Isotonic subgroup selection

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12$^{\text{th}}$ April 2024

Collaborators

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University of Edinburgh

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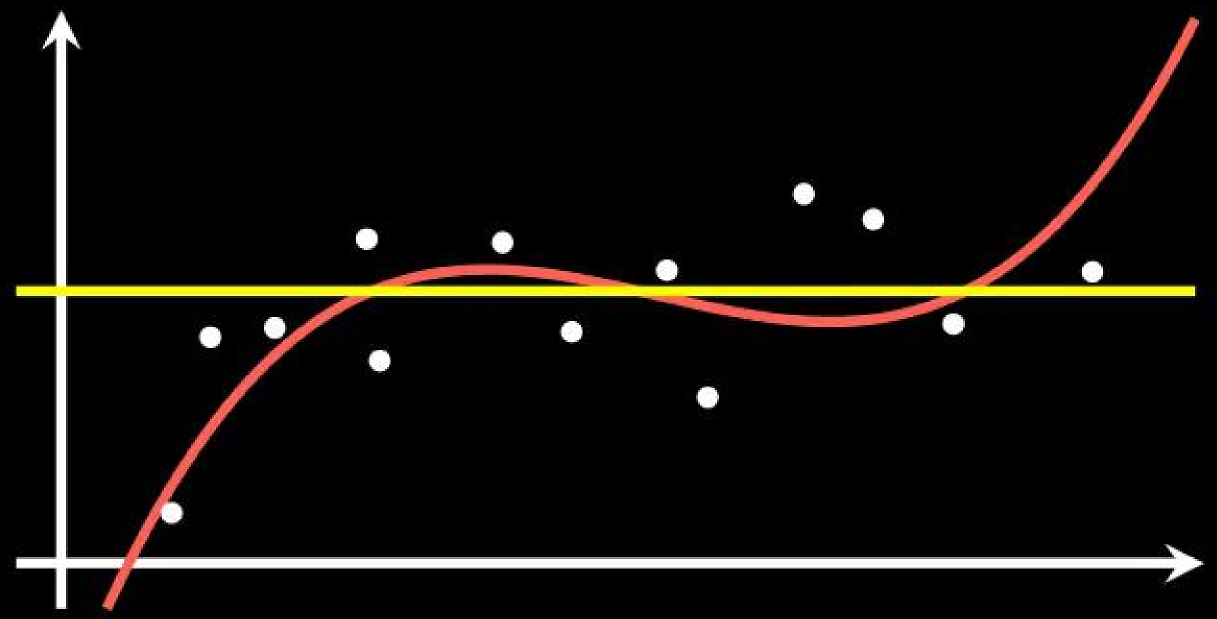

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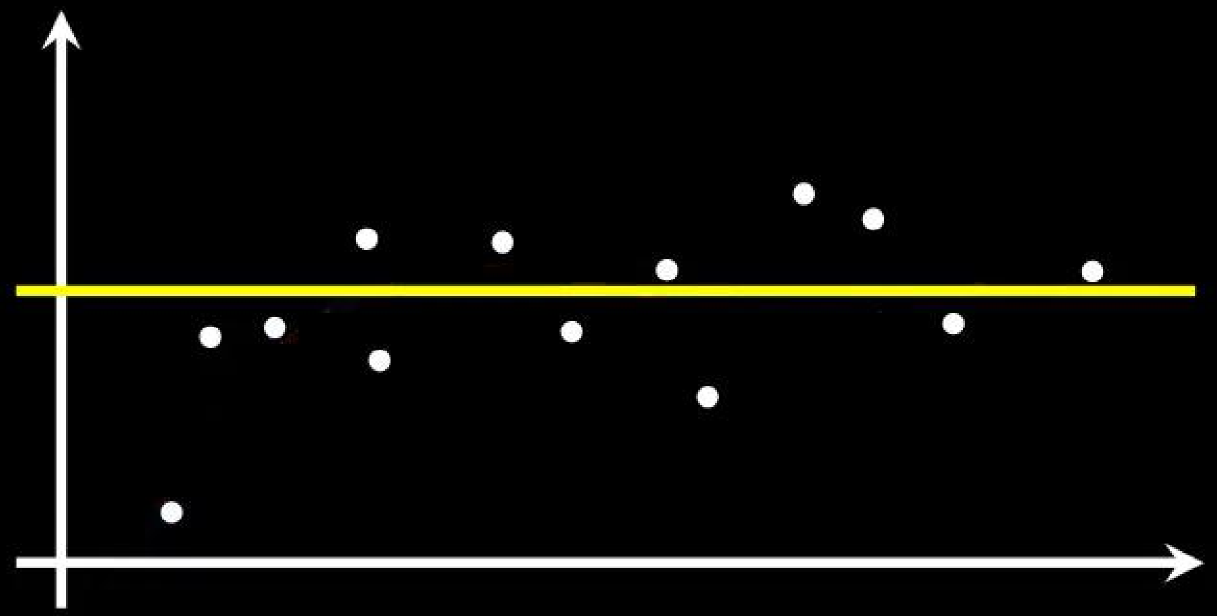

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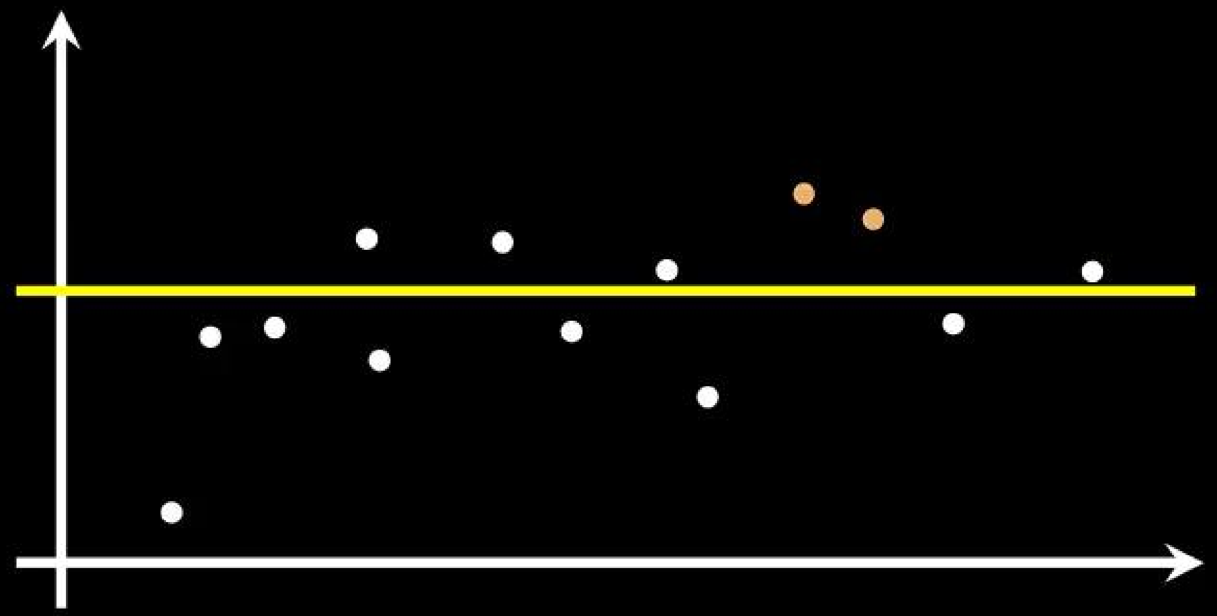

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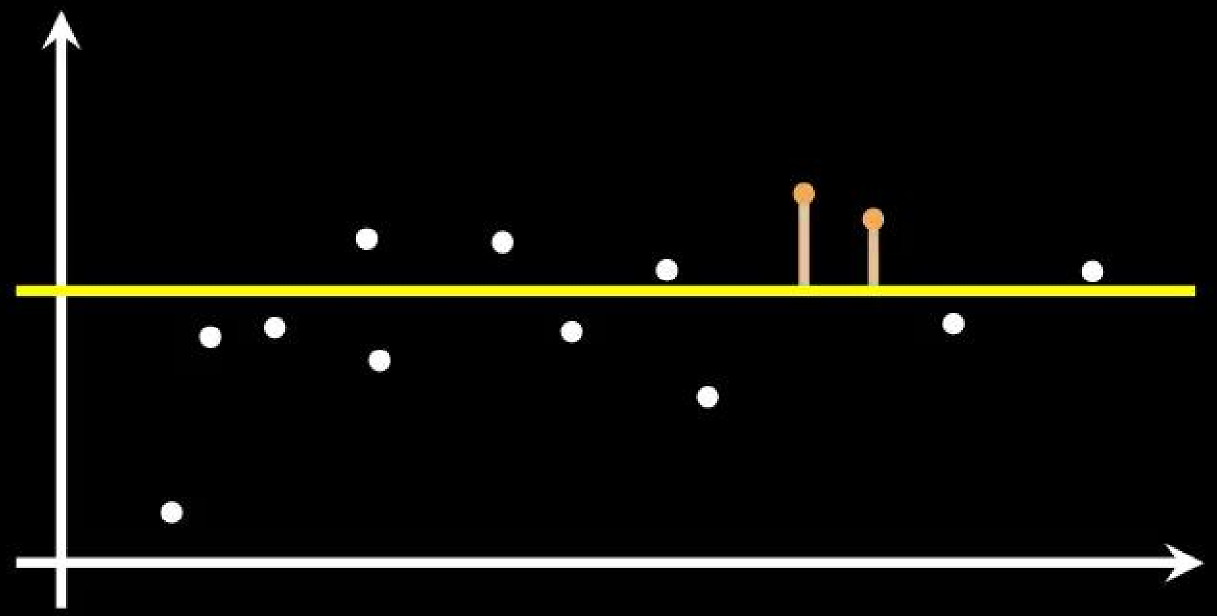

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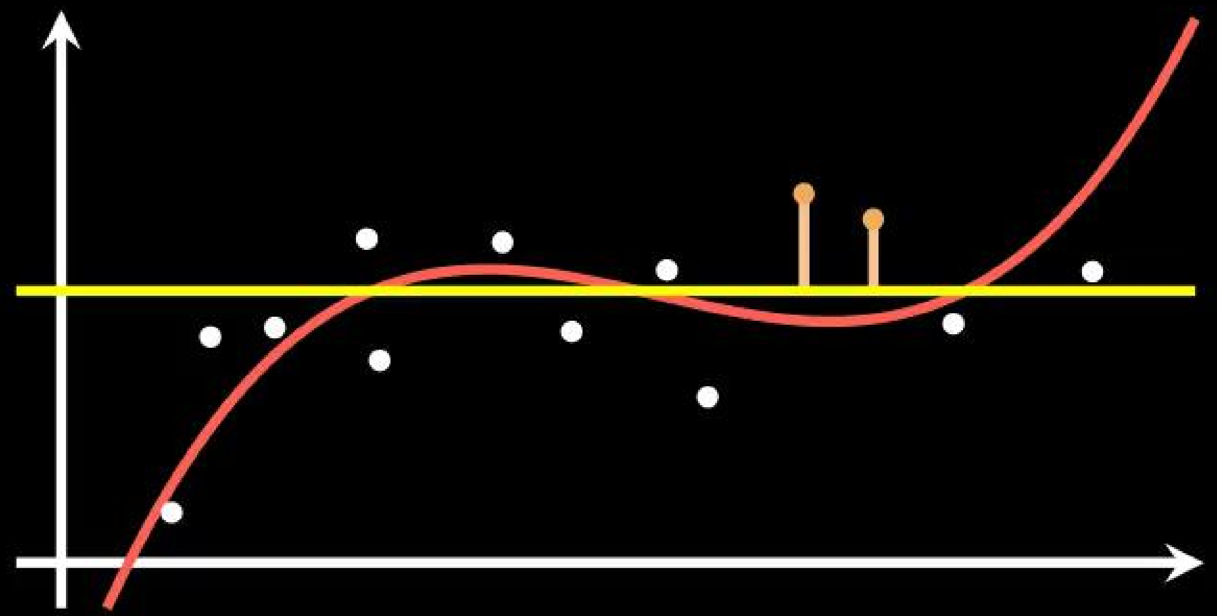

Example. Efficacy of a new vaccine.

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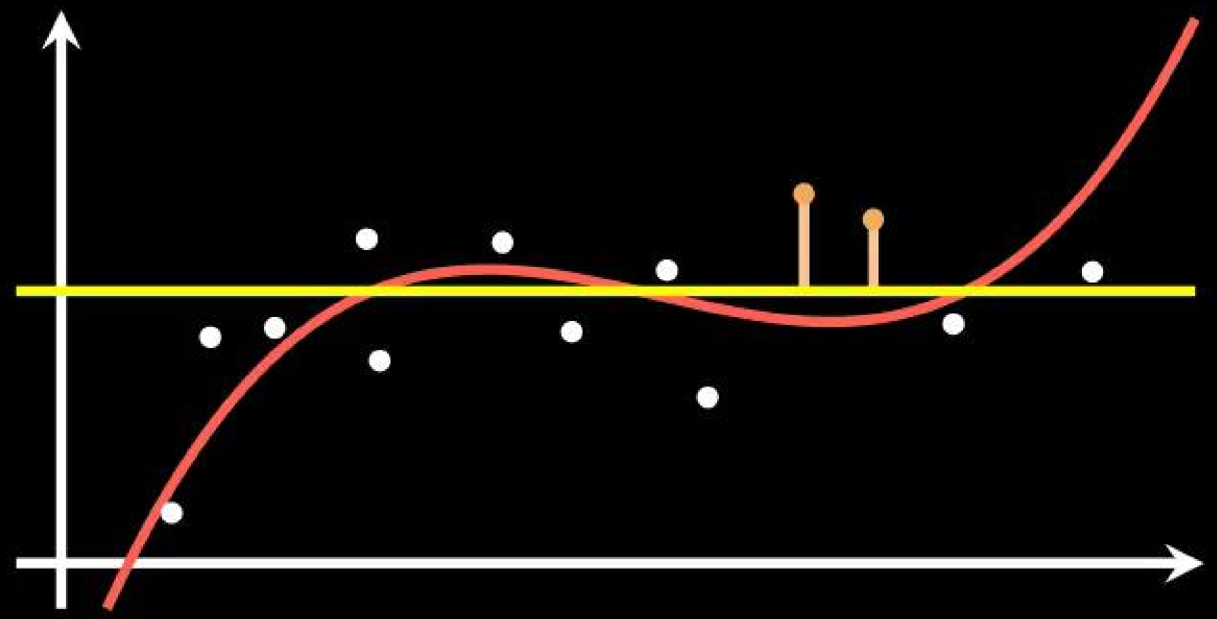

