Olivier's Ricci curvature and applications

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Goal

- We introduce three generalized notions of the Ricci curvature.
- We argue that these curvatures and **robustness** of networks are positively correlated. So one can measure robustness of a network by computing its curvatures.
- We test our hypothesis by computing curvatures of **cancer networks** and get compatible results.

Ricci curvature and entropy

- The Ricci curvature tensor on a Riemannian manifold (M, g) provides a way of measuring the degree to which the geometry determined by a given Riemannian metric might differ from that of ordinary Euclidean space.

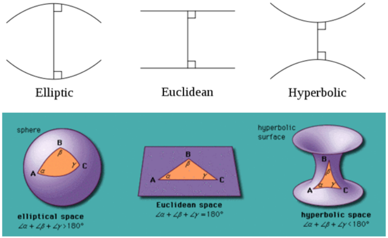

Figure: Pictures of positive, zero, negative curvatures

Ricci curvature and entropy

- For the measure μ on a Riemannian manifold (M, g), the Boltzmann entropy is defined as follows:

$$\mathrm{Ent}(\mu) := -\int_M \rho \log \rho \, d\mathrm{vol}_M,$$

  where vol is the standard Riemannian measure and $\rho = d\mu / d\mathrm{vol}_M$.
- It measures how much "uniform" the measure is. To get intuition, compute for finite spaces.

Ricci curvature and entropy

- A metric space (X, d_X) is a compact length space iff $P_2(X) := (P(X), W_2)$ is a compact length space [LV09, Stu06].
- Lott, Sturm and Villani discovered following connection between Ricci curvature and entropy [LV09, Stu06].
- $\mathrm{Ric}_M(v) \geq k\|v\|^2$ for any $v \in \mathrm{TM}$ if and only if

$$\mathrm{Ent}(\mu_t) \geq (1-t)\,\mathrm{Ent}(\mu_0) + t\,\mathrm{Ent}(\mu_1) + k\,\frac{t(1-t)}{2}\,W_2(\mu_0, \mu_1)^2,$$

  where $(\mu_t)_{0 \leq t \leq 1}$ is the 2-Wasserstein geodesics between μ_0 and μ_1.
- This inequality indicates the positive correlation between entropy and curvature.

$$\Delta\mathrm{Ent} \times \Delta\mathrm{Ric} \geq 0.$$

Entropy and robustness

- The **robustness** of a network (here, a positively weighted finite graph without direction) is the ability to remain functional in the face of random perturbations [DM05, PMT17].
- In many cases, robustness is measured empirically.
- Example) Experimental perturbation studies in yeast cells [HMJ$^+$00].
- Example) Computational analysis of network observables under node deletion [AJB00].
- In [DGO04, DM05], the authors argued that the entropy and the robustness of networks are positively correlated by invoking theory of large deviations and suggesting some computational results.

$$\Delta \mathrm{Ent} \times \Delta R \geq 0.$$

Robustness and Ricci curvature

- Hence, in [TSZ+15, PMT17], the authors argue that the curvature and the robustness of networks are positively correlated.

$$\Delta R \times \Delta \mathrm{Ric} \geq 0.$$

- BUT, what is notion of curvature for networks?

Three generalized notions of curvature

There are three candidates for generalized version of the Ricci curvature. All of them are applicable to networks.

- **Ollivier-Ricci curvature** are defined for metric spaces with Markov chain structure, or metric measure spaces. For networks, we will get curvature value $k_{OR}(x, y) \in \mathbb{R}$ for each edge xy.
- **Bakry-Émery Ricci curvature** are defined for graphs. We will get curvature value $k_{BER}(x) \in \mathbb{R}$ for each vertice x.
- **Forman-Ricci curvature** are defined for CW-complexes. For networks, we will get curvature value $k_{FR}(e) \in \mathbb{R}$ for each edge e.

