KOÇ ÜNİVERSİTESİ

Yaşam bilimleri için yapay öğrenme

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2 Temmuz 2018

- Çok az eğitim örneği ile karmaşık problemlerin çözülmesi

Giriş
Yaşam bilimleri uygulamalarındaki zorluklar

- Çok az eğitim örneği ile karmaşık problemlerin çözülmesi
- Çeşitli veri kaynaklarının beraberce modellenmesi

Giriş

Yaşam bilimleri uygulamalarındaki zorluklar

- Çok az eğitim örneği ile karmaşık problemlerin çözülmesi
- Çeşitli veri kaynaklarının beraberce modellenmesi
- Test edilebilir hipotezler üretilmesi

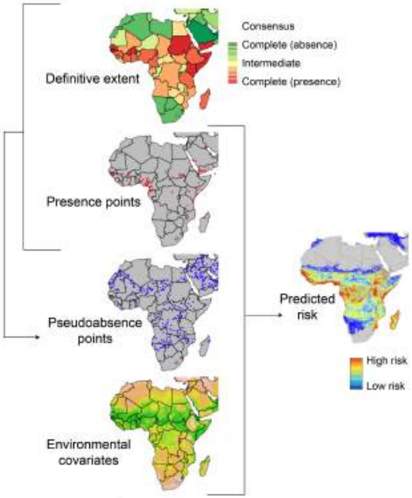
Giriş

Yaşam bilimleri uygulamalarındaki zorluklar

- Çok az eğitim örneği ile karmaşık problemlerin çözülmesi
- Çeşitli veri kaynaklarının beraberce modellenmesi
- Test edilebilir hipotezler üretilmesi
- **Çekirdek tabanlı yapay öğrenme yöntemleri**

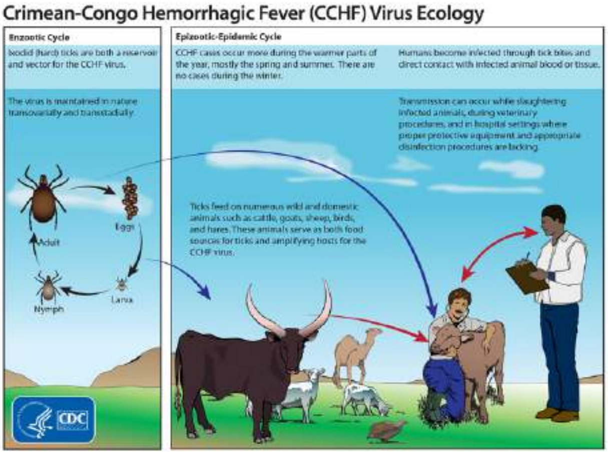
Enfeksiyon hastalıklarının modellenmesi

Enfeksiyon hastalıklarının modellenmesi



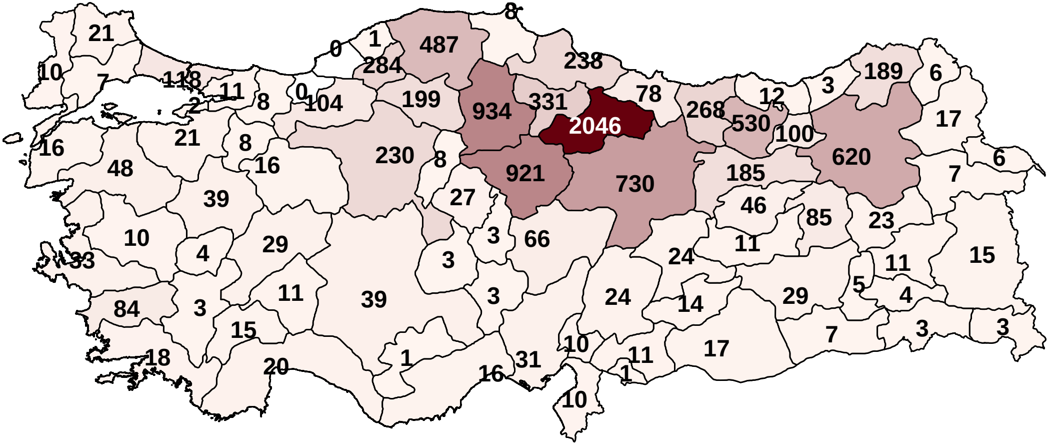
Enfeksiyon hastalıklarının modellenmesi

Kırım–Kongo Kanamalı Ateşi (KKKA) hastalığı



Enfeksiyon hastalıklarının modellenmesi

Türkiye’de KKKA



Enfeksiyon hastalıklarının modellenmesi

Türkiye'de KKKA

Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total	Season
0	0	2	9	24	62	101	44	6	1	0	0	249	2004
0	0	0	8	27	77	95	51	3	4	0	0	265	2005
0	0	1	19	65	160	114	72	8	0	0	0	439	2006
0	0	2	25	119	216	224	90	40	1	0	0	717	2007
0	0	1	37	241	432	411	151	40	2	0	0	1315	2008
0	0	0	37	205	496	366	177	33	3	1	0	1318	2009
0	0	0	61	240	272	222	59	11	2	0	0	867	2010
0	0	1	29	149	341	349	180	19	5	2	0	1075	2011
0	0	1	31	223	233	201	90	13	3	1	0	796	2012
0	0	1	74	225	260	254	81	11	2	2	0	910	2013
0	4	6	95	218	238	280	108	13	5	0	0	967	2014
0	0	2	16	97	231	218	119	20	12	2	1	718	2015
0	4	17	441	1833	3018	2835	1222	217	40	8	1	9636	Total

$$\begin{aligned} \boldsymbol{y} &= \boldsymbol{f} + \boldsymbol{\xi} \\ \boldsymbol{f} | \mathbf{X} &\sim \text{Normal}(\boldsymbol{f}; \mathbf{0}, \mathbf{K}) \\ \boldsymbol{\xi} | \sigma_y^2 &\sim \text{Normal}(\boldsymbol{\xi}; \mathbf{0}, \sigma_y^2 \mathbf{I}) \end{aligned}$$

$$
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\boldsymbol{f} | \mathbf{X} &\sim \text{Normal}(\boldsymbol{f}; \mathbf{0}, \mathbf{K}) \\
\boldsymbol{\xi} | \sigma_y^2 &\sim \text{Normal}(\boldsymbol{\xi}; \mathbf{0}, \sigma_y^2 \mathbf{I})
\end{aligned}
$$

$$
\mathbf{K} = \begin{bmatrix} k(\boldsymbol{x}_1, \boldsymbol{x}_1) & k(\boldsymbol{x}_2, \boldsymbol{x}_1) & \cdots & k(\boldsymbol{x}_N, \boldsymbol{x}_1) \\ k(\boldsymbol{x}_1, \boldsymbol{x}_2) & k(\boldsymbol{x}_2, \boldsymbol{x}_2) & \cdots & k(\boldsymbol{x}_N, \boldsymbol{x}_2) \\ \vdots & \vdots & \ddots & \vdots \\ k(\boldsymbol{x}_1, \boldsymbol{x}_N) & k(\boldsymbol{x}_2, \boldsymbol{x}_N) & \cdots & k(\boldsymbol{x}_N, \boldsymbol{x}_N) \end{bmatrix}
$$

$$
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\boldsymbol{y} &= \boldsymbol{f} + \boldsymbol{\xi} \\
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\end{aligned}
$$

$$
\mathbf{K} = \begin{bmatrix} k(\boldsymbol{x}_1, \boldsymbol{x}_1) & k(\boldsymbol{x}_2, \boldsymbol{x}_1) & \cdots & k(\boldsymbol{x}_N, \boldsymbol{x}_1) \\ k(\boldsymbol{x}_1, \boldsymbol{x}_2) & k(\boldsymbol{x}_2, \boldsymbol{x}_2) & \cdots & k(\boldsymbol{x}_N, \boldsymbol{x}_2) \\ \vdots & \vdots & \ddots & \vdots \\ k(\boldsymbol{x}_1, \boldsymbol{x}_N) & k(\boldsymbol{x}_2, \boldsymbol{x}_N) & \cdots & k(\boldsymbol{x}_N, \boldsymbol{x}_N) \end{bmatrix}
$$

$$
\begin{aligned}
\mathrm{E}[y_\star | \boldsymbol{x}_\star, \mathbf{X}, \boldsymbol{y}, \sigma_y^2] &= \boldsymbol{k}_\star^\top (\mathbf{K} + \sigma_y^2 \mathbf{I})^{-1} \boldsymbol{y} \\
\mathrm{Var}[y_\star | \boldsymbol{x}_\star, \mathbf{X}, \boldsymbol{y}, \sigma_y^2] &= k(x_\star, x_\star) - \boldsymbol{k}_\star^\top (\mathbf{K} + \sigma_y^2 \mathbf{I})^{-1} \boldsymbol{k}_\star
\end{aligned}
$$

$$k(\boldsymbol{x}_i, \boldsymbol{x}_j) = k((\boldsymbol{s}_l, \boldsymbol{t}_p), (\boldsymbol{s}_m, \boldsymbol{t}_q)) = k_s(\boldsymbol{s}_l, \boldsymbol{s}_m) k_t(\boldsymbol{t}_p, \boldsymbol{t}_q)$$

$$k(\boldsymbol{x}_i, \boldsymbol{x}_j) = k((\boldsymbol{s}_l, \boldsymbol{t}_p), (\boldsymbol{s}_m, \boldsymbol{t}_q)) = k_s(\boldsymbol{s}_l, \boldsymbol{s}_m) k_t(\boldsymbol{t}_p, \boldsymbol{t}_q)$$

$$\mathbf{K} = \mathbf{K}_s \otimes \mathbf{K}_t$$

Enfeksiyon hastalıklarının modellenmesi

Yapısal Gauss süreci regresyon modeli

$$k(\boldsymbol{x}_i, \boldsymbol{x}_j) = k((\boldsymbol{s}_l, \boldsymbol{t}_p), (\boldsymbol{s}_m, \boldsymbol{t}_q)) = k_s(\boldsymbol{s}_l, \boldsymbol{s}_m) k_t(\boldsymbol{t}_p, \boldsymbol{t}_q)$$