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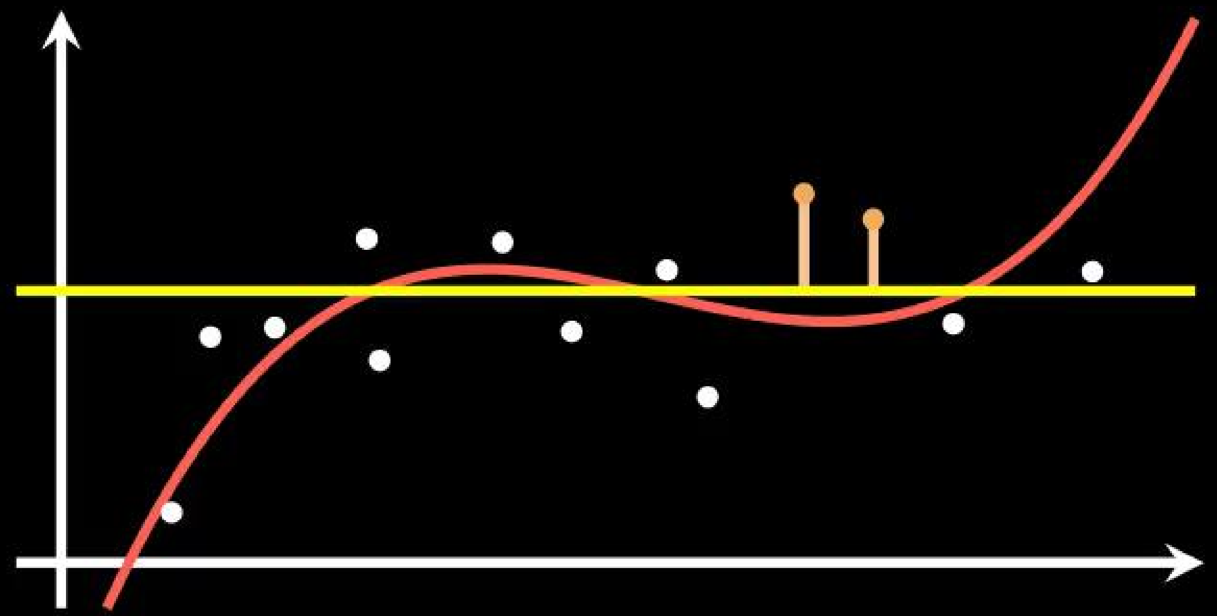

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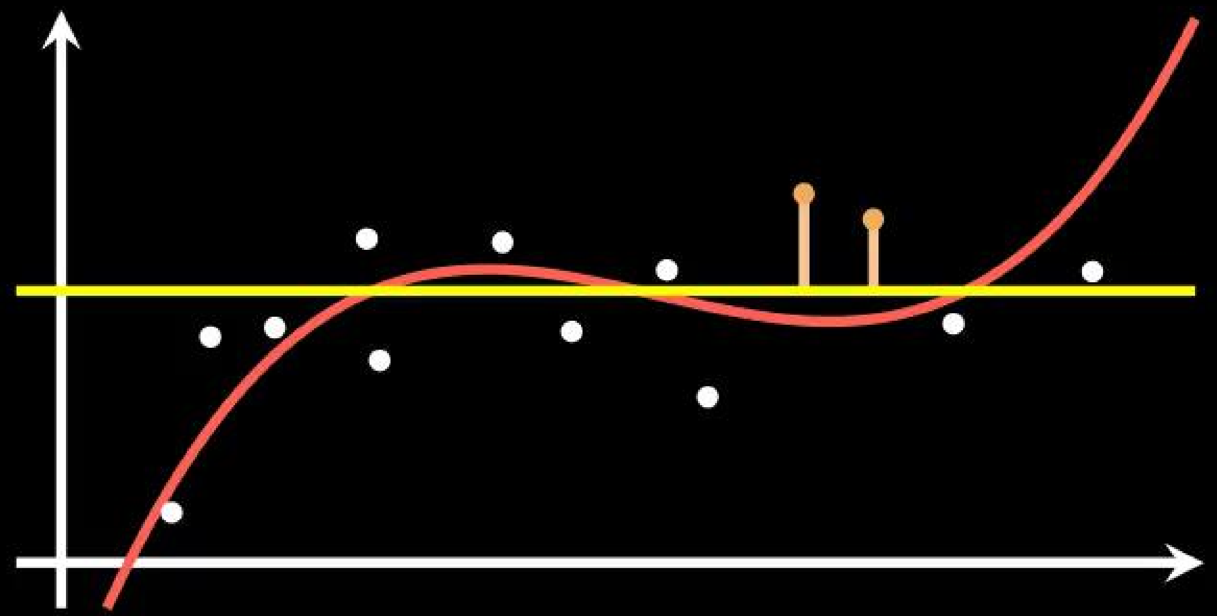

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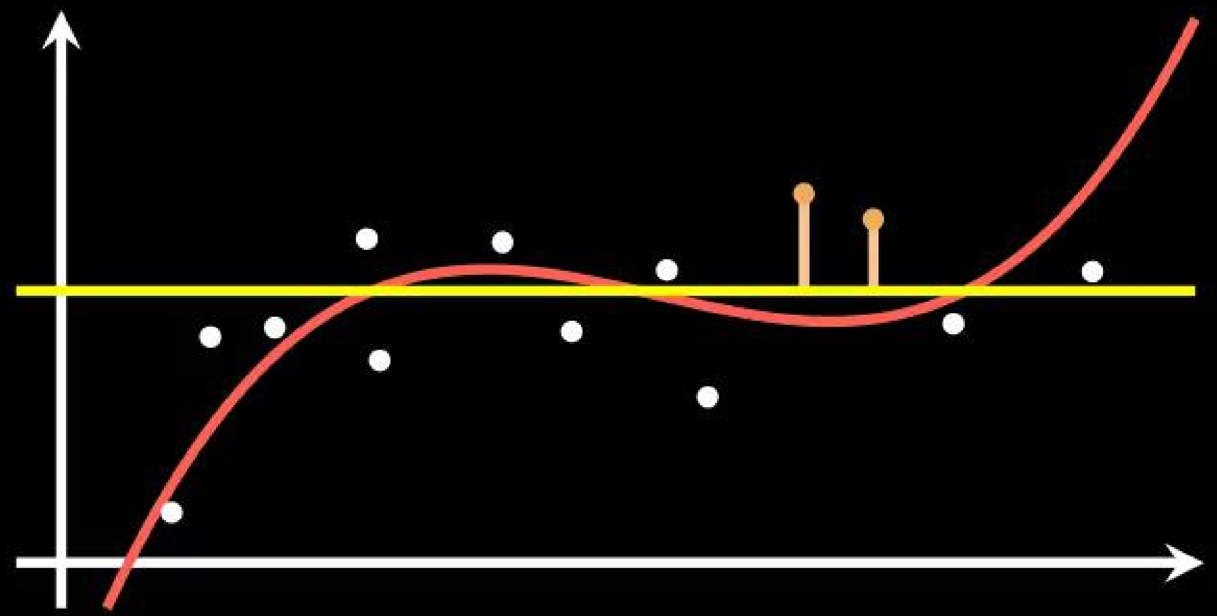

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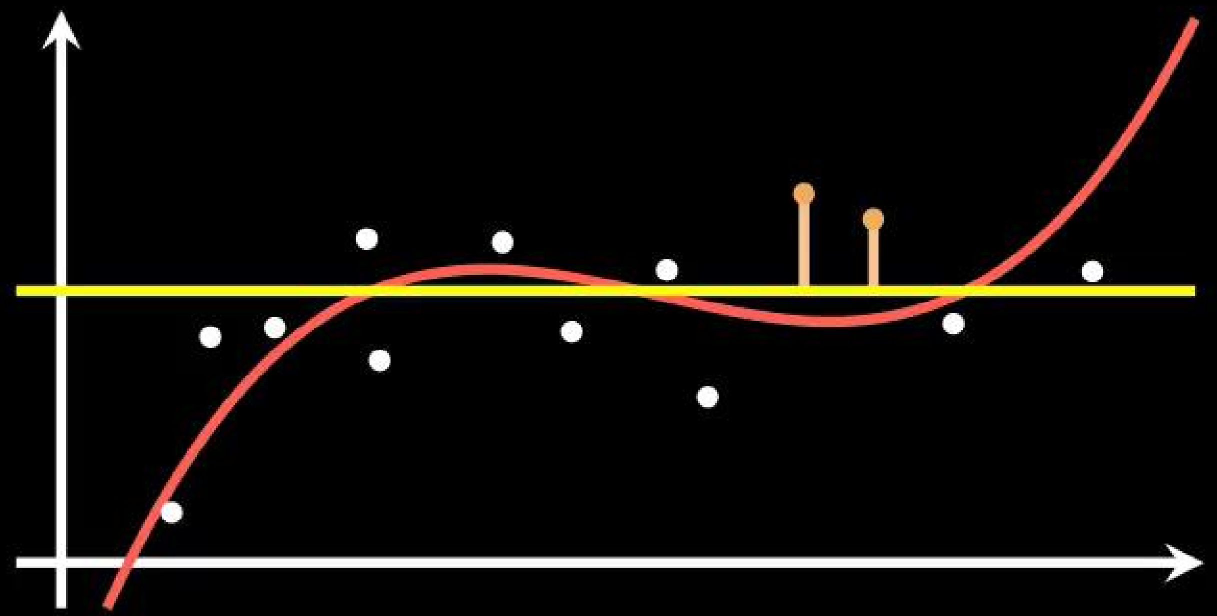

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$\longrightarrow$ Asymmetry of errors

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Fix $\sigma > 0$. Let $\mathcal{P}_{\mathrm{Mon},d}(\sigma)$ be the family of distributions P on $\mathbb{R}^d \times \mathbb{R}$ such that for $(X, Y) \sim P$,

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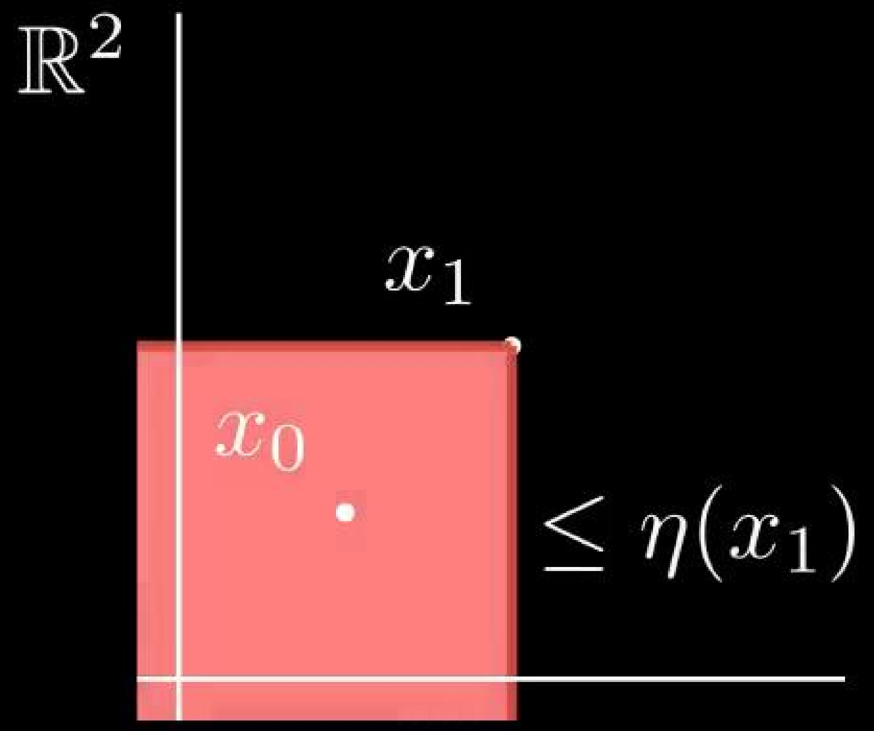

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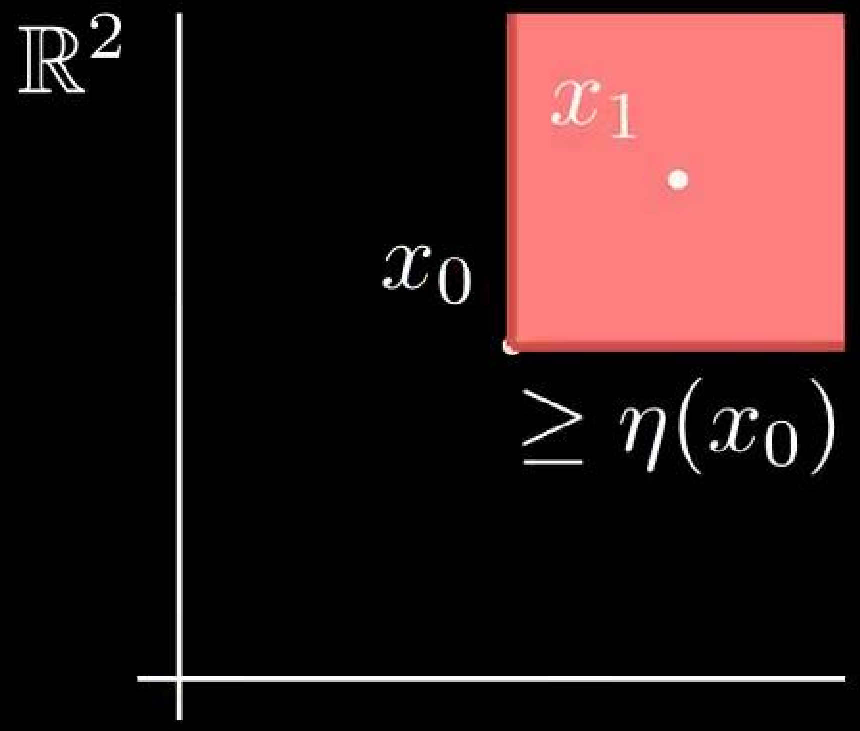