Curvatures on cell complexes

- It is already known that the normal gene interaction networks are less robust than their cancerous analogues [DM05, WBST12].
- To check the validity of the claim, the curvature and the robustness are positively correlated, the authors computed three curvatures for cell complexes.
- We will consider seven kinds of cancer types. Breast, Head/Neck, Kidney, Liver, Lung, Prostate and Thyroid cancers. For each cancer type, the authors used normal tissue and cancerous tissue data from 3000 samples.
- Then, we will have networks, depending on types and normal/cancerous. Vertices of the networks consist of 500 cancer related genes. Edges are weighted by correlation values of gene-to-gene expressions.
- Expression value of a gene measures activity of the gene.

Curvatures on cell complexes

Cancer Type	Δ Average OR Curvature	Δ Average BER Curvature	Δ Average FR Curvature
Breast Carcinoma	0.012	0.182	13.022
Head/Neck Carcinoma	0.004	0.116	9.100
Kidney Carcinoma	0.010	0.217	7.711
Liver Carcinoma	0.008	0.227	3.136
Lung Adenocarcinoma	0.013	0.320	7.898
Prostate Adenocarcinoma	0.009	0.179	7.368
Thyroid Carcinoma	0.006	0.133	2.969

Table 1: All seven cancer networks have a higher average Ricci Curvature than the complementary normal networks.

Curvatures on cell complexes

Gene Ranking	Gene A	Gene B	Δ OR Curvature (Cancer-Normal)
1	RNF43	RSPO3	0.3504
2	RNF43	RSPO2	0.3444
3	ERG	ETV1	0.3012
4	GPC3	PTCH1	0.3001
5	SDC4	GPC3	0.2901
6	POT1	SBDS	0.2796
7	FGFR2	KDR	0.2538
8	ERG	FOXA1	0.2460
9	SDC4	EXT1	0.2410
10	MYC	SDHD	0.2408
11	TAL1	RUNX1	0.2167
12	SDC4	EXT2	0.2165
13	NUP214	ELN	0.2132
14	TAL1	TCF3	0.2123
15	PDGFB	COL2A1	0.2036
16	IDH1	IDH2	0.2012
17	SDHB	HMGA1	0.2007
18	TAL1	TRIM27	0.1929
19	EPS15	MLLT4	0.1909
20	FUBP1	PICALM	0.1899

Table 3: The top 20 pairs of genes with respect to Olivier-Ricci curvature.

Curvatures on cell complexes

Gene Ranking	Gene	Δ BER Curvature (Cancer-Normal)	Gene Ranking	Gene	Δ BER Curvature (Cancer-Normal)
1	PICALM	7.4910	21	PDGFRB	2.8796
2	CLTCL1	4.9102	22	JAK2	2.7667
3	EPS15	4.3210	23	RPN1	2.6685
4	KIF5B	4.1284	24	DCTN	2.4304
5	CLTC	4.0657	25	TBL1XR1	2.3959
6	PTPN11	4.0465	26	ABL1	2.3943
7	YWHAE	3.8416	27	PIM1	2.3879
8	EGFR	3.8357	28	PBRM1	2.3454
9	JAK1	3.7590	29	TFRC	2.3162
10	MSN	3.6079	30	NDRG1	2.2251
11	CDC73	3.5274	31	LCK	2.1788
12	PIK3CA	3.4499	32	KIT	2.1602
13	XPO1	3.4274	33	FGFR1	2.1367
14	ALDH2	3.3854	34	STAT5B	2.0506
15	SDHB	3.2626	35	ERG	2.0441
16	GNAS	3.1372	36	KDR	2.0387
17	AKT1	3.1279	37	PPARG	2.0034
18	MAP2K1	3.0754	38	SYK	1.9919
19	CBL	3.0287	39	HIP1	1.9897
20	PML	3.0043	40	CUX1	1.9819

Table 4: The top 40 genes with respect to local BER curvature.