$$\mathbf{K} = \mathbf{K}_s \otimes \mathbf{K}_t$$

$$\begin{aligned} \mathrm{E}[y_\star | \boldsymbol{x}_\star, \mathbf{X}, \mathbf{Y}, \sigma_y^2] &= (\boldsymbol{k}_{s,\star} \otimes \boldsymbol{k}_{t,\star})^\top (\mathbf{K}_s \otimes \mathbf{K}_t + \sigma_y^2 \mathbf{I})^{-1} \operatorname{vec}(\mathbf{Y}) \\ \mathrm{Var}[y_\star | \boldsymbol{x}_\star, \mathbf{X}, \mathbf{Y}, \sigma_y^2] &= k_s(s_\star, s_\star) k_t(t_\star, t_\star) - (\boldsymbol{k}_{s,\star} \otimes \boldsymbol{k}_{t,\star})^\top (\mathbf{K}_s \otimes \mathbf{K}_t + \sigma_y^2 \mathbf{I})^{-1} (\boldsymbol{k}_{s,\star} \otimes \boldsymbol{k}_{t,\star}) \end{aligned}$$

$$\mathbf{K}_s = \mathbf{U}_s \mathbf{D}_s \mathbf{U}_s^\top$$

$$\mathbf{K}_t = \mathbf{U}_t \mathbf{D}_t \mathbf{U}_t^\top$$

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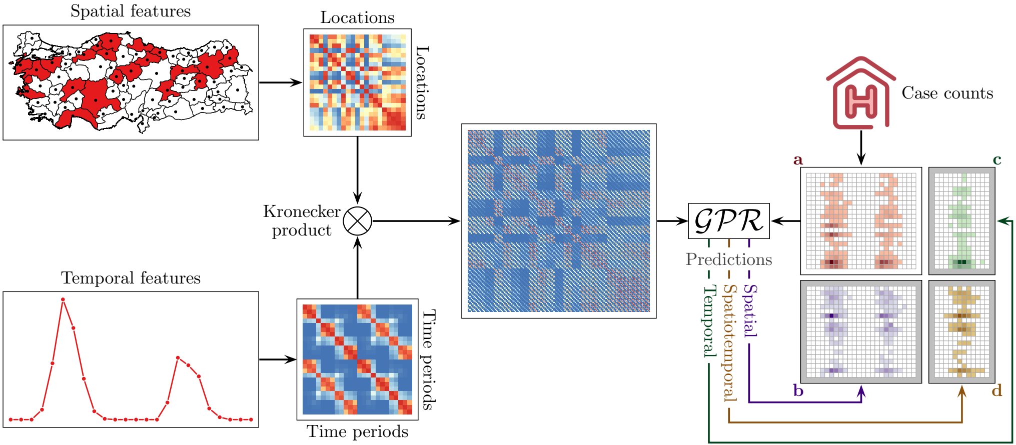
$$\mathbf{K}_s \otimes \mathbf{K}_t = (\mathbf{U}_s \otimes \mathbf{U}_t)(\mathbf{D}_s \otimes \mathbf{D}_t)(\mathbf{U}_s \otimes \mathbf{U}_t)^\top$$

$$\mathbf{K}_s = \mathbf{U}_s \mathbf{D}_s \mathbf{U}_s^\top$$
$$\mathbf{K}_t = \mathbf{U}_t \mathbf{D}_t \mathbf{U}_t^\top$$

$$\mathbf{K}_s \otimes \mathbf{K}_t = (\mathbf{U}_s \otimes \mathbf{U}_t)(\mathbf{D}_s \otimes \mathbf{D}_t)(\mathbf{U}_s \otimes \mathbf{U}_t)^\top$$

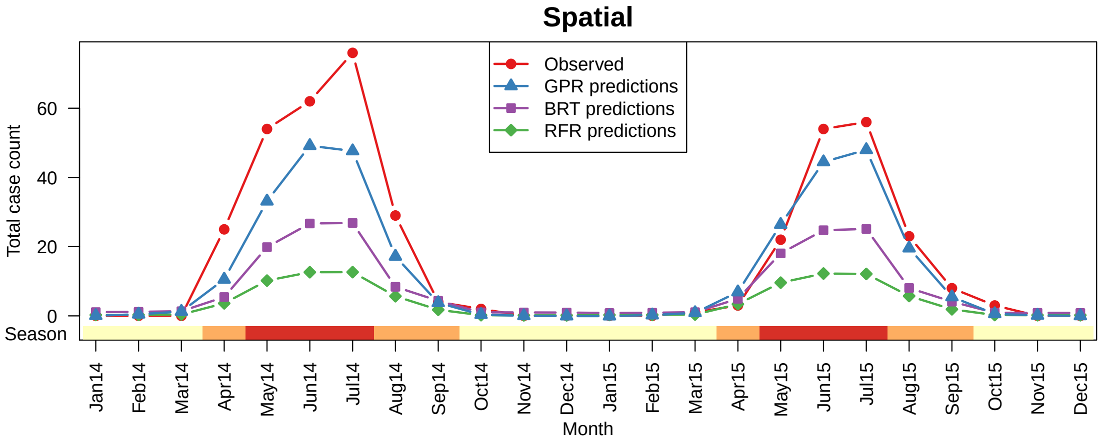
$$(\mathbf{K}_s \otimes \mathbf{K}_t + \sigma_y^2 \mathbf{I})^{-1} = (\mathbf{U}_s \otimes \mathbf{U}_t)(\mathbf{D}_s \otimes \mathbf{D}_t + \sigma_y^2 \mathbf{I})^{-1}(\mathbf{U}_s \otimes \mathbf{U}_t)^\top$$

Enfeksiyon hastalıklarının modellenmesi
Önerdiğimiz ilk model

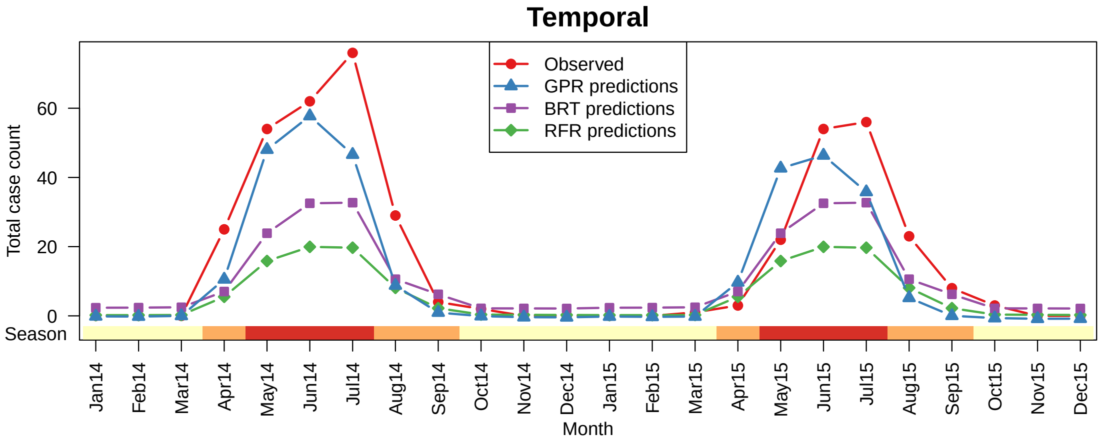


Enfeksiyon hastalıklarının modellenmesi

Kestirim sonuçları

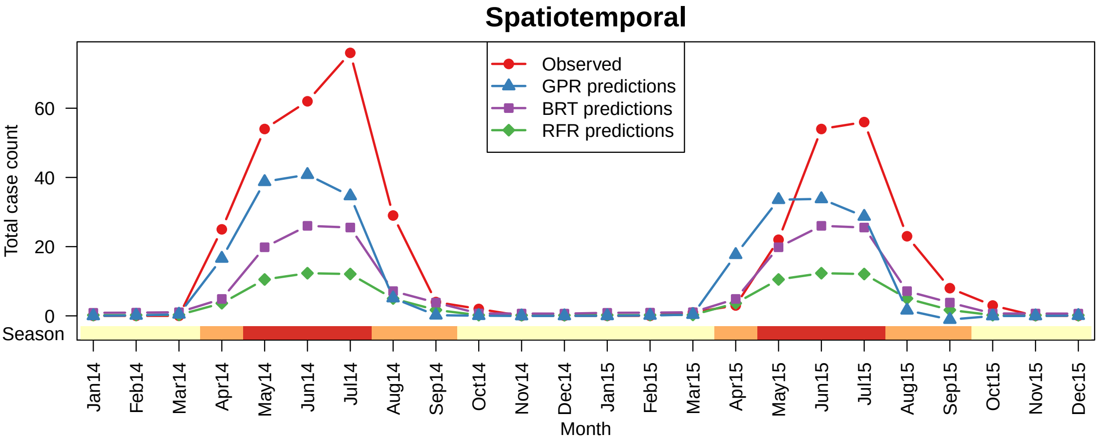


Enfeksiyon hastalıklarının modellenmesi
Kestirim sonuçları

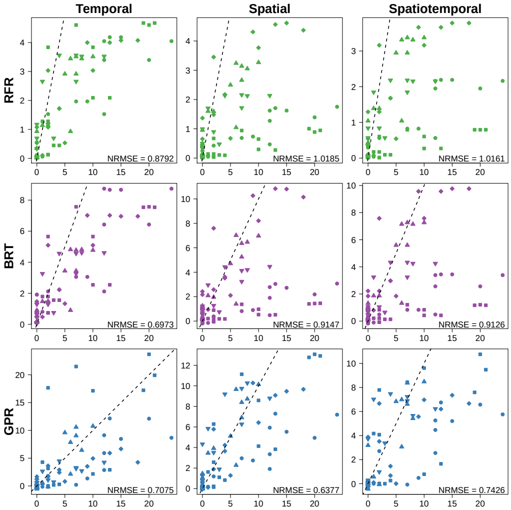


Enfeksiyon hastalıklarının modellenmesi

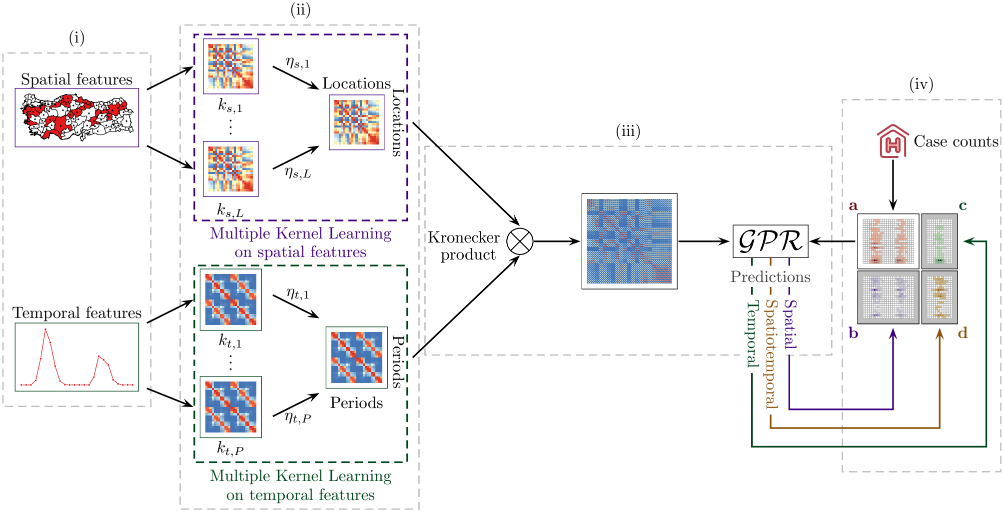
Kestirim sonuçları



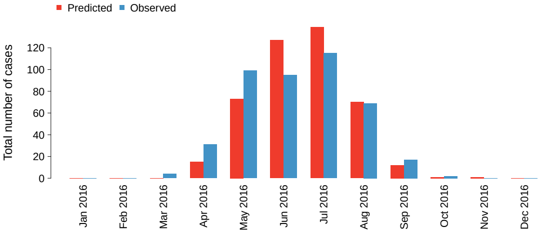
Enfeksiyon hastalıklarının modellenmesi
Kestirim sonuçları