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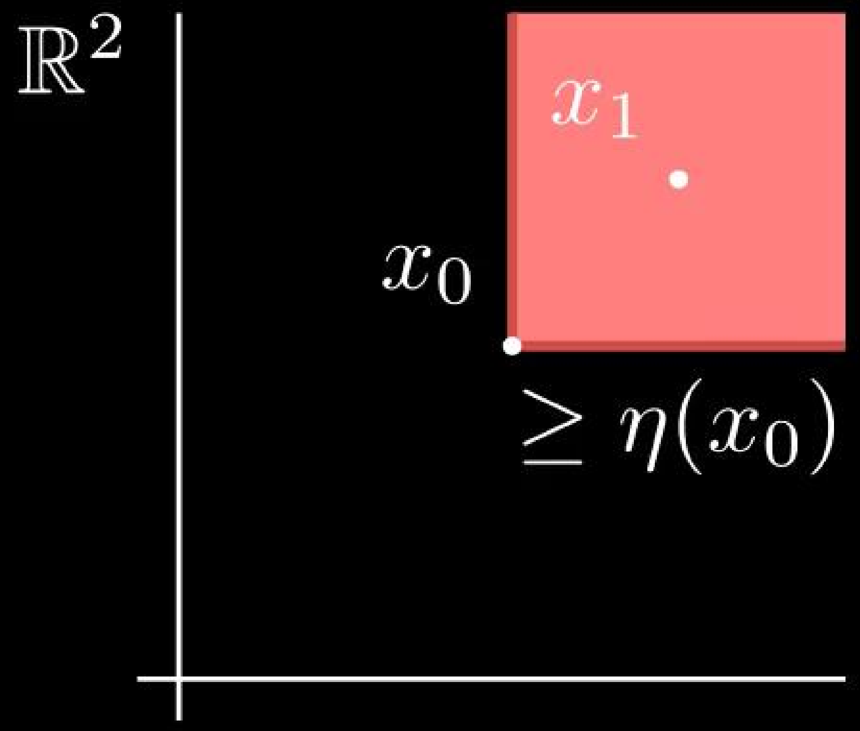

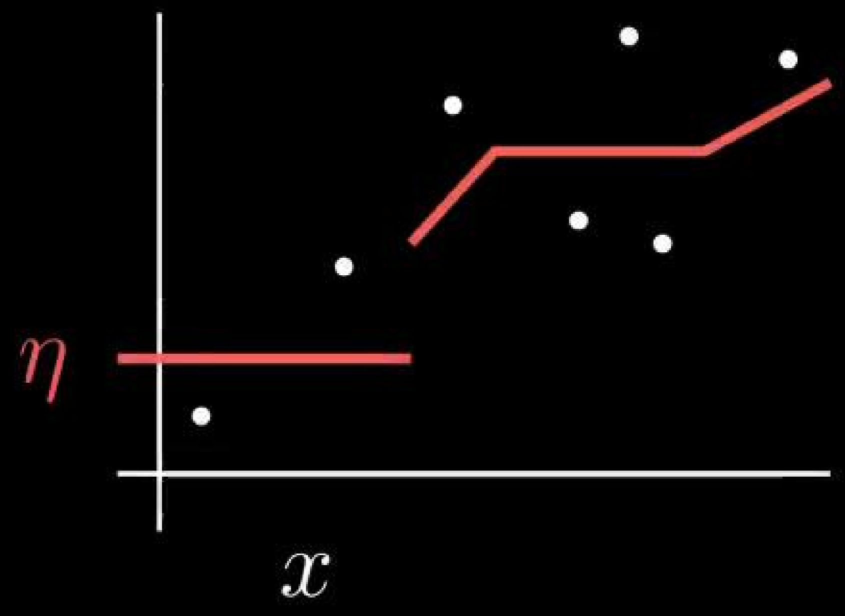

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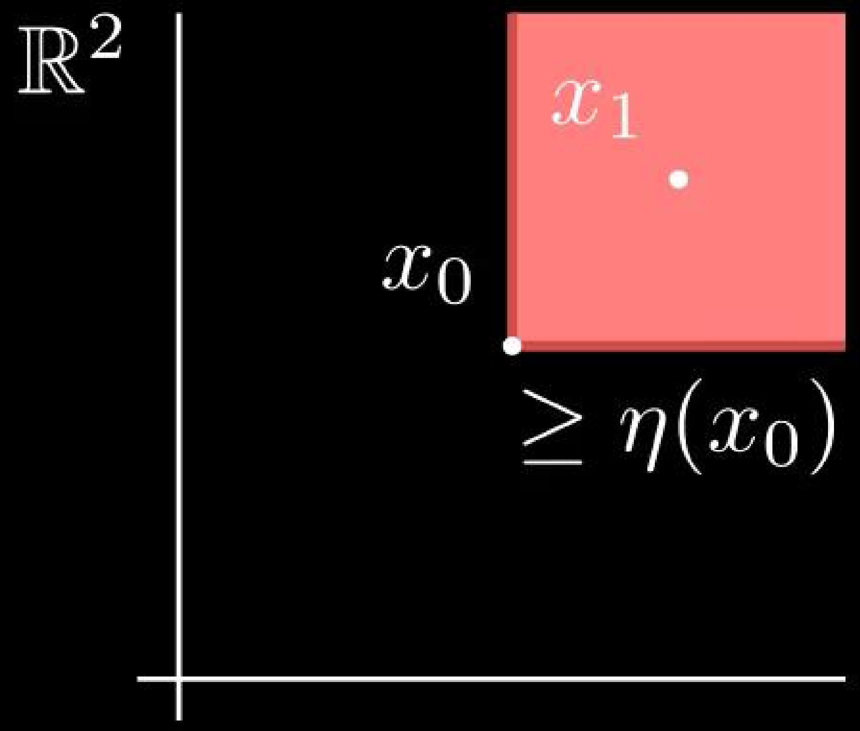
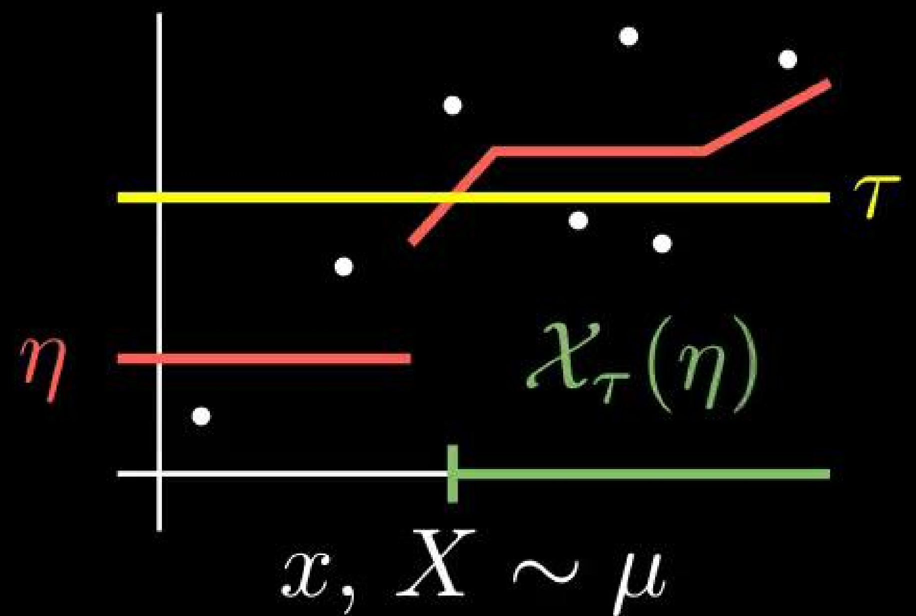


Notation:

- Fix $\tau \in \mathbb{R}$. Define τ-superlevel set by

$$\mathcal{X}_\tau(\eta) := \{x \in \mathbb{R}^d : \eta(x) \geq \tau\}$$

- Denote the marginal distribution of X by μ.



Goal

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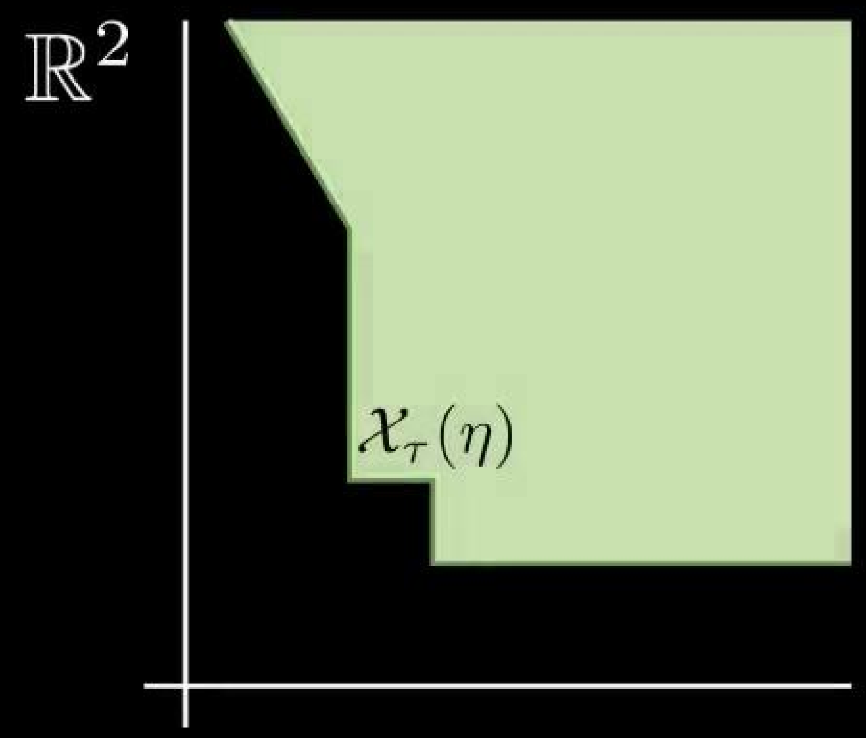

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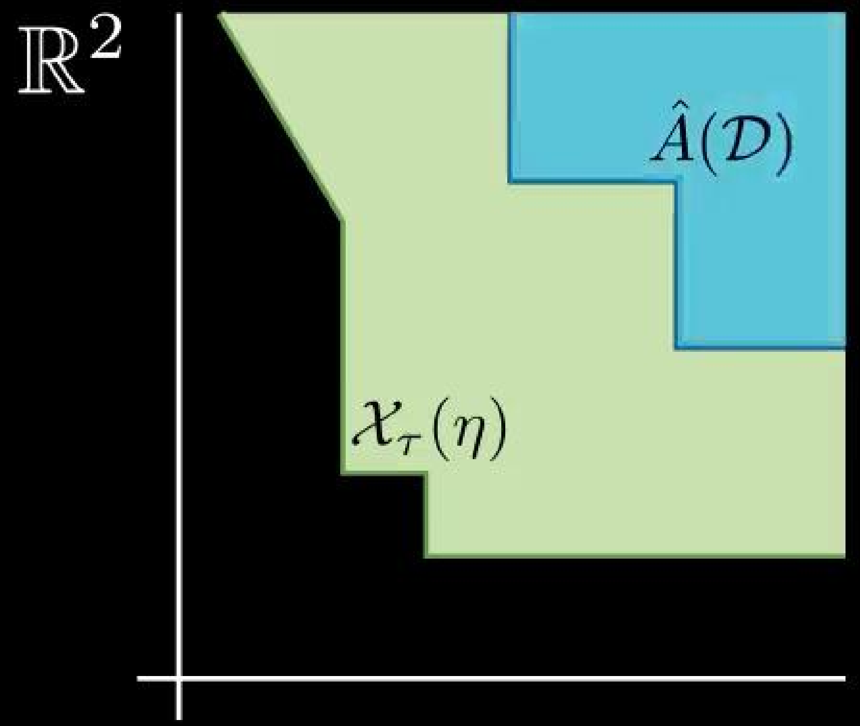
Type I error control: Fix $\alpha \in (0, 1)$. Require

$$\inf_{P \in \mathcal{P}_{\mathrm{Mon},d}(\sigma)} \mathbb{P}\big\{\hat{A}(\mathcal{D}) \subseteq \mathcal{X}_\tau(\eta)\big\} \geq 1 - \alpha.$$



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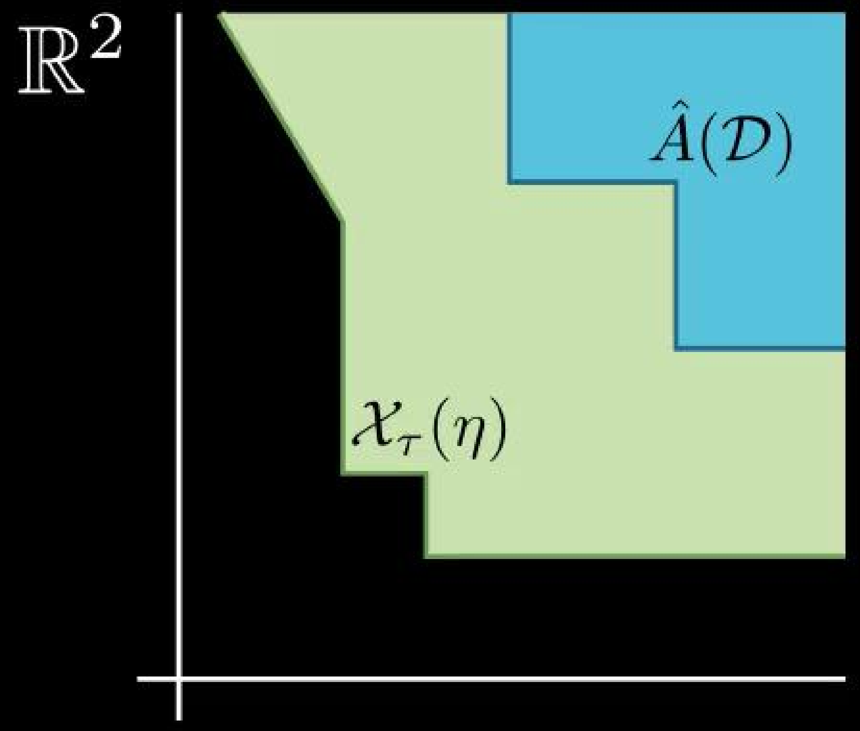

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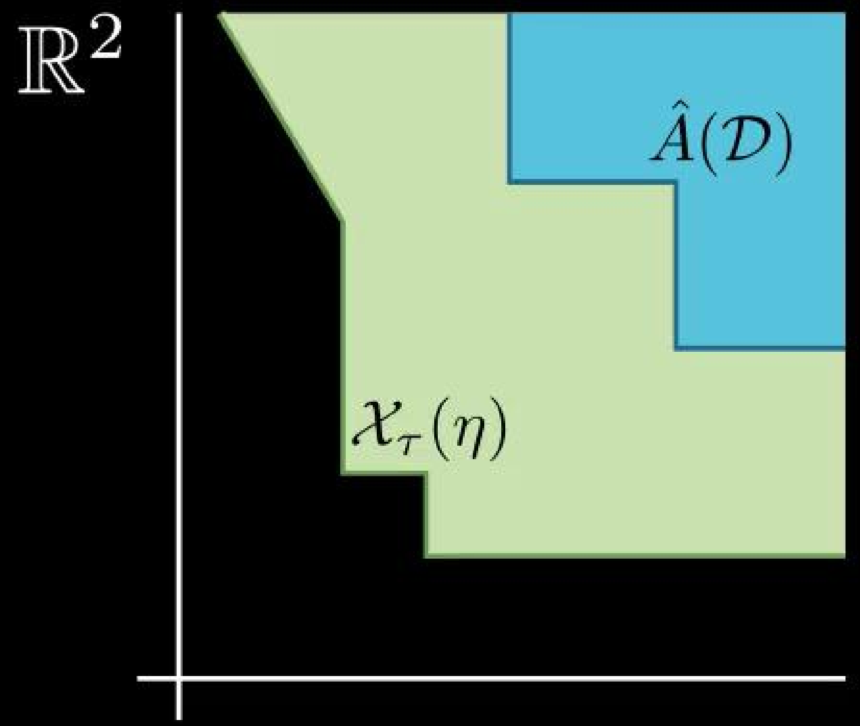

Example:

Type I error: $\hat{A}$ should contain only those HIV-patients for whom the conditional probability of not facing a negative event within the next 5 years is at least 98%.

