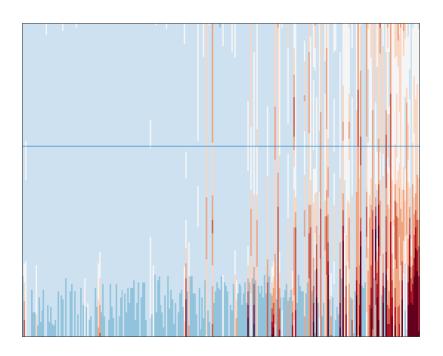
Below is the heatmap of transition gene



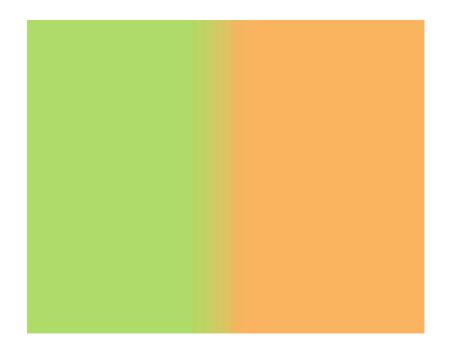
Below is the heatmap of down-regulated

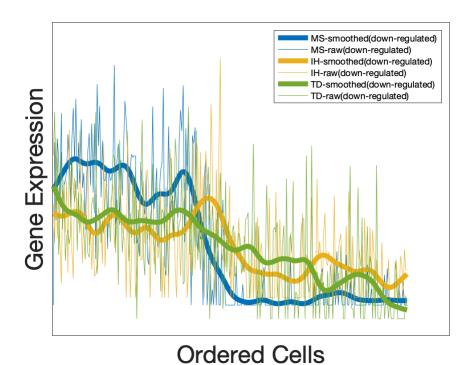


Below is the heatmap of up-regulated MS



Below is the gradual cell indentity cha





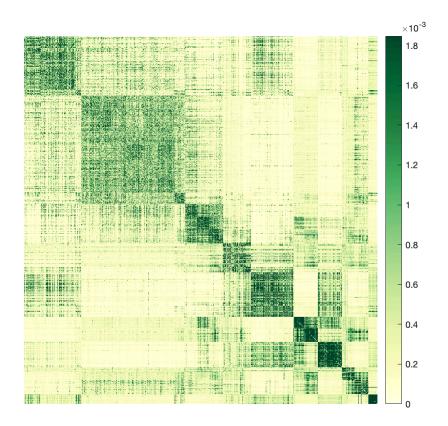
MS(up-regulated)
MS-raw(up-regulated)
IH-smoothed(up-regulated)
IH-raw(up-regulated)

Ordered Cells

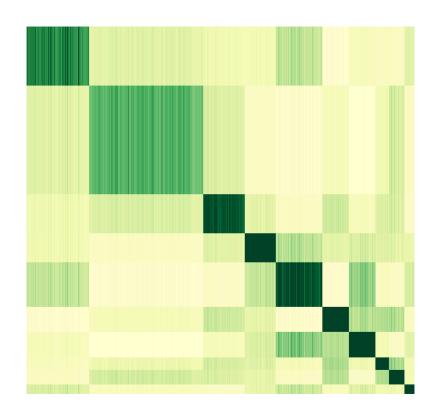
output other data in Supplementary

rho_class = Output.rho_class;

```
perm_class = Output.perm_class;
P_hat = Output.P_hat;
P_appr_perm = Output.P_appr_perm;
P_perm = Output.P_perm;
P_rho = Output.P_rho;
labs_perm = Output.labs_perm;
mu_hat = Output.mu_hat;
k = Output.k;
H = Output.H;
max_P = 0.2* max(max(P_rho));
c_{lim} = [0 max_P];
cmp = 'ylgn';
figure('rend','painters','pos',[10 10 5
colormap(brewermap([],cmp))
imagesc(P_perm);
axis off
set(gca,'xtick',[],'ytick',[]);
caxis(c_lim)
colorbar;
```

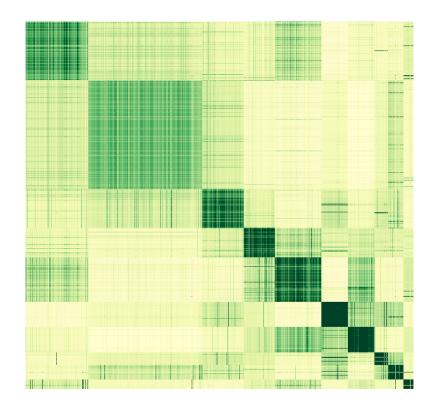


```
figure('rend','painters','pos',[10 10 5
colormap(brewermap([],cmp))
imagesc(P_appr_perm);
axis off
set(gca,'xtick',[],'ytick',[]);
caxis(c_lim)
```

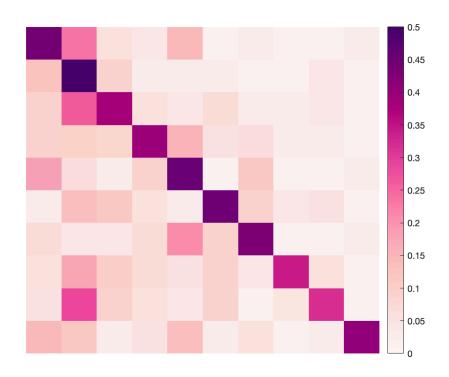


```
%colorbar;

figure('rend','painters','pos',[10 10 5]
colormap(brewermap([],cmp))
imagesc(P_rho);
axis off
set(gca,'xtick',[],'ytick',[]);
caxis(c_lim)
%colorbar;
box off
```

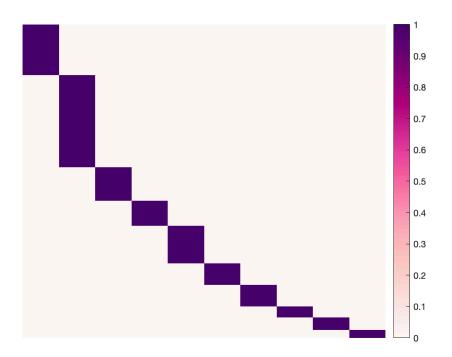


```
cmp = 'rdpu';
figure('rend','painters','pos',[10 10 5]
colormap(brewermap([],cmp))
imagesc(P_hat);
caxis([0 0.5])
axis off
set(gca,'xtick',[],'ytick',[]);
box off
colorbar;
```



```
figure;
for id_cluster = 1:k
member(:,id_cluster) = (class_order == end
colormap(brewermap([],cmp))
imagesc(member);
caxis([0 1])
colorbar;
axis off
set(gca,'xtick',[],'ytick',[]);
```

box off



```
figure;
colormap(brewermap([],cmp))
imagesc(rho_class);
caxis([0 1])
colorbar;
axis off
set(gca,'xtick',[],'ytick',[]);
box off
```