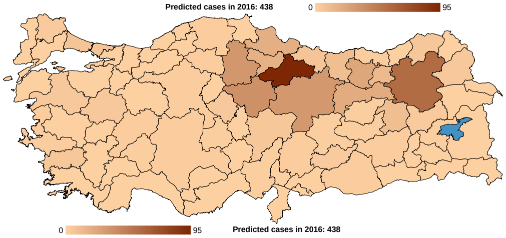


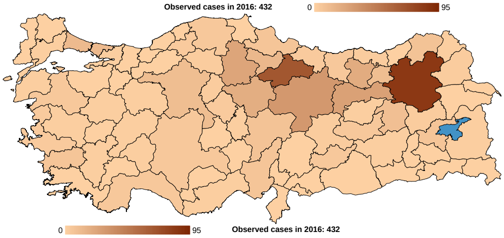
Enfeksiyon hastalıklarının modellenmesi
Önerdiğimiz ikinci model



Enfeksiyon hastalıklarının modellenmesi
2016 yılı için kestirim sonuçları

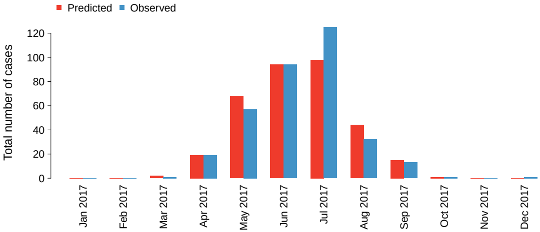


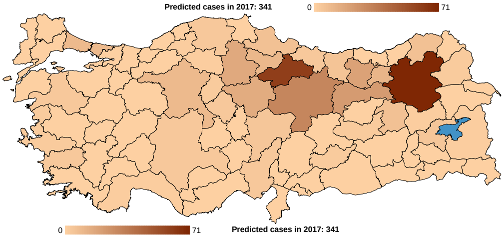


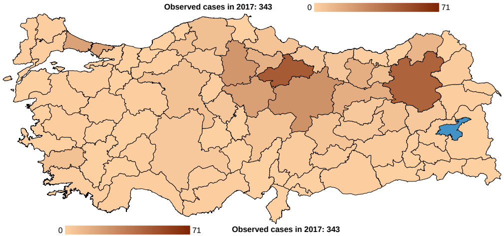


Enfeksiyon hastalıklarının modellenmesi

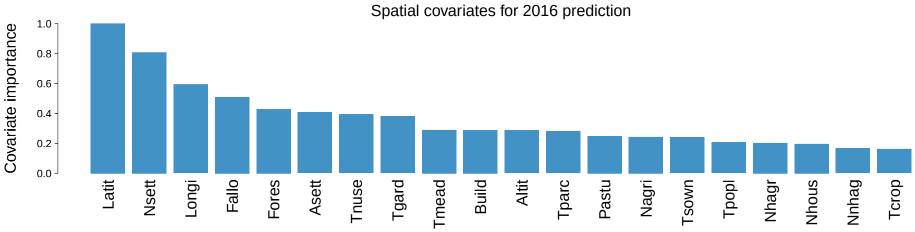
2017 yılı için kestirim sonuçları

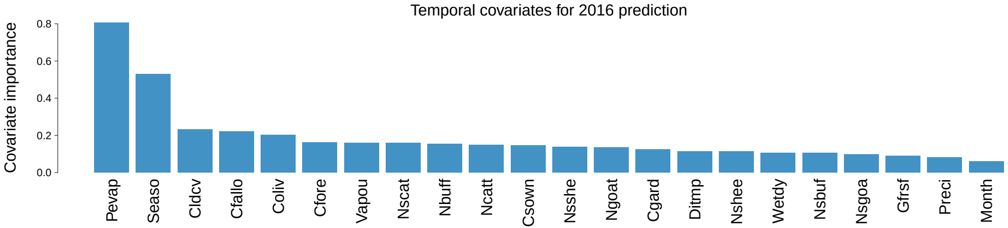




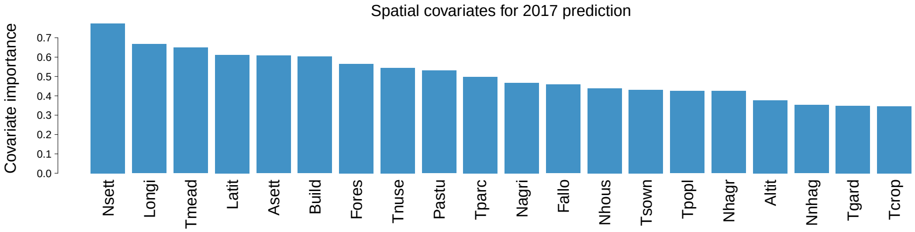


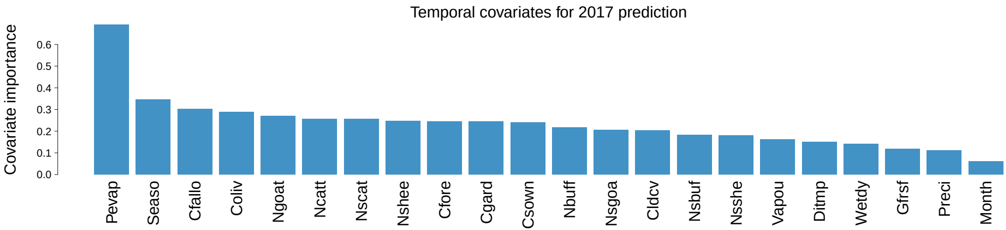
Enfeksiyon hastalıklarının modellenmesi
Öznitelik ağırlıkları





Enfeksiyon hastalıklarının modellenmesi
Öznitelik ağırlıkları

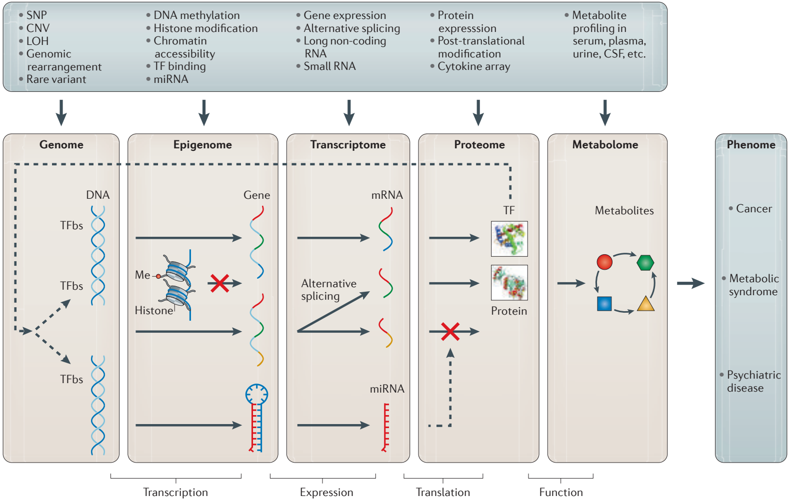




Karmaşık hastalıkların modellenmesi

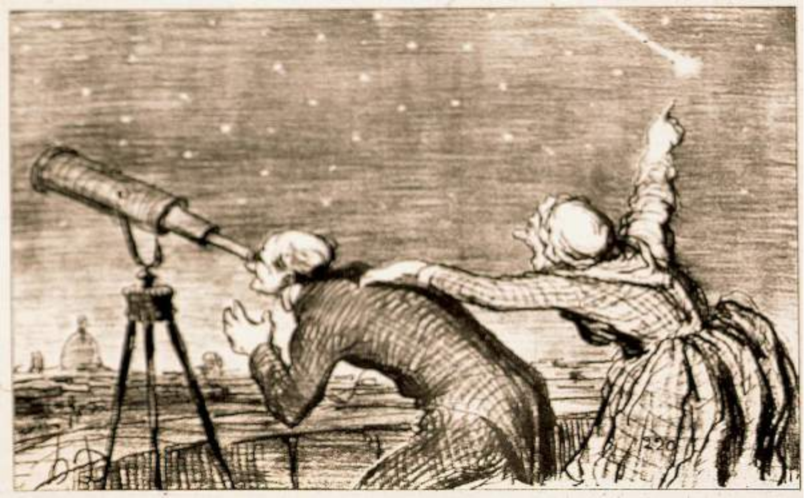
Karmaşık hastalıkların modellenmesi

Karmaşıklık nereden geliyor?



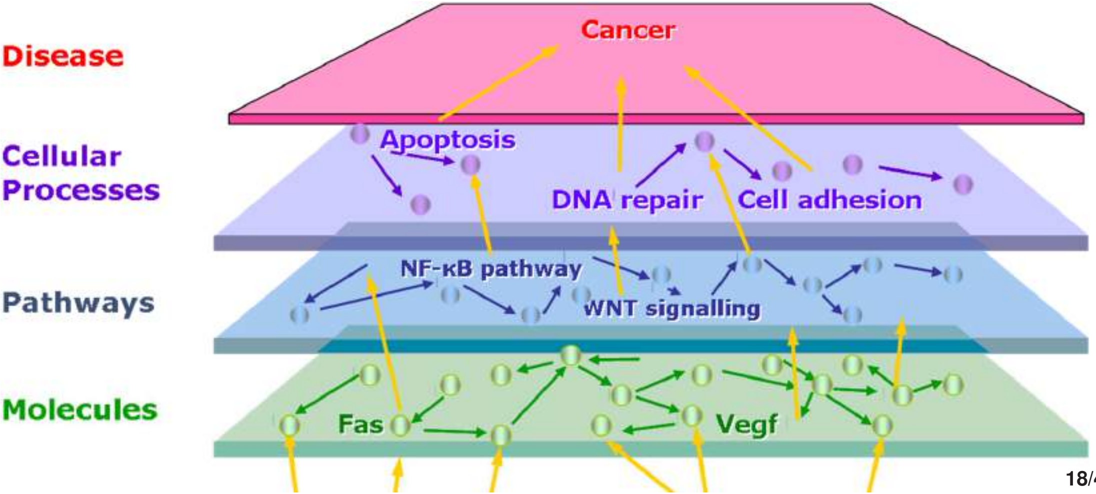
Karmaşık hastalıkların modellenmesi

Nereye bakmalıyız?