High-level strategy

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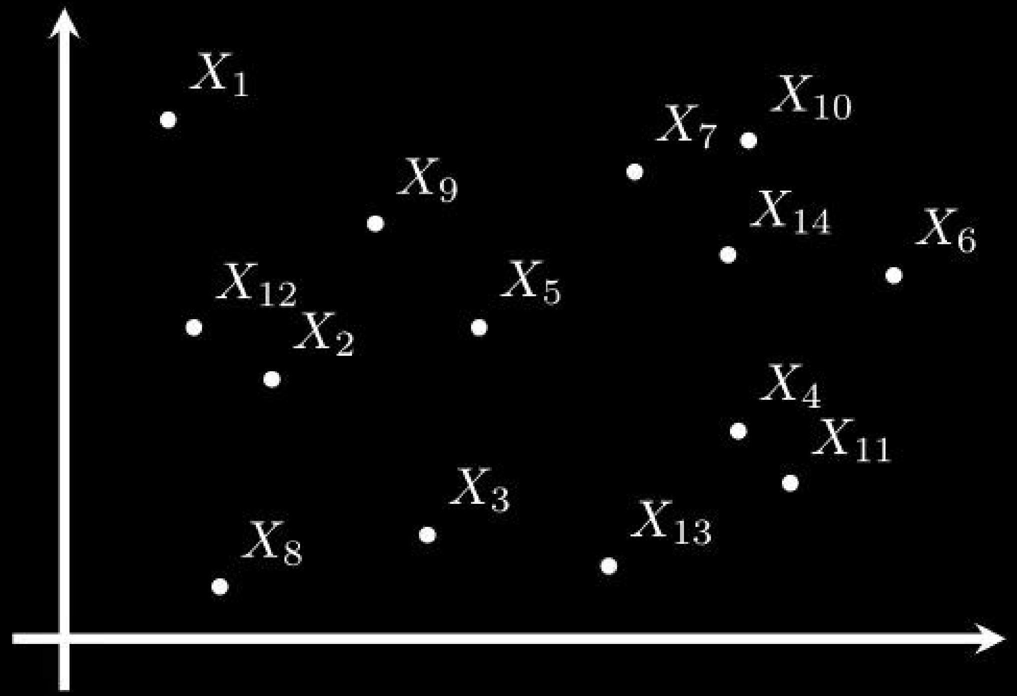

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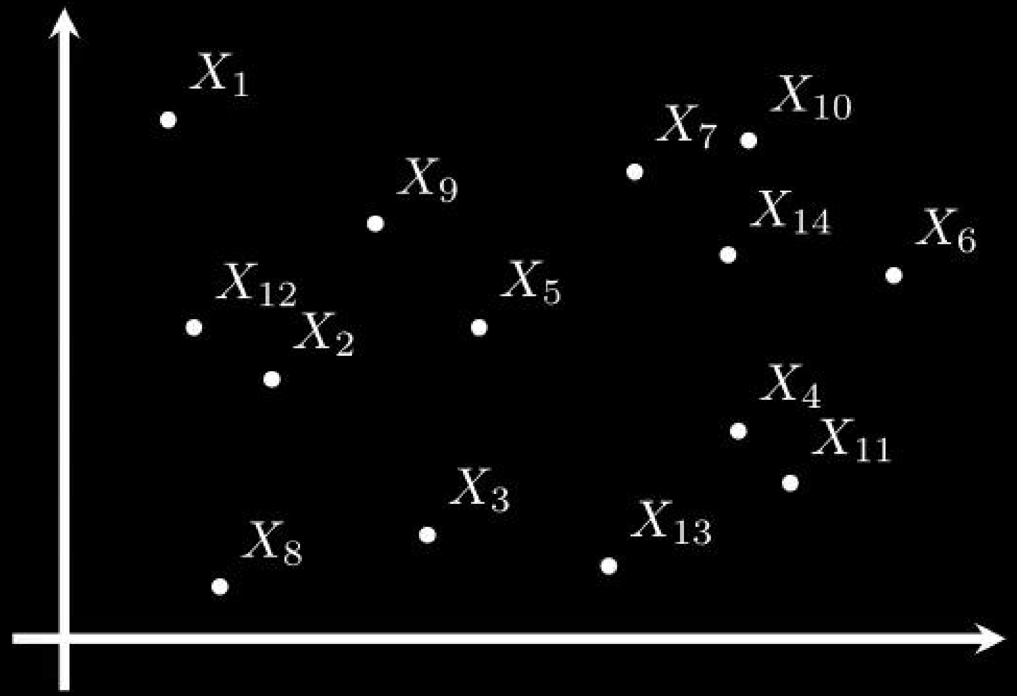

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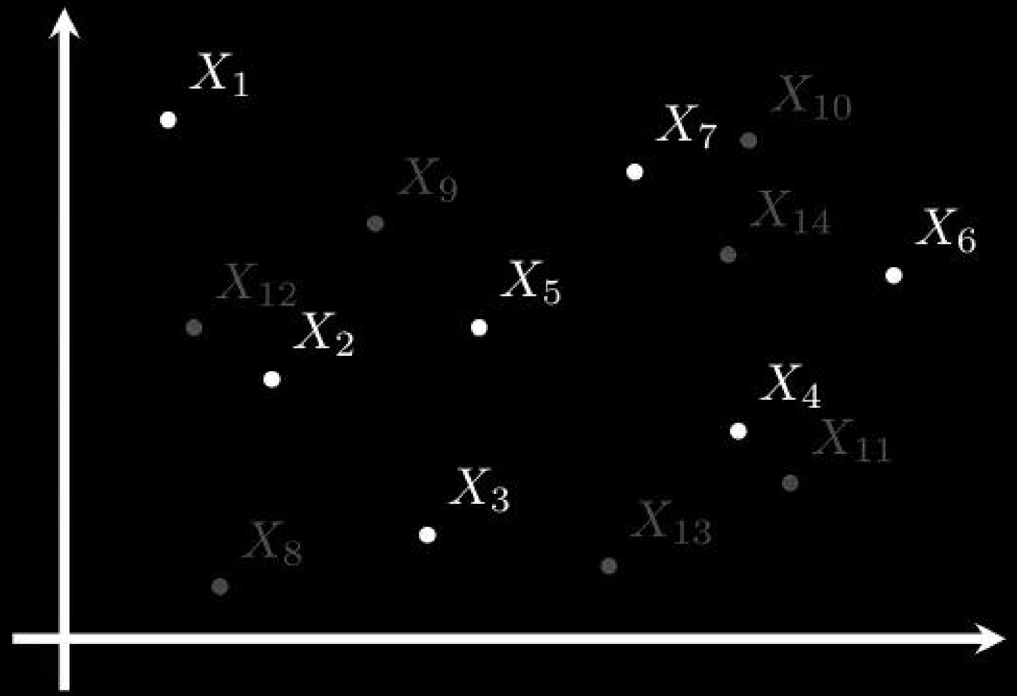

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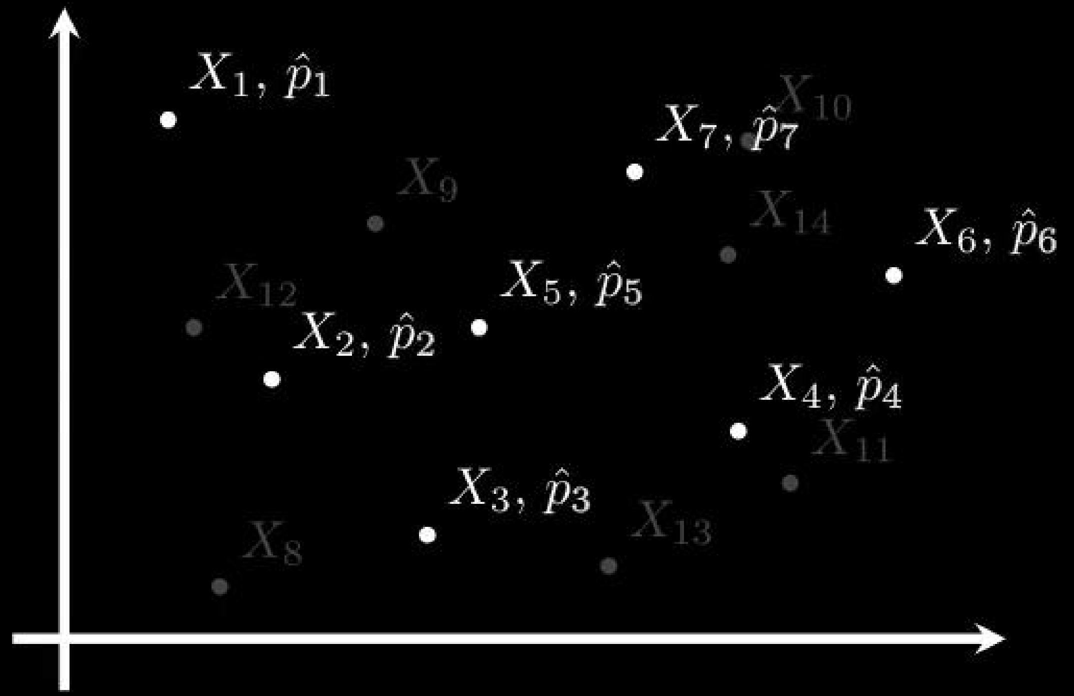

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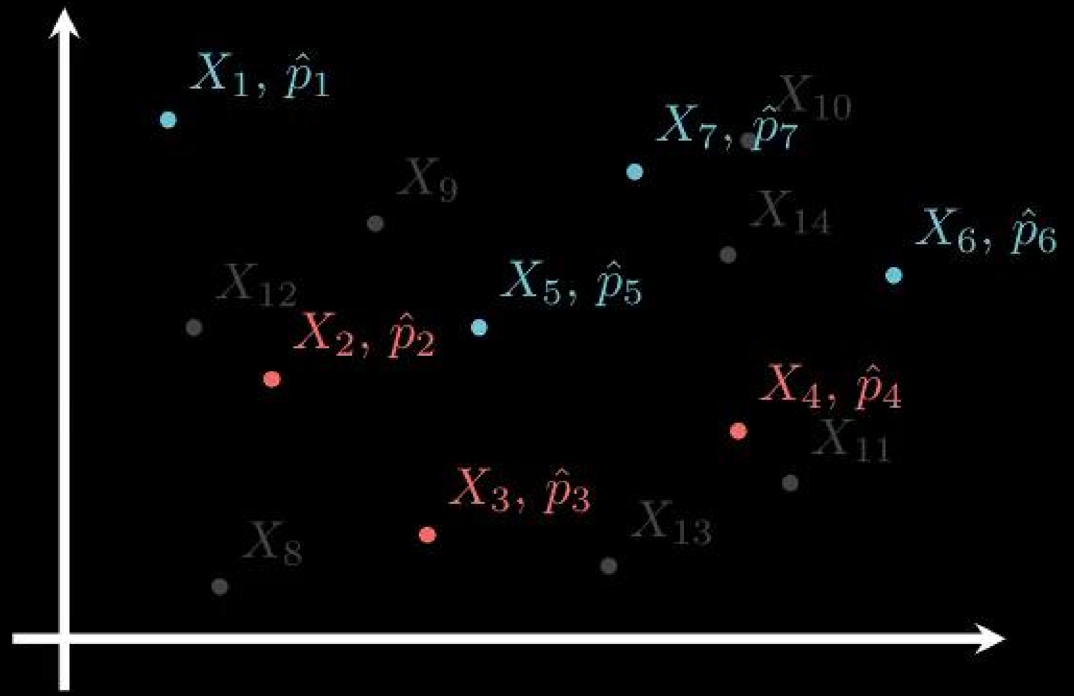

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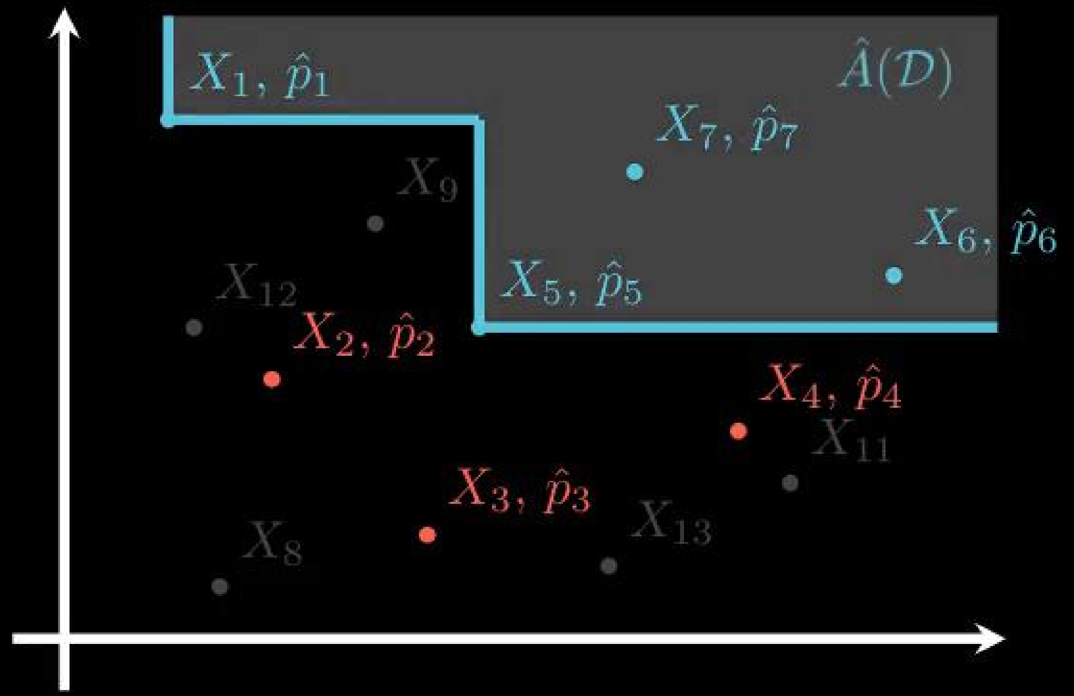