Curvatures on cell complexes

Gene Rank-ing	Gene A	Gene B	Δ FR Curvature (Cancer-Normal)
1	CARS	ALDH2	256.904
2	NDRG1	ARNT	252.955
3	ALDH2	SDHB	239.857
4	CLTCL1	ALDH2	227.896
5	ALDH2	KIF5B	219.595
6	EBF1	CEBPA	218.589
7	CLTCL1	SDHB	212.586
8	CEBPA	PPARG	209.869
9	PTPN11	PTPRB	208.132
10	ALDH2	IDH1	198.918
11	EPS15	SDHB	195.605
12	CDH1	FUS	193.463
13	SDHB	PTPN11	191.581
14	JAK1	AKT2	191.086
15	ELF4	ERG	188.118
16	AKT2	PIK3CA	187.711
17	NONO	RUNX1	186.994
18	HMGA1	RARA	186.925
19	CLTCL1	HIP1	186.329
20	ERBB2	ATP1A1	185.469

Table 5: The top 20 pairs of genes with respect to FR curvature.

Curvatures on cell complexes

- In Table 1, all three generalized curvatures have higher values in the seven cancer networks to the normal ones. Hence, the result is consistent with the authors' hypothesis.
- Table 3,4 and 5 shows top ranked genes in breast cancer. It shows, what kinds of genes are most contributing for "robustness" of the cell complexes.
- There are three genes, SDHB, EPS15, and ERG found among the top ranked genes with respect to all three FR, BER and OR curvatures.
- There are some similarities between the top ranked genes with respect to FR curvature and BER curvature, namely, ALDH2, NDRG, CLTCL1, KIF5B, PPARG, PTPN11, JAK1, PIK3CA, SDHB, EPS15, ERG, and HIP.
- There are some similarities between the top ranked genes with respect to FR curvature and OR curvature, namely IDH1, RUNX1, HMGA1, SDHB, EPS15, and ERG.

Curvatures on cell complexes

- A number of genes have known clinical implications with regards to breast cancer. For example, EPS15 plays a crucial role in the degradation of growth factor receptions. It is reported that over-expression of EPS15 is significantly associated with a favorable clinical outcome.
- SDHB gene is another known tumor suppressor.
- BUT, there are some important cancer-related gene mutations known to play a significant role in breast cancer such as BRCA1 and BRCA2 which are not ranked among the top ranked genes.

Ollivier-Ricci curvature, details

Theorem

[vRS05] For any compact connected Riemannian manifold M and $k \in \mathbb{R}$, the following properties are equivalent:

1. $\mathrm{Ric}_M(v) \geq k\|v\|^2$ *for any* $v \in \mathrm{TM}$
2. *The normalized Riemannian uniform distribution on balls*

   $$m_{x,r}(A) := \mathrm{vol}_M(A \cap B(x,r))/\mathrm{vol}_M(B(x,r))$$

   satisfies the asymptotic estimate

   $$W_1(m_{r,x}, m_{y,r}) \leq \left(1 - \frac{k}{2(n+2)} r^2 + o(r^2)\right) \cdot d_M(x,y)$$

   where the error term is uniform with respect to $x, y \in M$.

In particular, if $k > 0$, small balls are closer in transportation distance than their centers are.

Ollivier-Ricci curvature, details

Definition (Ollivier-Ricci curvature)

[Oll09] Let (X, d_X) be a metric space with a Markov chain m_X. Let $x, y \in X$ be two distinct points. The **coarse Ricci curvature** of (X, d_X, m_X) along (xy) is:

$$k_{OR}(x, y) := 1 - \frac{W_1\big(m_X(x, \cdot), m_X(y, \cdot)\big)}{d_X(x, y)}.$$

Ollivier-Ricci curvature, details

- In this paper, we only consider positively weighted finite graphs $G = (V, E)$.
- For each $x, y \in V$, define $m_X(x, y) := \frac{w_{xy}}{\sum_{z \in V} w_{xz}}$ where w_{xy} is the weight on edge (xy).
- The metric on G is usual graph metric, the number of edges in the shortest path.

The End

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