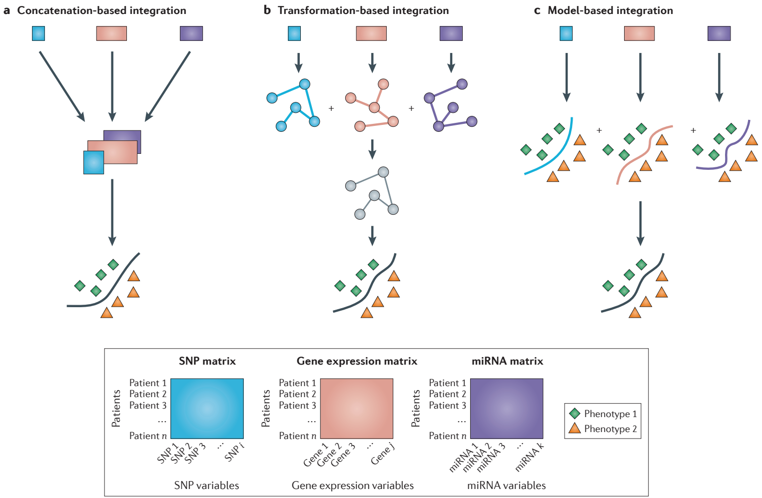
Karmaşık hastalıkların modellenmesi

Neleri gözlemlemeliyiz?



Karmaşık hastalıkların modellenmesi

Verileri nasıl birleştirmeliyiz?



Pan-cancer transcriptional signatures predictive of oncogenic mutations reveal that Fbw7 regulates cancer cell oxidative metabolism

Ryan J. Davis[a,b,c,1], Mehmet Gönen[d,e,f,1], Daciana H. Margineantu[a,b,1], Shlomo Handeli[a,b], Jherek Swanger[a,b], Pia Hoellerbauer[a], Patrick J. Paddison[a], Haiwei Gu[g,h], Daniel Raftery[g,h], Jonathan E. Grim[b], David M. Hockenbery[a,b,2], Adam A. Margolin[d,2], and Bruce E. Clurman[a,b,2,3]

[a]Division of Human Biology, Fred Hutchinson Cancer Research Center, Seattle, WA 98109; [b]Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, WA 98109; [c]Molecular and Cellular Biology Graduate Program, University of Washington, Seattle, WA 98195; [d]Department of Biomedical Engineering, Oregon Health & Science University, Portland, OR 97239; [e]Department of Industrial Engineering, College of Engineering, Koç University, 34450 Istanbul, Turkey; [f]School of Medicine, Koç University, 34450 Istanbul, Turkey; [g]Northwest Metabolomics Research Center, University of Washington, Seattle, WA 98109; and [h]Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA 98109

c

Kernelized Bayesian Transfer Learning*

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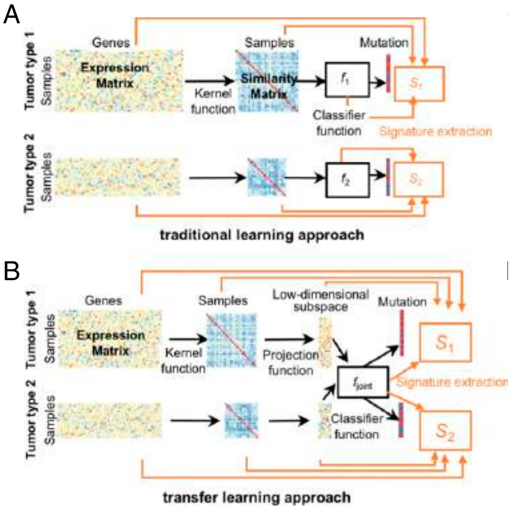
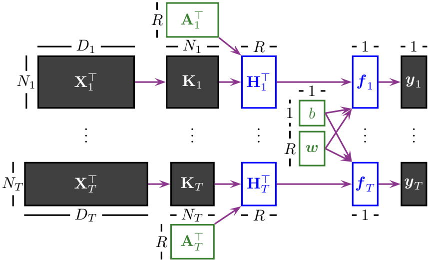
Karmaşık hastalıkların modellenmesi

Farklı hastalıkların transfer öğrenimi ile modellenmesi



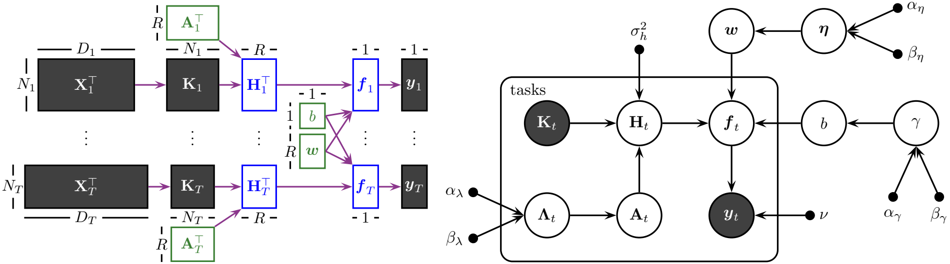
Karmaşık hastalıkların modellenmesi

Önerilen model



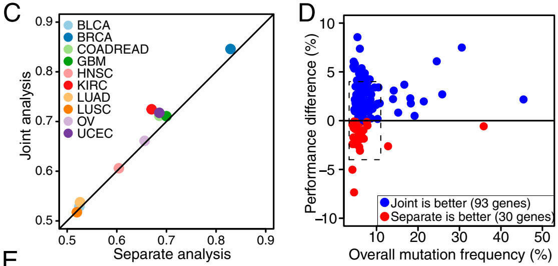
Karmaşık hastalıkların modellenmesi

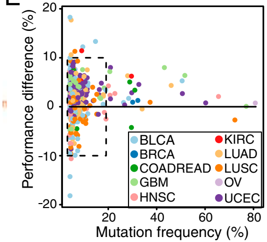
Önerilen model



Karmaşık hastalıkların modellenmesi

Farklı hastalıkların transfer öğrenimi ile modellenmesi



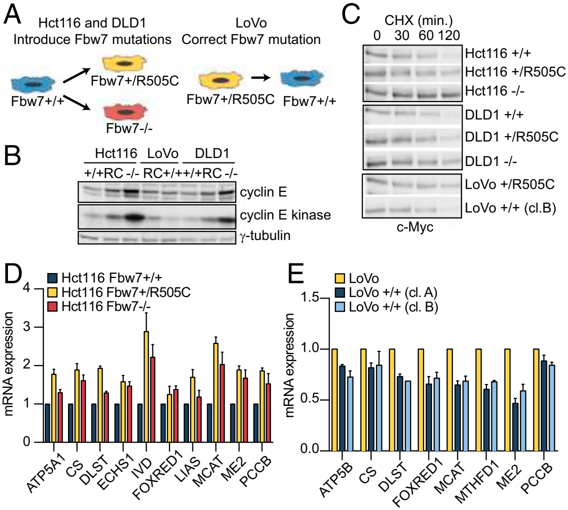


F

Tumor Type	Separate Analysis Rank	Joint Analysis Rank
Consensus	**56**	**1**
BLCA	54	3
COADRED	7	1
HNSC	1	2
LUSC	NA	67
UCEC	2	1

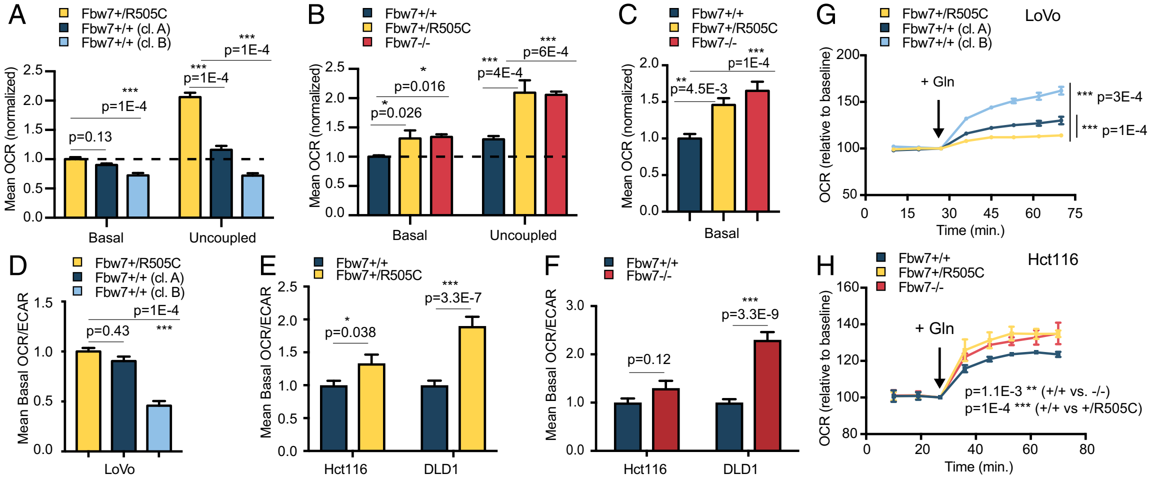
Karmaşık hastalıkların modellenmesi

Farklı hastalıkların transfer öğrenimi ile modellenmesi



Karmaşık hastalıkların modellenmesi

Farklı hastalıkların transfer öğrenimi ile modellenmesi



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doi: 10.1093/bioinformatics/bty239
ISMB 2018

OXFORD

Discriminating early- and late-stage cancers using multiple kernel learning on gene sets