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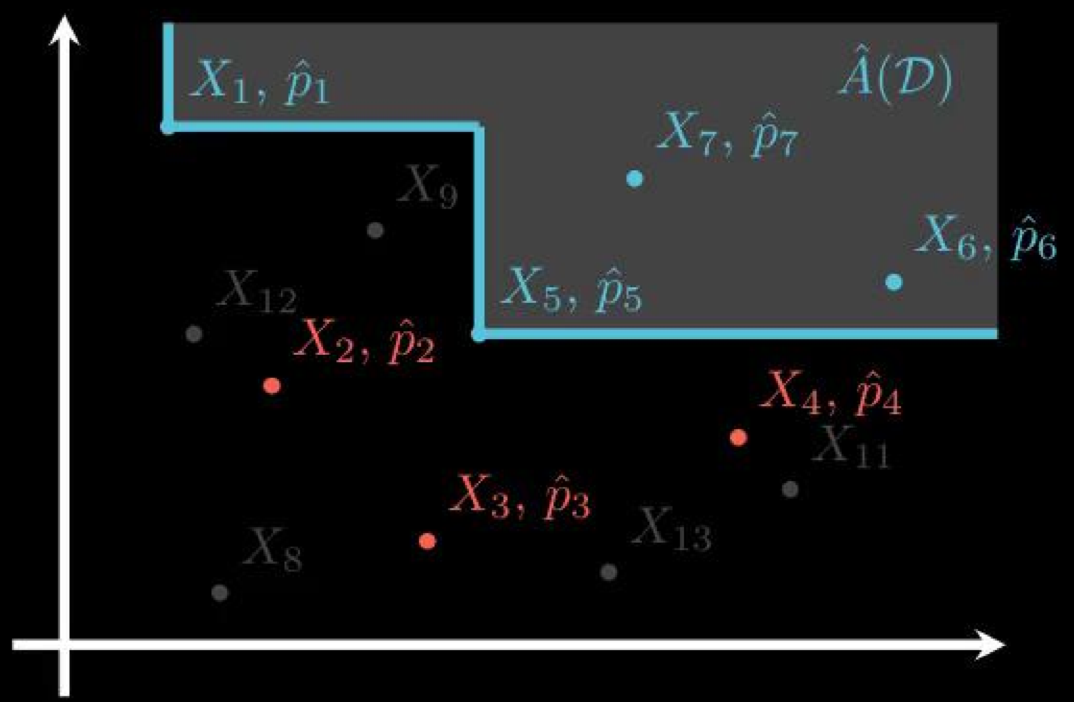

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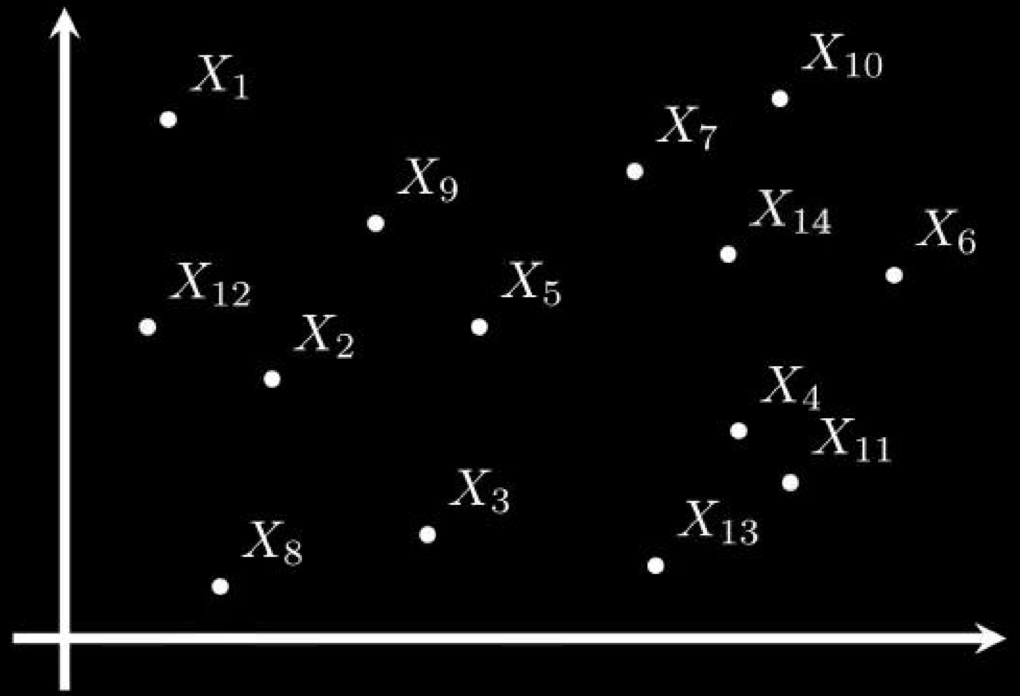

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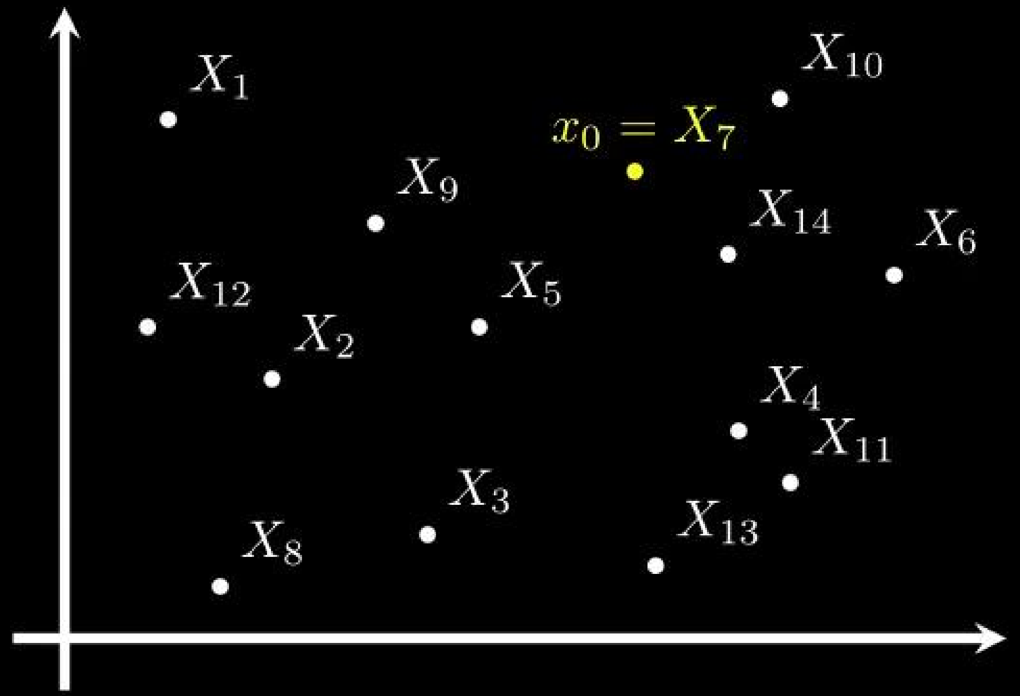

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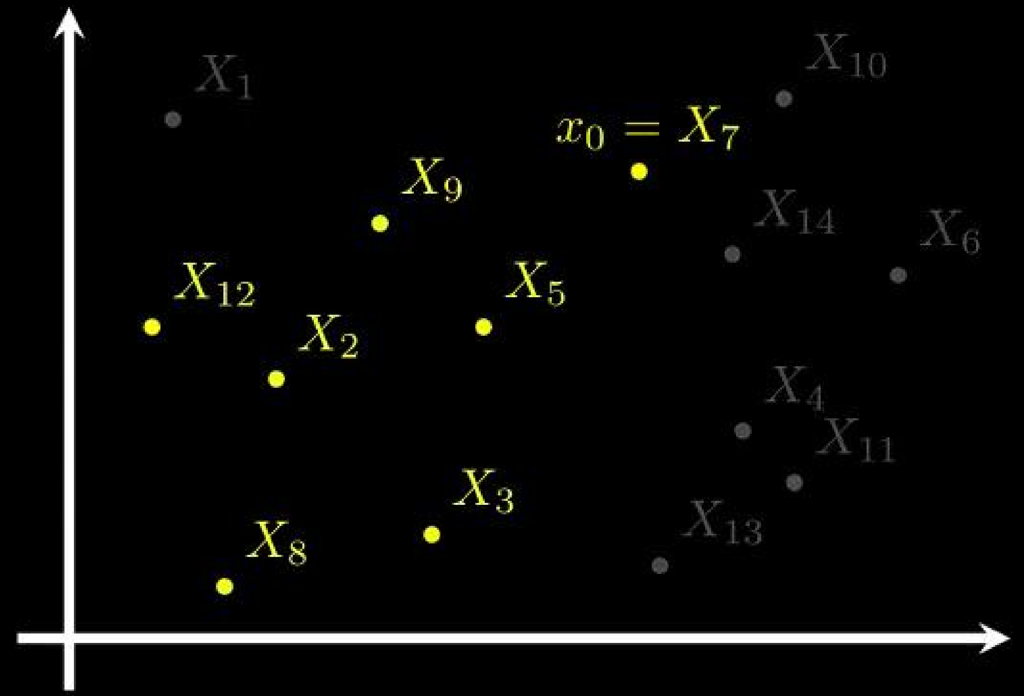

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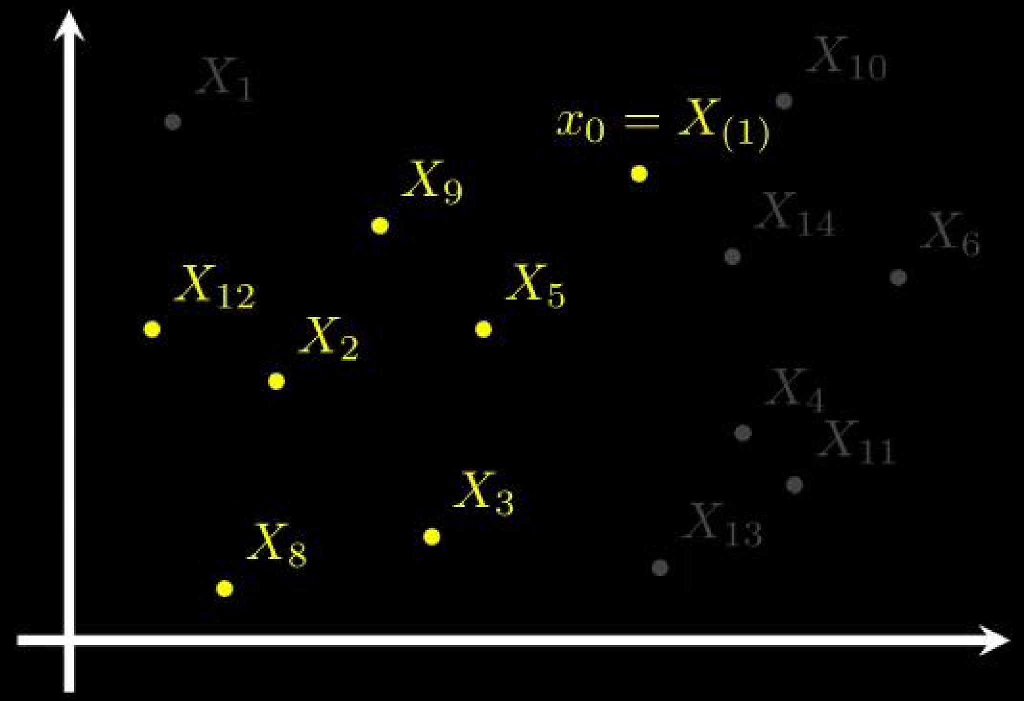

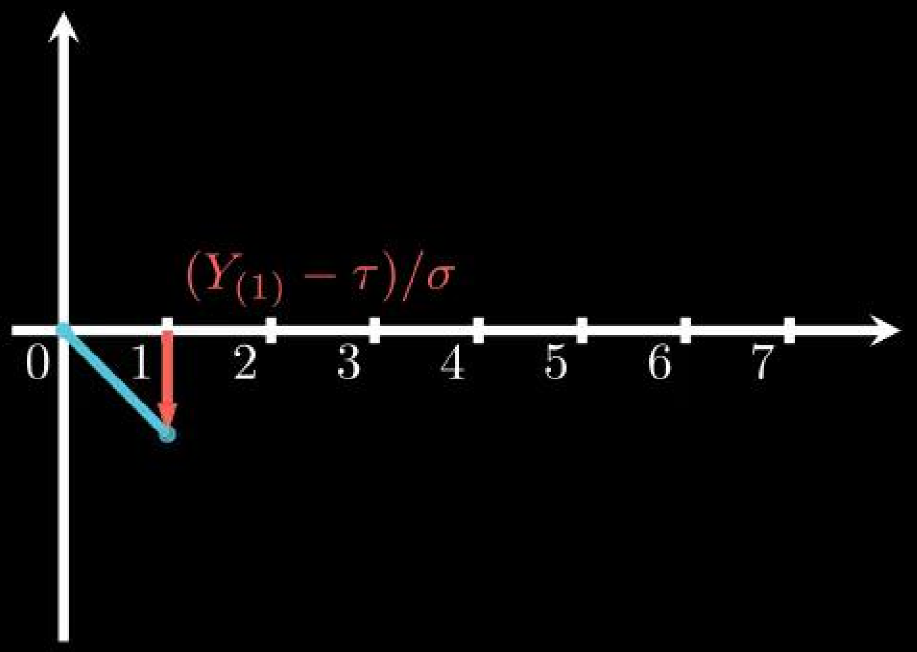

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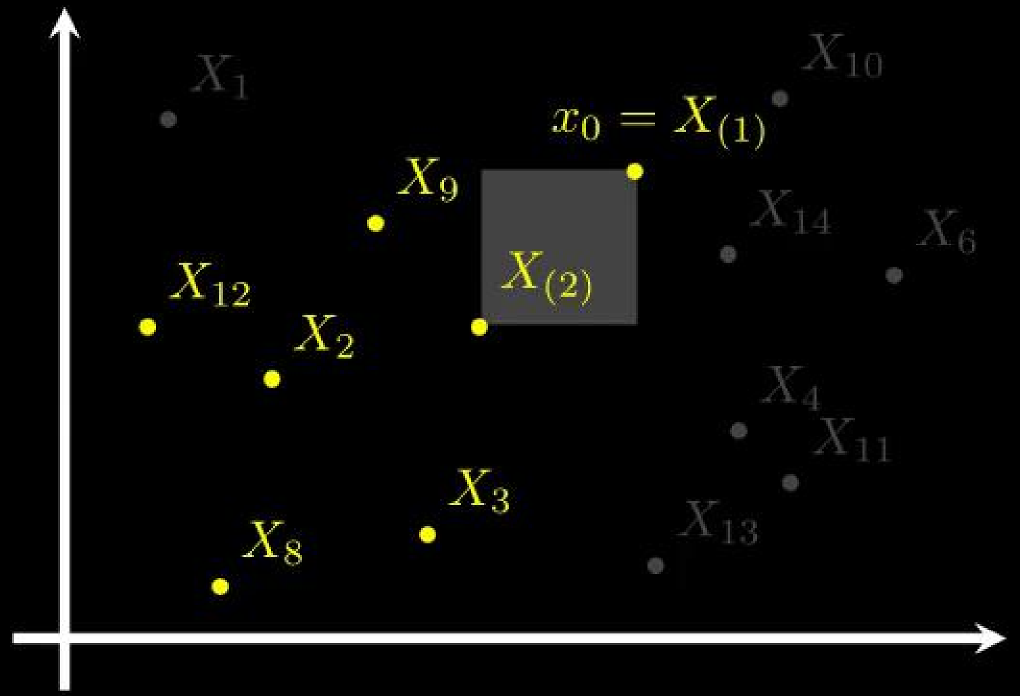