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Cohort	Disease name	Stage I	Stage II	Stage III	Stage IV	Early (E1)	Late (E1)	Total (E1)	Early (E2)	Late (E2)	Total (E2)
ACC	Adrenocortical carcinoma	9	37	16	15	—	—	—	46	31	77
BLCA	Bladder urothelial carcinoma	2	130	140	134	—	—	—	132	274	406
BRCA	Breast invasive carcinoma	181	619	247	20	181	886	1067	800	267	1067
COAD	Colon adenocarcinoma	75	176	128	64	75	368	443	251	192	443
ESCA	Esophageal carcinoma	16	69	49	8	16	126	142	85	57	142
HNSC	Head and neck squamous cell carcinoma	25	70	78	259	25	407	429	95	337	429
KICH	Kidney chromophobe	20	25	14	6	20	45	65	45	20	65
KIRC	Kidney renal clear cell carcinoma	265	57	123	82	265	262	527	322	205	527
KIRP	Kidney renal papillary cell carcinoma	172	21	51	15	172	87	259	193	66	259
LIHC	Liver hepatocellular carcinoma	171	86	85	5	171	176	347	257	90	347
LUAD	Lung adenocarcinoma	274	121	84	26	274	231	505	395	110	505
LUSC	Lung squamous cell carcinoma	244	162	84	7	244	253	497	406	91	497
MESO	Mesothelioma	10	16	44	16	—	—	—	26	60	86
PAAD	Pancreatic adenocarcinoma	21	146	3	4	21	153	174	—	—	—
READ	Rectum adenocarcinoma	30	51	51	24	30	126	156	81	75	156
SKCM	Skin cutaneous melanoma	2	66	27	3	—	—	—	68	30	98
STAD	Stomach adenocarcinoma	53	111	150	38	53	299	352	164	188	352
TGCT	Testicular germ cell tumours	55	12	14	0	55	26	81	—	—	—
THCA	Thyroid carcinoma	281	52	112	55	281	219	500	333	167	500
UVM	Uveal melanoma	0	39	36	4	—	—	—	39	40	79
					Total	1883	3664	5547	3738	2300	6038

$$
\begin{aligned}
\text{min.} \quad & \frac{1}{2}\boldsymbol{w}^\top \boldsymbol{w} + C \sum_{i=1}^{N} \xi_i \\
\text{w.r.t.} \quad & \boldsymbol{w} \in \mathbb{R}^D, \quad \boldsymbol{\xi} \in \mathbb{R}^N, \quad b \in \mathbb{R} \\
\text{s.t.} \quad & y_i(\boldsymbol{w}^\top \boldsymbol{x}_i + b) \geq 1 - \xi_i \qquad \forall i \\
& \xi_i \geq 0 \qquad \forall i
\end{aligned}
$$

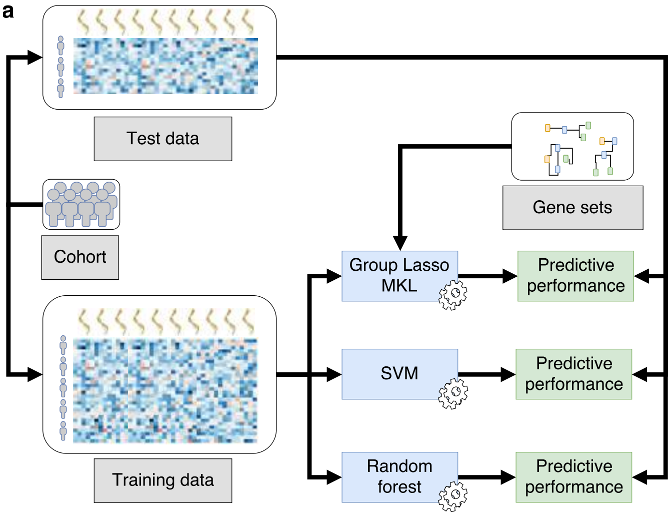
$$\begin{aligned}
\text{min.} \quad & -\sum_{i=1}^{N} \alpha_i + \frac{1}{2} \sum_{i=1}^{N} \sum_{j=1}^{N} \alpha_i \alpha_j y_i y_j \boldsymbol{x}_i^\top \boldsymbol{x}_j \\
\text{w.r.t.} \quad & \boldsymbol{\alpha} \in \mathbb{R}^N \\
\text{s.t.} \quad & \sum_{i=1}^{N} \alpha_i y_i = 0 \\
& C \geq \alpha_i \geq 0 \qquad \forall i
\end{aligned}$$

$$
\begin{aligned}
\text{min.} \quad & -\sum_{i=1}^{N} \alpha_i + \frac{1}{2} \sum_{i=1}^{N} \sum_{j=1}^{N} \alpha_i \alpha_j y_i y_j \sum_{m=1}^{P} \eta_m k_m(\boldsymbol{x}_i, \boldsymbol{x}_j) \\
\text{w.r.t.} \quad & \boldsymbol{\alpha} \in \mathbb{R}^N, \quad \boldsymbol{\eta} \in \mathbb{R}^P \\
\text{s.t.} \quad & \sum_{i=1}^{N} \alpha_i y_i = 0 \\
& C \geq \alpha_i \geq 0 \qquad \forall i \\
& \sum_{m=1}^{P} \eta_m = 1 \\
& \eta_m \geq 0 \qquad \forall m
\end{aligned}
$$

$$\eta_m^{(t+1)} = \frac{\eta_m^{(t)} \sqrt{\sum_{i=1}^{N} \sum_{j=1}^{N} \alpha_i^{(t)} \alpha_j^{(t)} y_i y_j k_m(\boldsymbol{x}_i, \boldsymbol{x}_j)}}{\sum_{o=1}^{P} \eta_o^{(t)} \sqrt{\sum_{i=1}^{N} \sum_{j=1}^{N} \alpha_i^{(t)} \alpha_j^{(t)} y_i y_j k_o(\boldsymbol{x}_i, \boldsymbol{x}_j)}} \qquad \forall m$$

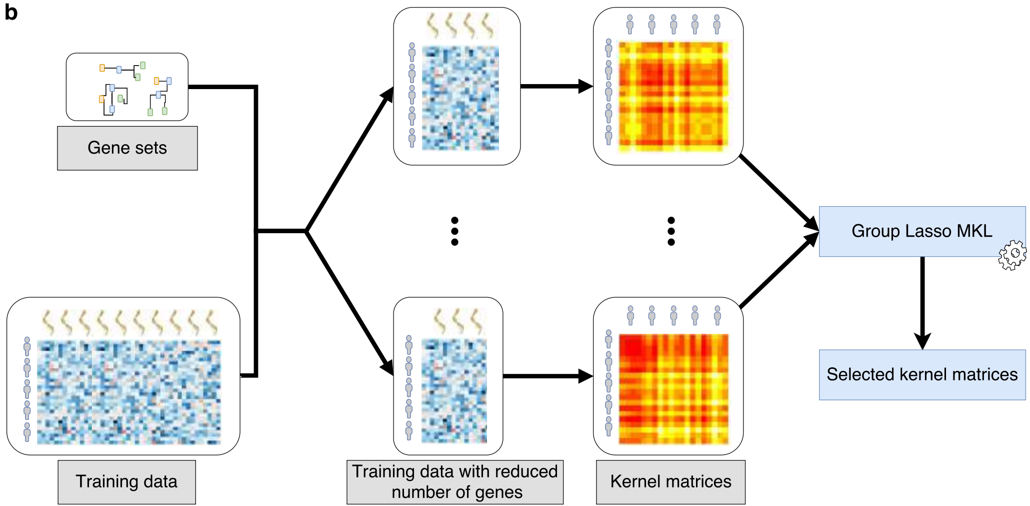
Karmaşık hastalıkların modellenmesi

Önerdiğimiz yöntem



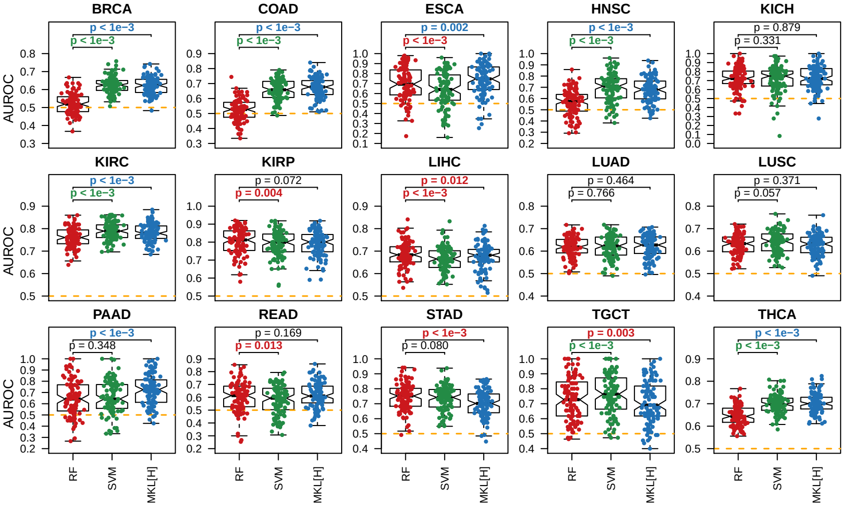
Karmaşık hastalıkların modellenmesi

Önerdiğimiz yöntem



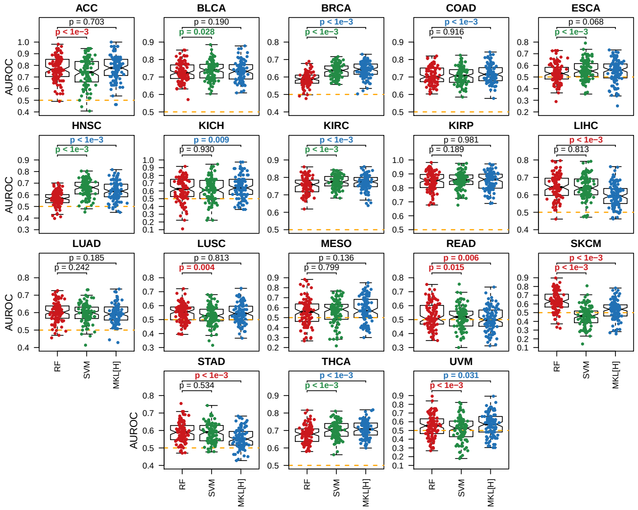
Karmaşık hastalıkların modellenmesi

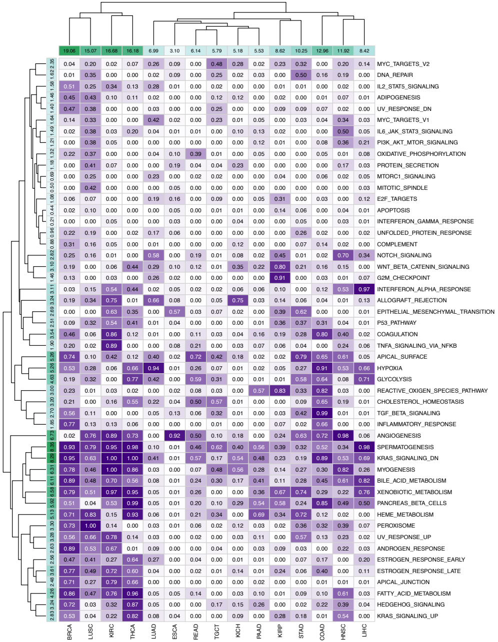
Kestirim sonuçları (Erken aşama: I. Geç aşama: II, III ve IV)