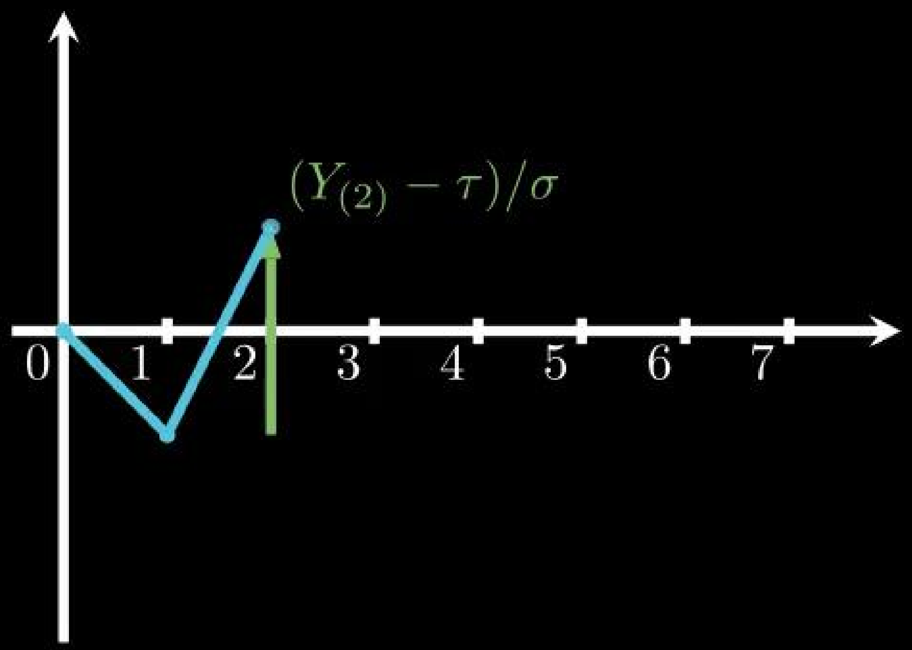

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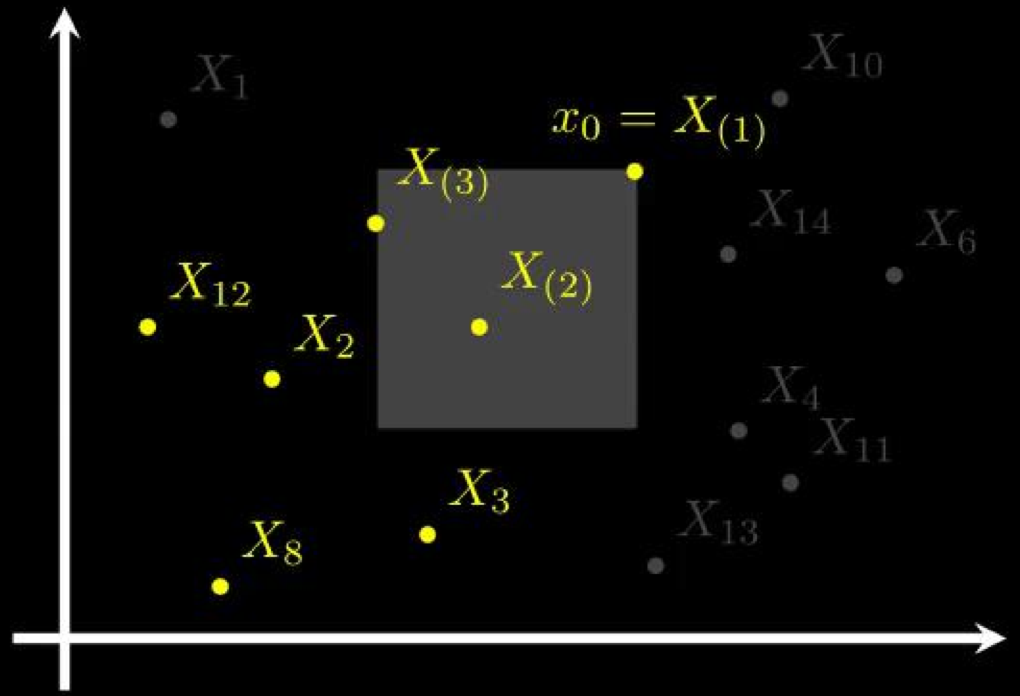

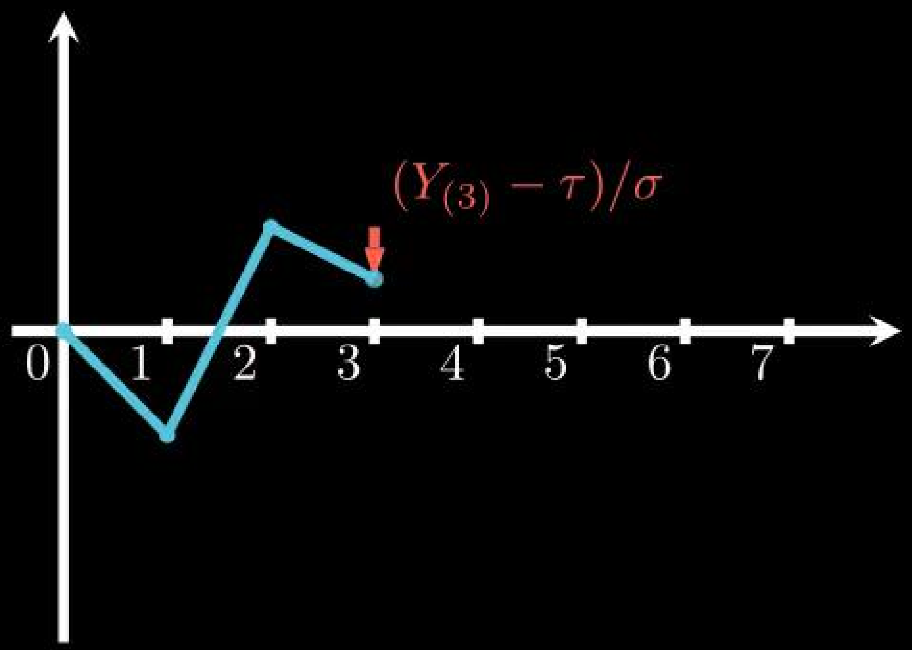

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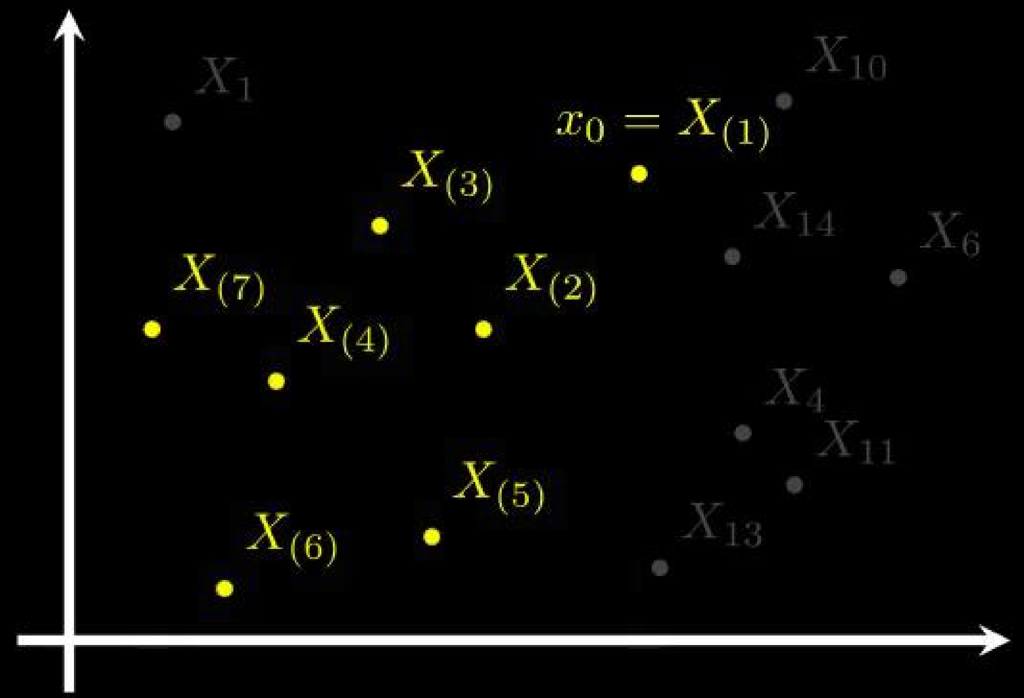

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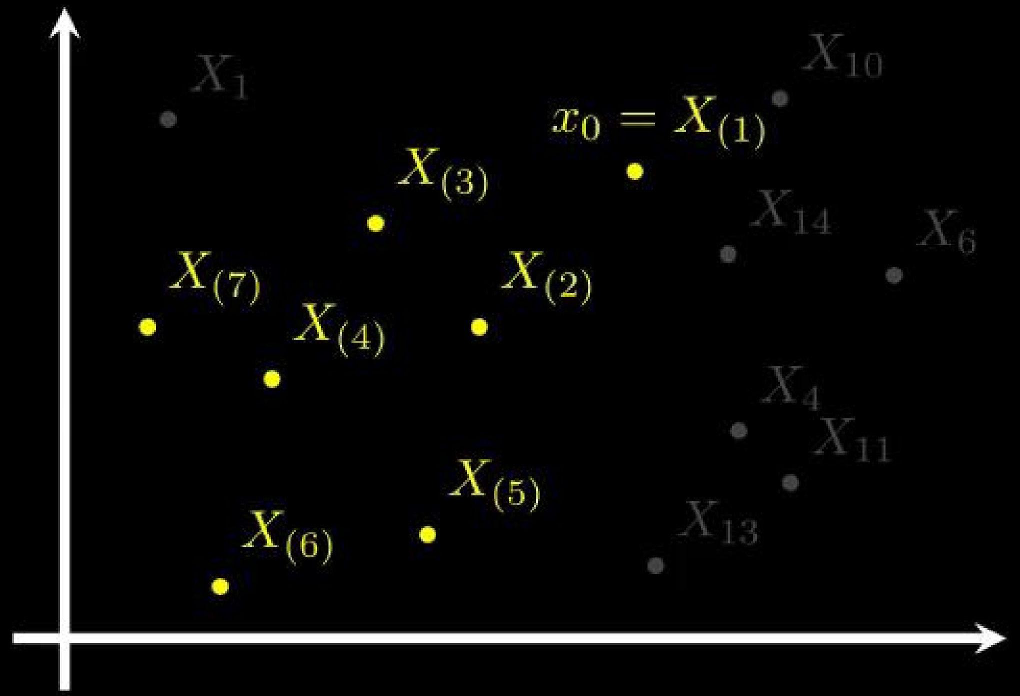

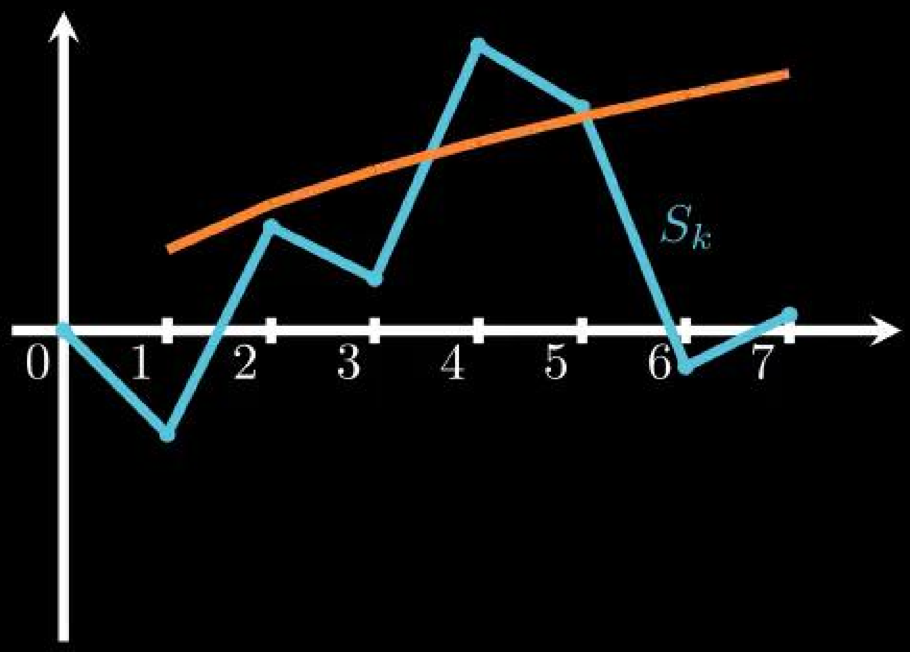

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$$S_k := \sum_{j=1}^{k} \frac{Y_{(j)} - \tau}{\sigma}.$$