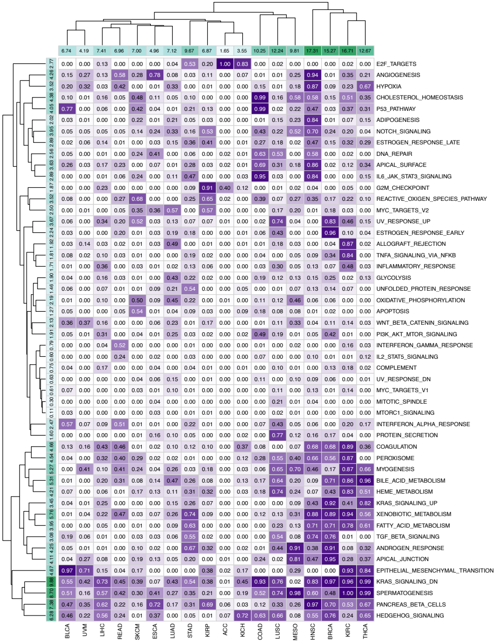


Karmaşık hastalıkların modellenmesi

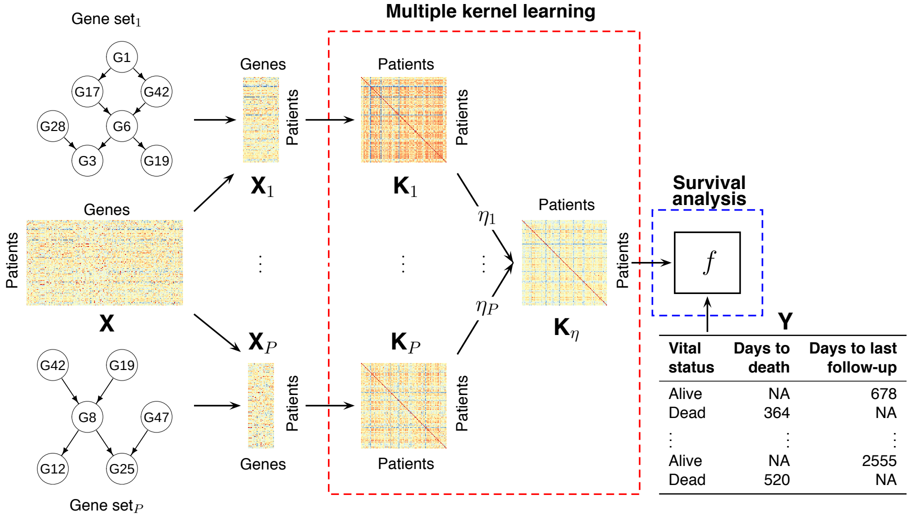
Kestirim sonuçları (Erken aşama: I ve II. Geç aşama: III ve IV)




19.06 15.07 16.68 16.18 6.99 3.10 6.14 5.79 5.18 5.53 8.62 10.25 12.96 11.92 8.42
MYC_TARGETS_V2
DNA_REPAIR
IL2_STAT5_SIGNALING
ADIPOGENESIS
UV_RESPONSE_DN
MYC_TARGETS_V1
IL6_JAK_STAT3_SIGNALING
PI3K_AKT_MTOR_SIGNALING
OXIDATIVE_PHOSPHORYLATION
PROTEIN_SECRETION
MTORC1_SIGNALING
MITOTIC_SPINDLE
E2F_TARGETS
APOPTOSIS
INTERFERON_GAMMA_RESPONSE
UNFOLDED_PROTEIN_RESPONSE
COMPLEMENT
NOTCH_SIGNALING
WNT_BETA_CATENIN_SIGNALING
G2M_CHECKPOINT
INTERFERON_ALPHA_RESPONSE
ALLOGRAFT_REJECTION
EPITHELIAL_MESENCHYMAL_TRANSITION
P53_PATHWAY
COAGULATION
TNFA_SIGNALING_VIA_NFKB
APICAL_SURFACE
HYPOXIA
GLYCOLYSIS
REACTIVE_OXIGEN_SPECIES_PATHWAY
CHOLESTEROL_HOMEOSTASIS
TGF_BETA_SIGNALING
INFLAMMATORY_RESPONSE
ANGIOGENESIS
SPERMATOGENESIS
KRAS_SIGNALING_DN
MYOGENESIS
BILE_ACID_METABOLISM
XENOBIOTIC_METABOLISM
PANCREAS_BETA_CELLS
HEME_METABOLISM
PEROXISOME
UV_RESPONSE_UP
ANDROGEN_RESPONSE
ESTROGEN_RESPONSE_EARLY
ESTROGEN_RESPONSE_LATE
APICAL_JUNCTION
FATTY_ACID_METABOLISM
HEDGEHOG_SIGNALING
KRAS_SIGNALING_UP
BRCA LUSC KIRC THCA LUAD ESCA READ TGCT KICH PAAD KIRP STAD COAD HNSC LIHC

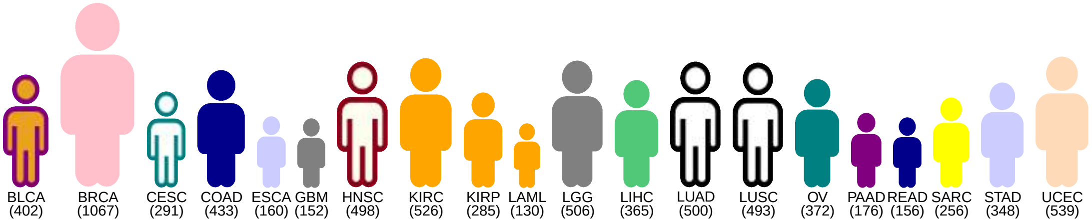

6.74 4.19 7.41 6.96 7.00 4.96 7.12 9.67 6.87 1.65 3.55 10.25 12.24 9.81 17.31 15.27 16.71 12.67
E2F_TARGETS
ANGIOGENESIS
HYPOXIA
CHOLESTEROL_HOMEOSTASIS
P53_PATHWAY
ADIPOGENESIS
NOTCH_SIGNALING
ESTROGEN_RESPONSE_LATE
DNA_REPAIR
APICAL_SURFACE
IL6_JAK_STAT3_SIGNALING
G2M_CHECKPOINT
REACTIVE_OXIGEN_SPECIES_PATHWAY
MYC_TARGETS_V2
UV_RESPONSE_UP
ESTROGEN_RESPONSE_EARLY
ALLOGRAFT_REJECTION
TNFA_SIGNALING_VIA_NFKB
INFLAMMATORY_RESPONSE
GLYCOLYSIS
UNFOLDED_PROTEIN_RESPONSE
OXIDATIVE_PHOSPHORYLATION
APOPTOSIS
WNT_BETA_CATENIN_SIGNALING
PI3K_AKT_MTOR_SIGNALING
INTERFERON_GAMMA_RESPONSE
IL2_STAT5_SIGNALING
COMPLEMENT
UV_RESPONSE_DN
MYC_TARGETS_V1
MITOTIC_SPINDLE
MTORC1_SIGNALING
INTERFERON_ALPHA_RESPONSE
PROTEIN_SECRETION
COAGULATION
PEROXISOME
MYOGENESIS
BILE_ACID_METABOLISM
HEME_METABOLISM
KRAS_SIGNALING_UP
XENOBIOTIC_METABOLISM
FATTY_ACID_METABOLISM
TGF_BETA_SIGNALING
ANDROGEN_RESPONSE
APICAL_JUNCTION
EPITHELIAL_MESENCHYMAL_TRANSITION
KRAS_SIGNALING_DN
SPERMATOGENESIS
PANCREAS_BETA_CELLS
HEDGEHOG_SIGNALING
BLCA UVM LIHC READ SKCM ESCA LUAD STAD KIRP ACC KICH COAD LUSC MESO HNSC BRCA KIRC THCA

Karmaşık hastalıkların modellenmesi
Kanser hastalarının sağ kalım analizi



Karmaşık hastalıkların modellenmesi

Kanser hastalarının sağ kalım analizi



- 20 cancer types
- 7,655 patients

$$
\begin{aligned}
\text{min.} \quad & \frac{1}{2}\boldsymbol{w}^\top \boldsymbol{w} + C \sum_{i=1}^{N} (\xi_i^+ + (1 - \delta_i)\xi_i^-) \\
\text{w.r.t.} \quad & \boldsymbol{w} \in \mathbb{R}^D, \;\; \boldsymbol{\xi}^+ \in \mathbb{R}^N, \;\; \boldsymbol{\xi}^- \in \mathbb{R}^N, \;\; b \in \mathbb{R} \\
\text{s.t.} \quad & \epsilon + \xi_i^+ \geq y_i - \boldsymbol{w}^\top \boldsymbol{x}_i - b \qquad \forall i \\
& \epsilon + \xi_i^- \geq \boldsymbol{w}^\top \boldsymbol{x}_i + b - y_i \qquad \forall i \\
& \xi_i^+ \geq 0 \qquad \forall i \\
& \xi_i^- \geq 0 \qquad \forall i
\end{aligned}
$$

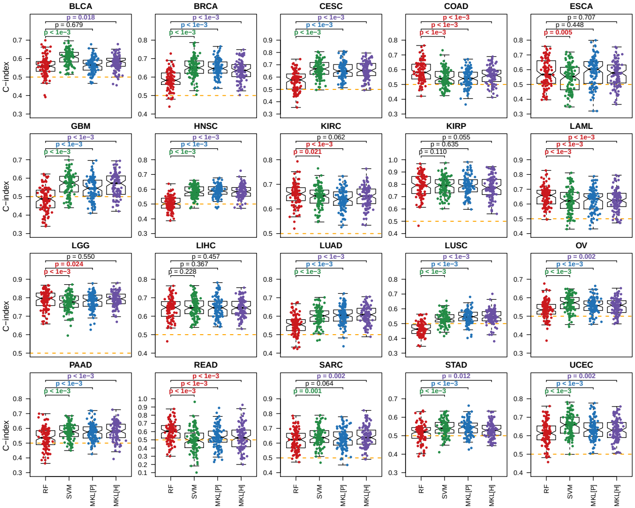
$$
\begin{aligned}
\text{min.} \quad & -\sum_{i=1}^{N} y_i(\alpha_i^{+} - \alpha_i^{-}) + \epsilon \sum_{i=1}^{N} (\alpha_i^{+} + \alpha_i^{-}) + \frac{1}{2} \sum_{i=1}^{N} \sum_{j=1}^{N} (\alpha_i^{+} - \alpha_i^{-})(\alpha_j^{+} - \alpha_j^{-}) \boldsymbol{x}_i^{\top} \boldsymbol{x}_j \\
\text{w.r.t.} \quad & \boldsymbol{\alpha}^{+} \in \mathbb{R}^N, \quad \boldsymbol{\alpha}^{-} \in \mathbb{R}^N \\
\text{s.t.} \quad & \sum_{i=1}^{N} (\alpha_i^{+} - \alpha_i^{-}) = 0 \\
& C \geq \alpha_i^{+} \geq 0 \qquad \forall i \\
& C(1 - \delta_i) \geq \alpha_i^{-} \geq 0 \qquad \forall i
\end{aligned}
$$