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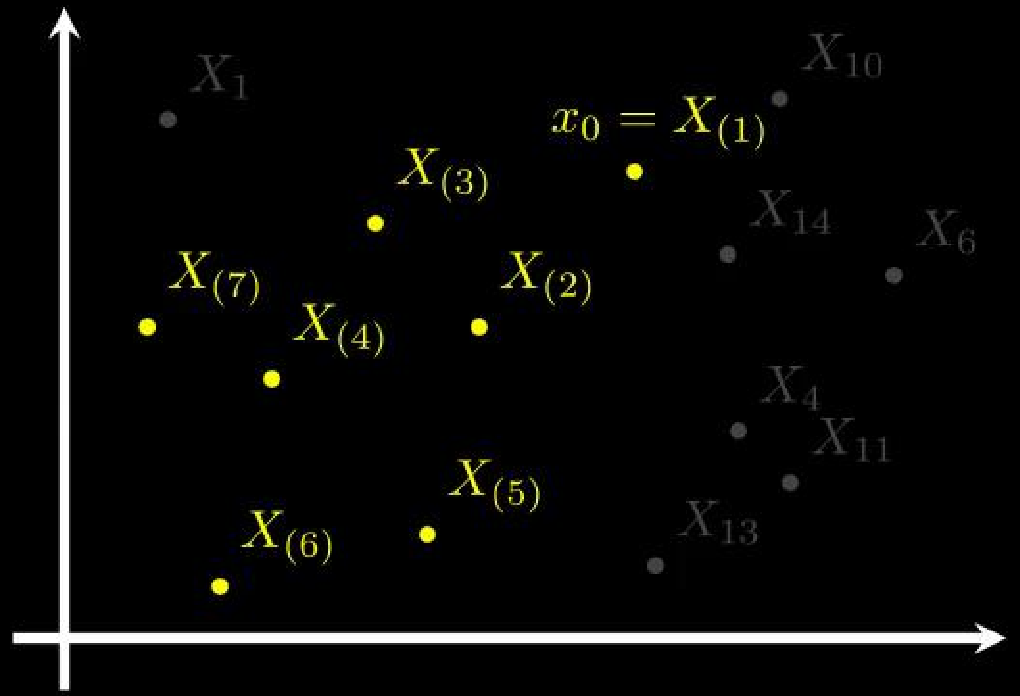

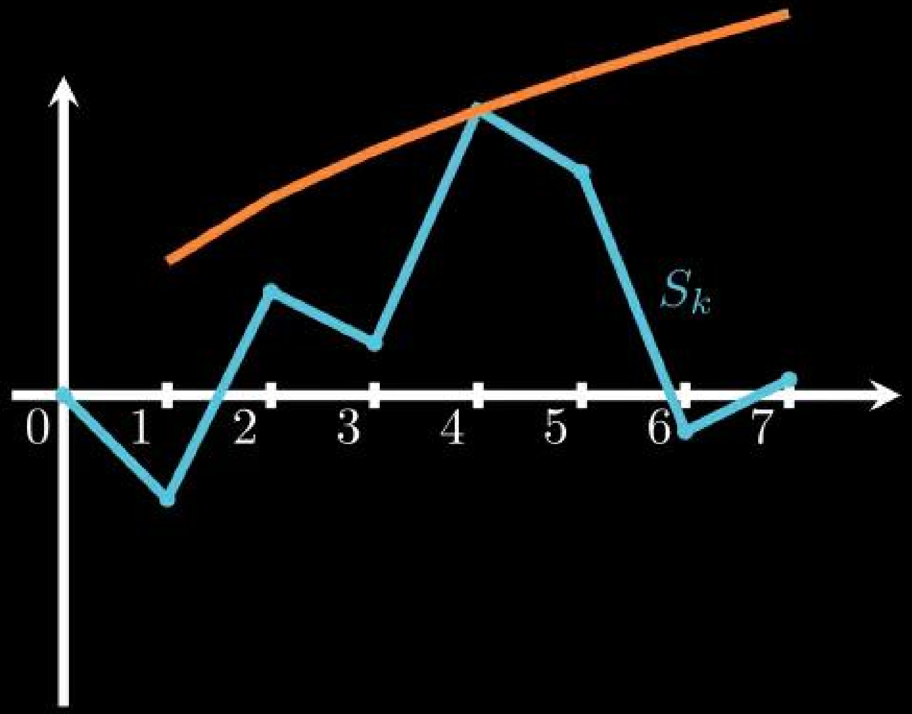

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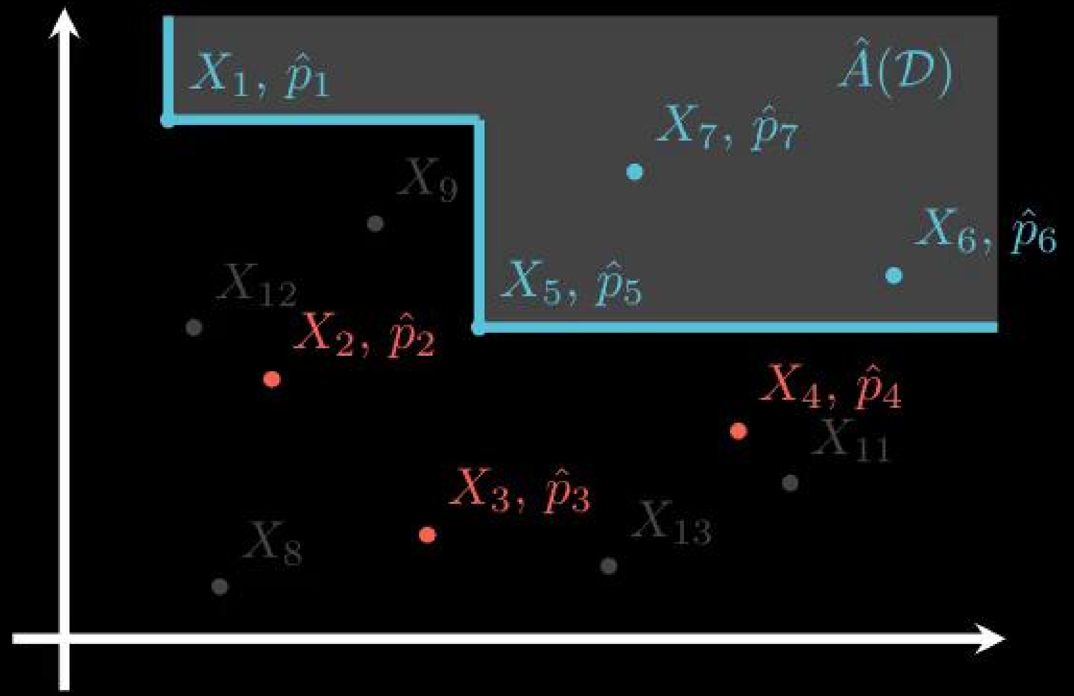

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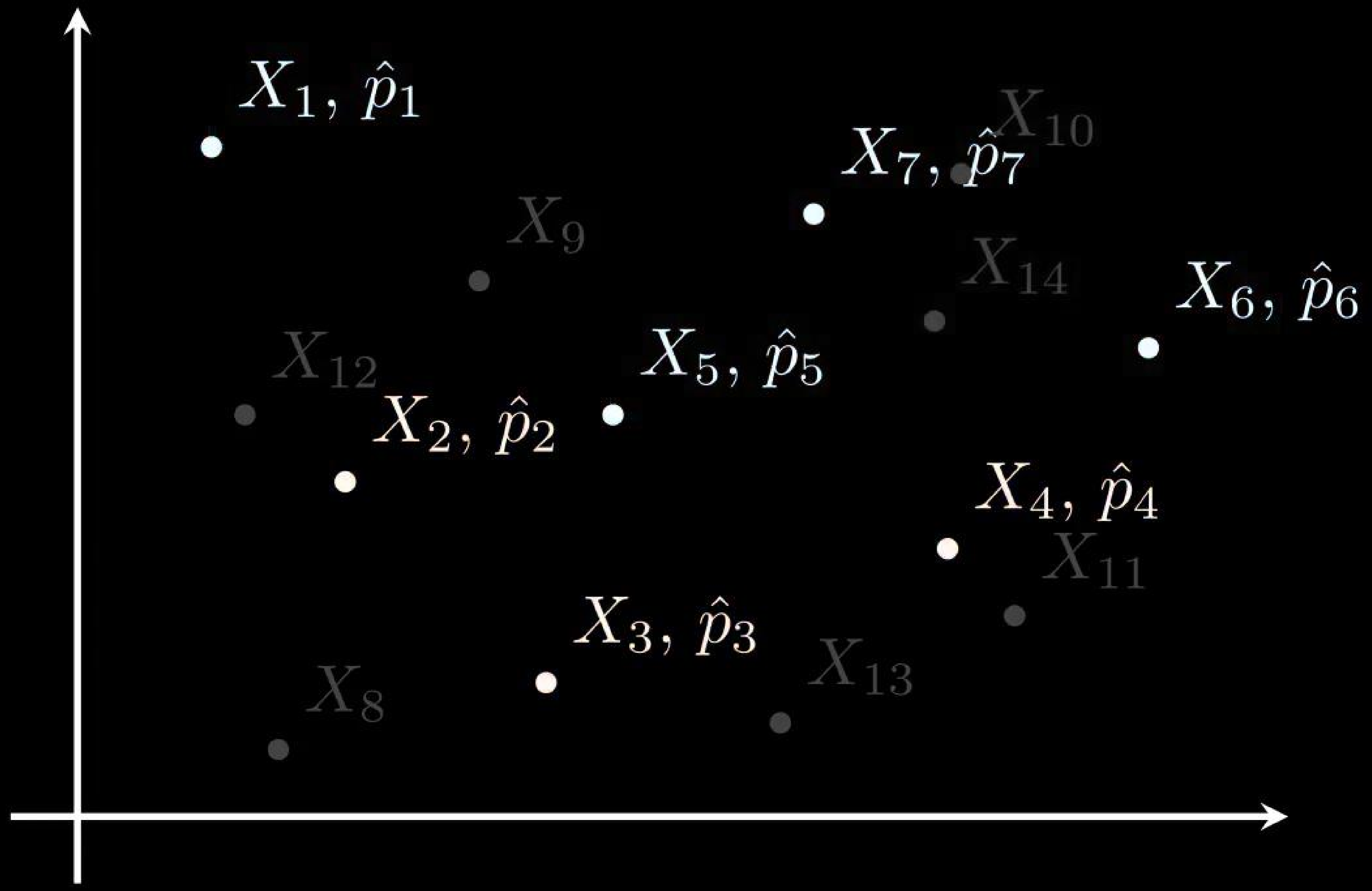

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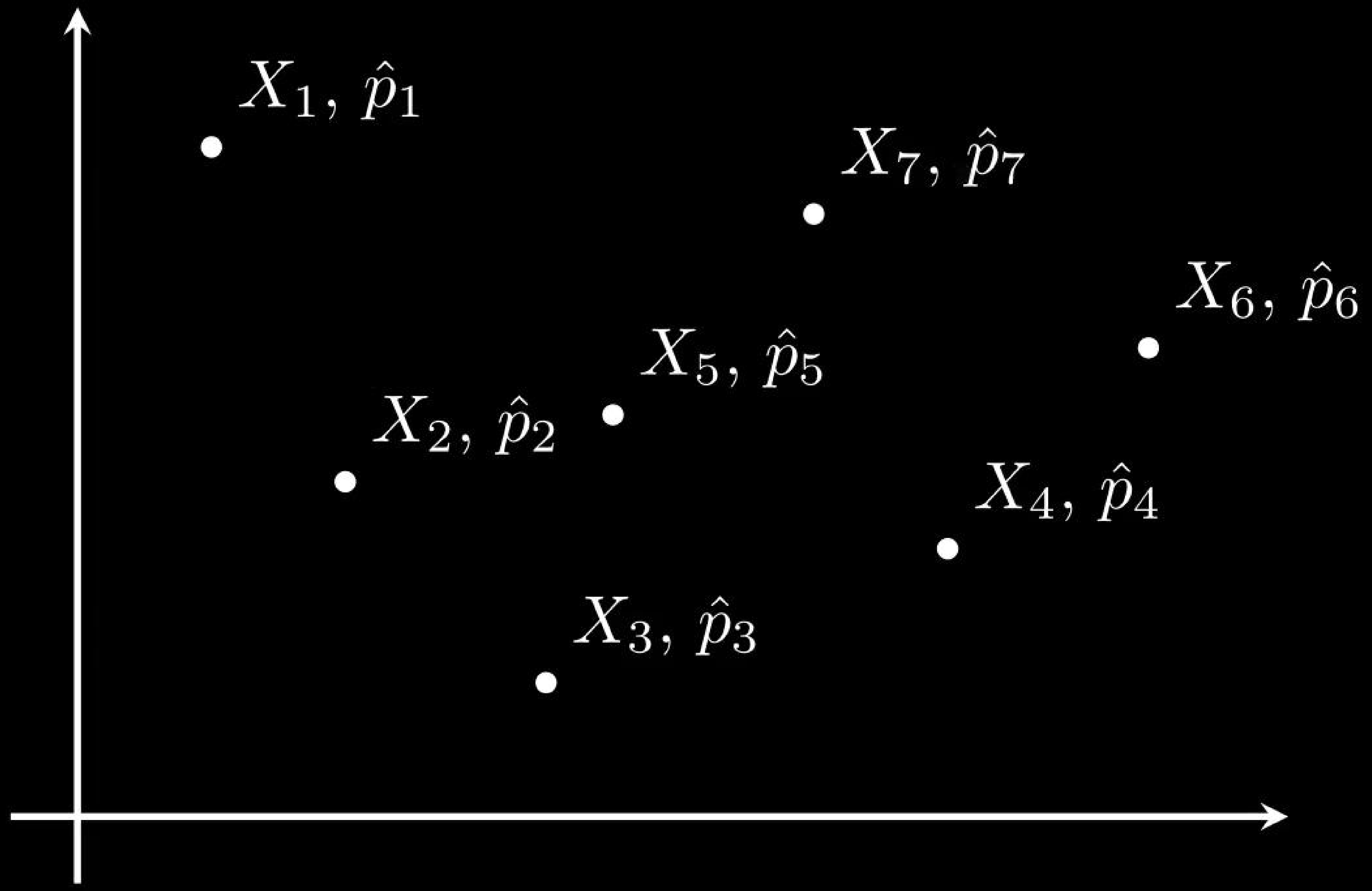