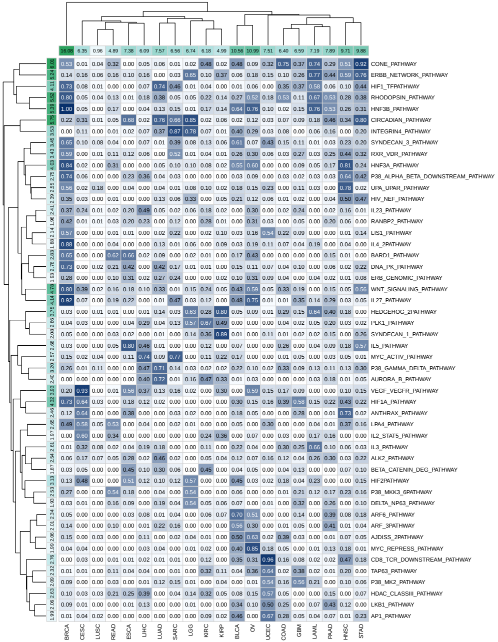
$$\begin{aligned}
\text{min.} \quad & -\sum_{i=1}^{N} y_i(\alpha_i^+ - \alpha_i^-) + \epsilon \sum_{i=1}^{N} (\alpha_i^+ + \alpha_i^-) + \frac{1}{2} \sum_{i=1}^{N} \sum_{j=1}^{N} (\alpha_i^+ - \alpha_i^-)(\alpha_j^+ - \alpha_j^-) \sum_{m=1}^{P} \eta_m k_m(\boldsymbol{x}_i, \boldsymbol{x}_j) \\
\text{w.r.t.} \quad & \boldsymbol{\alpha}^+ \in \mathbb{R}^N, \;\; \boldsymbol{\alpha}^- \in \mathbb{R}^N, \;\; \boldsymbol{\eta} \in \mathbb{R}^P \\
\text{s.t.} \quad & \sum_{i=1}^{N} (\alpha_i^+ - \alpha_i^-) = 0 \\
& C \geq \alpha_i^+ \geq 0 \qquad \forall i \\
& C(1 - \delta_i) \geq \alpha_i^- \geq 0 \qquad \forall i \\
& \sum_{m=1}^{P} \eta_m = 1 \\
& \eta_m \geq 0 \qquad \forall m
\end{aligned}$$

$$\eta_m^{(t+1)} = \frac{\eta_m^{(t)} \sqrt{\sum_{i=1}^{N} \sum_{j=1}^{N} (\alpha_i^{+(t)} - \alpha_i^{-(t)})(\alpha_j^{+(t)} - \alpha_j^{-(t)}) k_m(\boldsymbol{x}_i, \boldsymbol{x}_j)}}{\sum_{o=1}^{P} \eta_o^{(t)} \sqrt{\sum_{i=1}^{N} \sum_{j=1}^{N} (\alpha_i^{+(t)} - \alpha_i^{-(t)})(\alpha_j^{+(t)} - \alpha_j^{-(t)}) k_o(\boldsymbol{x}_i, \boldsymbol{x}_j)}} \qquad \forall m$$

Karmaşık hastalıkların modellenmesi

Sağ kalım analizi kestirim sonuçları

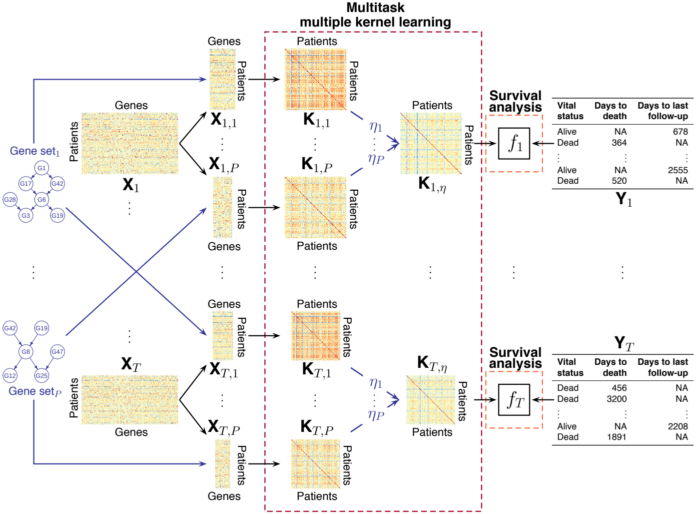


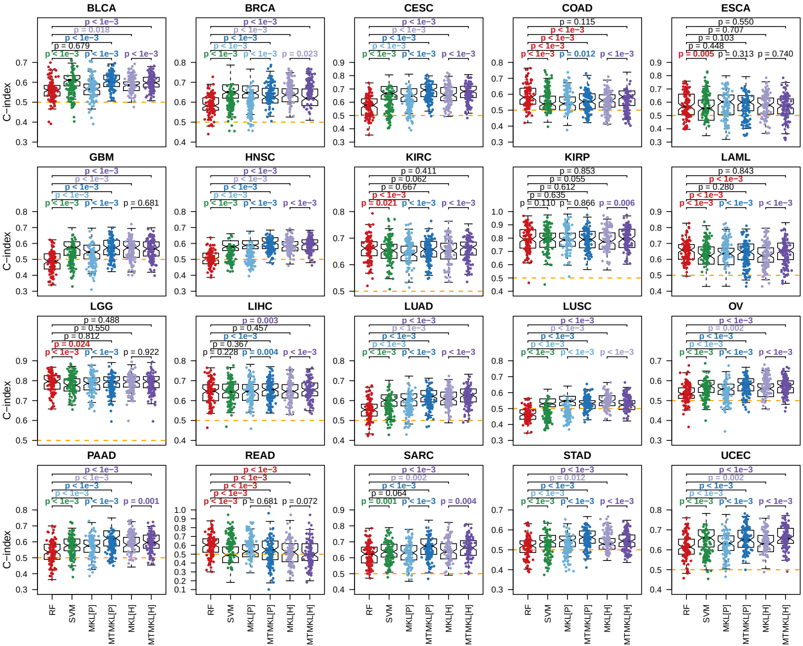

CONE_PATHWAY
ERBB_NETWORK_PATHWAY
HIF1_TFPATHWAY
RHODOPSIN_PATHWAY
HNF3B_PATHWAY
CIRCADIAN_PATHWAY
INTEGRIN4_PATHWAY
SYNDECAN_3_PATHWAY
RXR_VDR_PATHWAY
HNF3A_PATHWAY
P38_ALPHA_BETA_DOWNSTREAM_PATHWAY
UPA_UPAR_PATHWAY
HIV_NEF_PATHWAY
IL23_PATHWAY
RANBP2_PATHWAY
LIS1_PATHWAY
IL4_2PATHWAY
BARD1_PATHWAY
DNA_PK_PATHWAY
ERB_GENOMIC_PATHWAY
WNT_SIGNALING_PATHWAY
IL27_PATHWAY
HEDGEHOG_2PATHWAY
PLK1_PATHWAY
SYNDECAN_1_PATHWAY
IL5_PATHWAY
MYC_ACTIV_PATHWAY
P38_GAMMA_DELTA_PATHWAY
AURORA_B_PATHWAY
VEGF_VEGFR_PATHWAY
HIF1A_PATHWAY
ANTHRAX_PATHWAY
LPA4_PATHWAY
IL2_STAT5_PATHWAY
IL3_PATHWAY
ALK2_PATHWAY
BETA_CATENIN_DEG_PATHWAY
HIF2PATHWAY
P38_MKK3_6PATHWAY
DELTA_NP63_PATHWAY
ARF6_PATHWAY
ARF_3PATHWAY
AJDISS_2PATHWAY
MYC_REPRESS_PATHWAY
CD8_TCR_DOWNSTREAM_PATHWAY
TAP63_PATHWAY
P38_MK2_PATHWAY
HDAC_CLASSIII_PATHWAY
LKB1_PATHWAY
AP1_PATHWAY
BRCA CESC LUSC READ ESCA LIHC LUAD SARC LGG KIRC KIRP BLCA OV UCEC COAD GBM LAML PAAD HNSC STAD


BILE_ACID_METABOLISM
APICAL_SURFACE
KRAS_SIGNALING_DN
SPERMATOGENESIS
ANGIOGENESIS
WNT_BETA_CATENIN_SIGNALING
HYPOXIA
FATTY_ACID_METABOLISM
ESTROGEN_RESPONSE_LATE
COAGULATION
UNFOLDED_PROTEIN_RESPONSE
APOPTOSIS
P53_PATHWAY
XENOBIOTIC_METABOLISM
UV_RESPONSE_UP
REACTIVE_OXIGEN_SPECIES_PATHWAY
PANCREAS_BETA_CELLS
GLYCOLYSIS
HEDGEHOG_SIGNALING
KRAS_SIGNALING_UP
UV_RESPONSE_DN
EPITHELIAL_MESENCHYMAL_TRANSITION
E2F_TARGETS
G2M_CHECKPOINT
MYC_TARGETS_V1
MYC_TARGETS_V2
IL2_STAT5_SIGNALING
MTORC1_SIGNALING
ALLOGRAFT_REJECTION
IL6_JAK_STAT3_SIGNALING
OXIDATIVE_PHOSPHORYLATION
DNA_REPAIR
MYOGENESIS
PI3K_AKT_MTOR_SIGNALING
TNFA_SIGNALING_VIA_NFKB
INFLAMMATORY_RESPONSE
MITOTIC_SPINDLE
CHOLESTEROL_HOMEOSTASIS
NOTCH_SIGNALING
TGF_BETA_SIGNALING
COMPLEMENT
PROTEIN_SECRETION
ESTROGEN_RESPONSE_EARLY
INTERFERON_GAMMA_RESPONSE
PEROXISOME
INTERFERON_ALPHA_RESPONSE
HEME_METABOLISM
APICAL_JUNCTION
ADIPOGENESIS
ANDROGEN_RESPONSE
LGG KIRP LUAD HNSC READ UCEC CESC GBM LUSC STAD COAD LAML LIHC BLCA KIRC PAAD ESCA SARC BRCA OV

Karmaşık hastalıkların modellenmesi

Çoklu görev öğrenimi ile sağ kalım analizi




BLCA
p < 1e−3
p = 0.018
p < 1e−3
p = 0.679
p < 1e−3 p < 1e−3 p < 1e−3
BRCA
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p = 0.023
CESC
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
COAD
p = 0.115
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p = 0.012 p < 1e−3
ESCA
p = 0.550
p = 0.707
p = 0.103
p = 0.448
p = 0.005 p = 0.313 p = 0.740
GBM
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p = 0.681
HNSC
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
KIRC
p = 0.411
p = 0.062
p = 0.667
p < 1e−3
p = 0.021 p < 1e−3 p < 1e−3
KIRP
p = 0.853
p = 0.055
p = 0.612
p = 0.635
p = 0.110 p = 0.866 p = 0.006
LAML
p = 0.843
p < 1e−3
p = 0.280
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
LGG
p = 0.488
p = 0.550
p = 0.812
p = 0.024
p < 1e−3 p < 1e−3 p = 0.922
LIHC
p = 0.003
p = 0.457
p < 1e−3
p = 0.367
p = 0.228 p = 0.004 p < 1e−3
LUAD
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
LUSC
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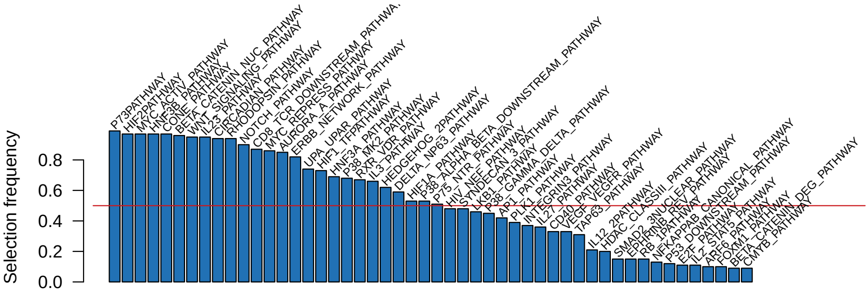
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
OV
p < 1e−3
p = 0.002
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
PAAD
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p = 0.001
READ
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3
p < 1e−3 p = 0.681 p = 0.072
SARC
p < 1e−3
p = 0.002
p < 1e−3
p = 0.064
p = 0.001 p < 1e−3 p = 0.004
STAD
p < 1e−3
p = 0.012
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
UCEC
p < 1e−3
p = 0.002
p < 1e−3
p < 1e−3
p < 1e−3 p < 1e−3 p < 1e−3
C−index
RF
SVM
MKL[P]
MTMKL[P]
MKL[H]
MTMKL[H]


Selection frequency
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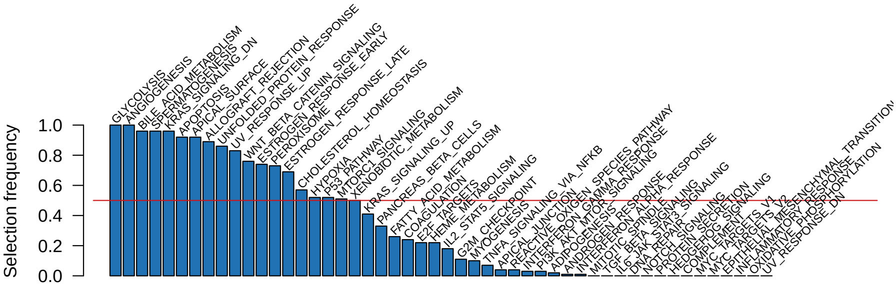
0.2
0.4
0.6
0.8
P73PATHWAY
HIF2PATHWAY
MYC_ACTIV_PATHWAY
HNF3B_PATHWAY
CONE_PATHWAY
BETA_CATENIN_NUC_PATHWAY
WNT_SIGNALING_PATHWAY
IL23_PATHWAY
CIRCADIAN_PATHWAY
RHODOPSIN_PATHWAY
NOTCH_PATHWAY
CD8_TCR_DOWNSTREAM_PATHWA
MYC_REPRESS_PATHWAY
AURORA_A_PATHWAY
ERBB_NETWORK_PATHWAY
UPA_UPAR_PATHWAY
HIF1_TFPATHWAY
HNF3A_PATHWAY
P38_MK2_PATHWAY
RXR_VDR_PATHWAY
IL3_PATHWAY
HEDGEHOG_2PATHWAY
DELTA_NP63_PATHWAY
HIF1A_PATHWAY
P38_ALPHA_BETA_DOWNSTREAM_PATHWAY
P75_NTR_PATHWAY
HIV_NEF_PATHWAY
SYNDECAN_3_PATHWAY
LKB1_PATHWAY
P38_GAMMA_DELTA_PATHWAY
AP1_PATHWAY
PLK1_PATHWAY
INTEGRIN3_PATHWAY
IL27_PATHWAY
CD40_PATHWAY
VEGF_VEGFR_PATHWAY
TAP63_PATHWAY
IL12_2PATHWAY
HDAC_CLASSIII_PATHWAY
SMAD2_3NUCLEAR_PATHWAY
EPHRINB_REV_PATHWAY
RB_1PATHWAY
NFKAPPAB_CANONICAL_PATHWAY
P53_DOWNSTREAM_PATHWAY
E2F_PATHWAY
IL2_STAT5_PATHWAY
ARF6_PATHWAY
FOXM1_PATHWAY
BETA_CATENIN_DEG_PATHWAY
CMYB_PATHWAY


Selection frequency
0.0
0.2
0.4
0.6
0.8
1.0
GLYCOLYSIS
ANGIOGENESIS
BILE_ACID_METABOLISM
SPERMATOGENESIS
KRAS_SIGNALING_DN
APOPTOSIS
APICAL_SURFACE
ALLOGRAFT_REJECTION
UNFOLDED_PROTEIN_RESPONSE
UV_RESPONSE_UP
WNT_BETA_CATENIN_SIGNALING
ESTROGEN_RESPONSE_EARLY
PEROXISOME
ESTROGEN_RESPONSE_LATE
CHOLESTEROL_HOMEOSTASIS
HYPOXIA
P53_PATHWAY
MTORC1_SIGNALING
XENOBIOTIC_METABOLISM
KRAS_SIGNALING_UP
PANCREAS_BETA_CELLS
FATTY_ACID_METABOLISM
COAGULATION
E2F_TARGETS
HEME_METABOLISM
IL2_STAT5_SIGNALING
G2M_CHECKPOINT
MYOGENESIS
TNFA_SIGNALING_VIA_NFKB
APICAL_JUNCTION
REACTIVE_OXIGEN_SPECIES_PATHWAY
INTERFERON_GAMMA_RESPONSE
PI3K_AKT_MTOR_SIGNALING
ADIPOGENESIS
ANDROGEN_RESPONSE
INTERFERON_ALPHA_RESPONSE
MITOTIC_SPINDLE
TGF_BETA_SIGNALING
IL6_JAK_STAT3_SIGNALING
DNA_REPAIR
NOTCH_SIGNALING
PROTEIN_SECRETION
HEDGEHOG_SIGNALING
COMPLEMENT
MYC_TARGETS_V1
MYC_TARGETS_V2
EPITHELIAL_MESENCHYMAL_TRANSITION
INFLAMMATORY_RESPONSE
OXIDATIVE_PHOSPHORYLATION
UV_RESPONSE_DN

Sonuç

- Yaşam bilimleri uygulamaları için çekirdek tabanlı yapay öğrenme yöntemleri

Sonuç

- Yaşam bilimleri uygulamaları için çekirdek tabanlı yapay öğrenme yöntemleri
- Az sayıda ve yüksek boyutlu örnekten öğrenebilme

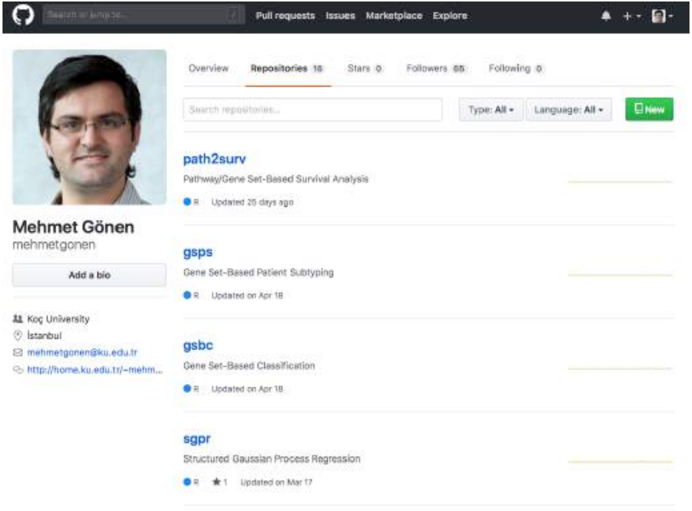
Sonuç

- Yaşam bilimleri uygulamaları için çekirdek tabanlı yapay öğrenme yöntemleri
- Az sayıda ve yüksek boyutlu örnekten öğrenebilme
- Farklı özellikteki veri kaynaklarını birleştirebilme

Sonuç

- Yaşam bilimleri uygulamaları için çekirdek tabanlı yapay öğrenme yöntemleri
- Az sayıda ve yüksek boyutlu örnekten öğrenebilme
- Farklı özellikteki veri kaynaklarını birleştirebilme
- Test edilebilir hipotezler üretmeye uygun bilgi çıkarımı

Sonuç
Kaynak kodlar



Destekler

- Türkiye Bilimsel ve Teknolojik Araştırma Kurumu (TÜBİTAK)
  - Hesaplamalı Onkoloji İçin Yolak Tabanlı Çekirdek Öğrenme Algoritmaları (EEEAG 117E181)
- Türkiye Bilimler Akademisi (TÜBA)
  - Üstün Başarılı Genç Bilim İnsanlarını Ödüllendirme Programı (GEBİP)
- Bilim Akademisi (BA)
  - Bilim Akademisi Genç Bilim İnsanları Ödül Programı (BAGEP)