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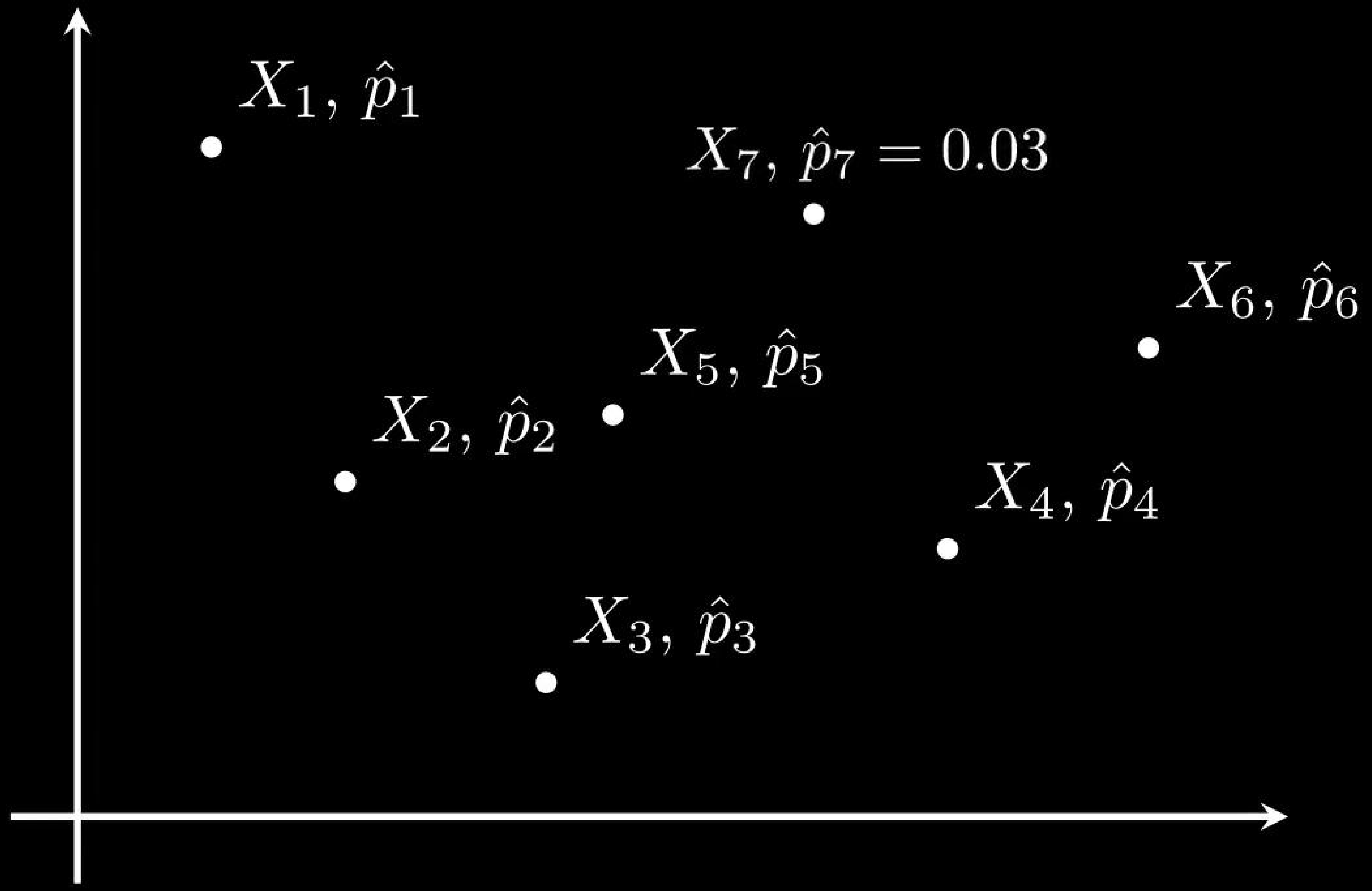

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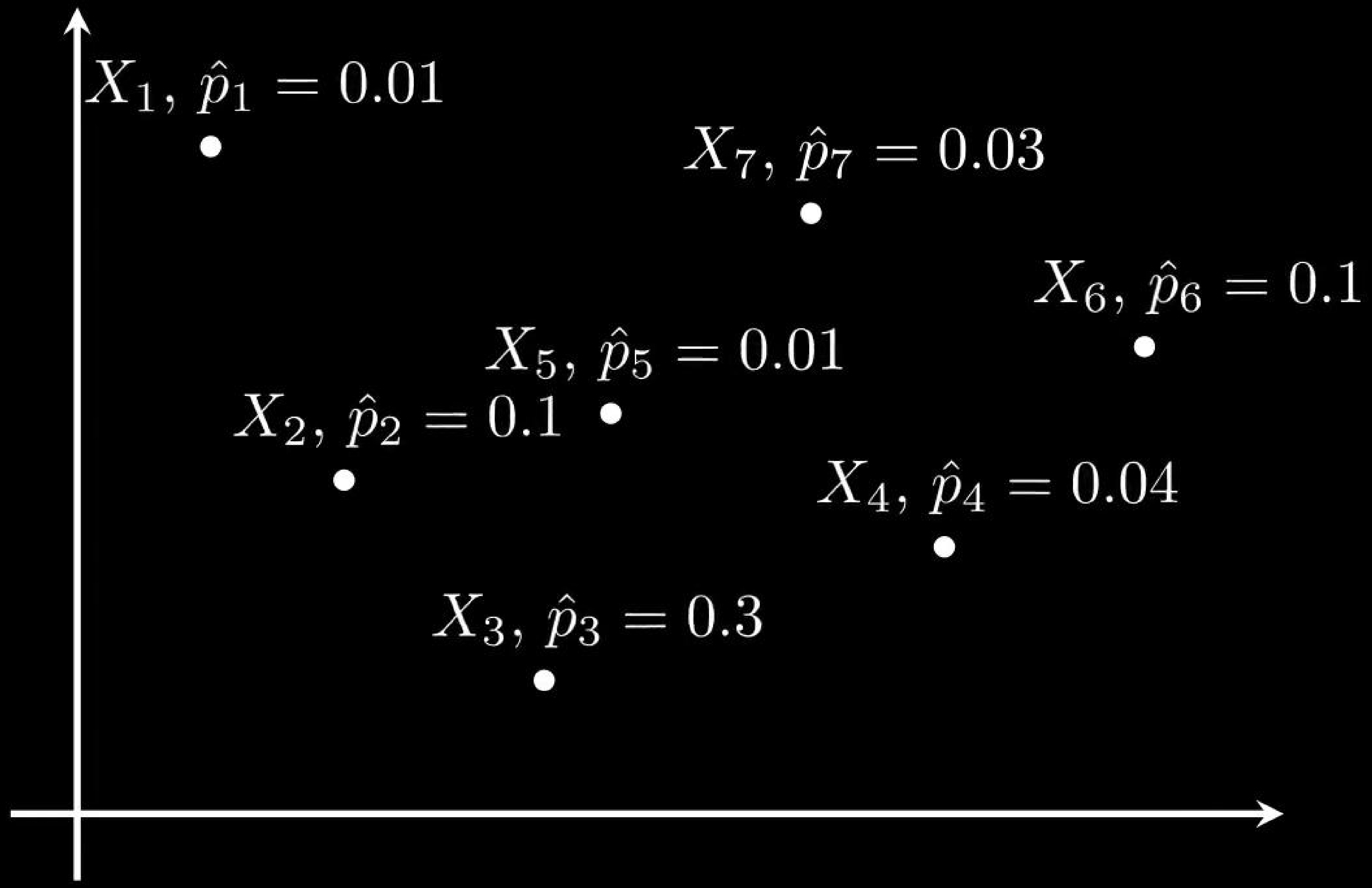

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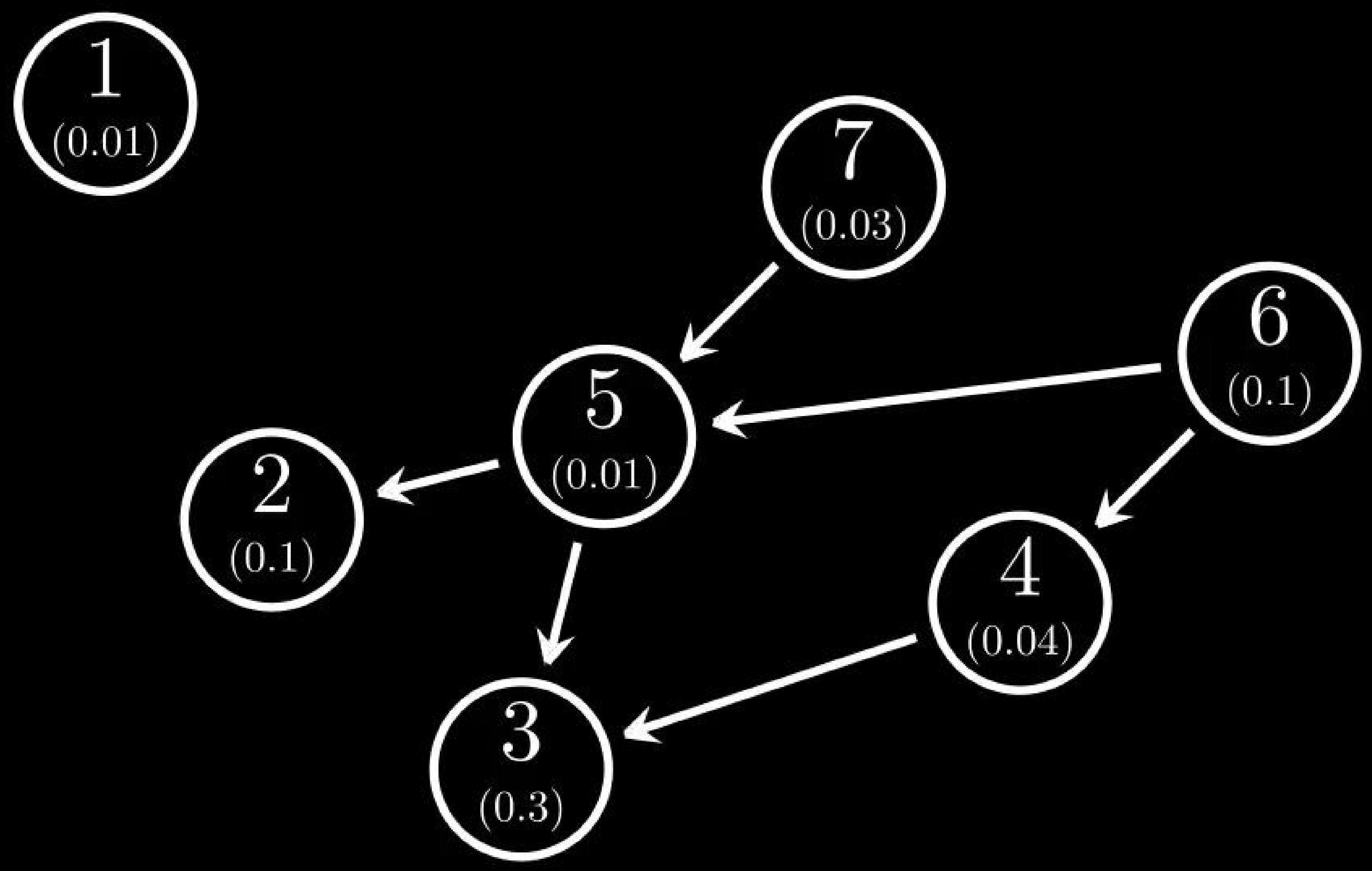

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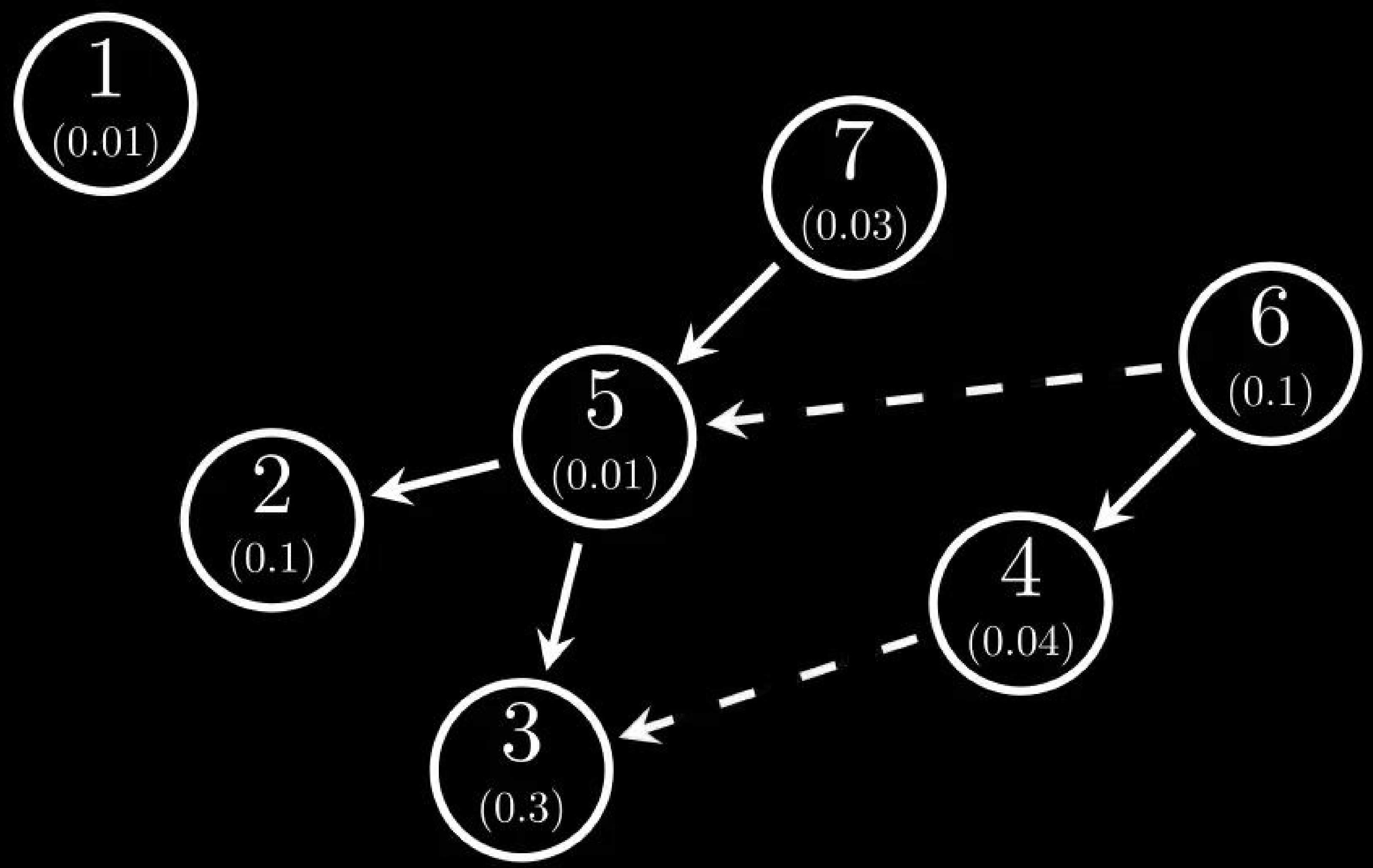

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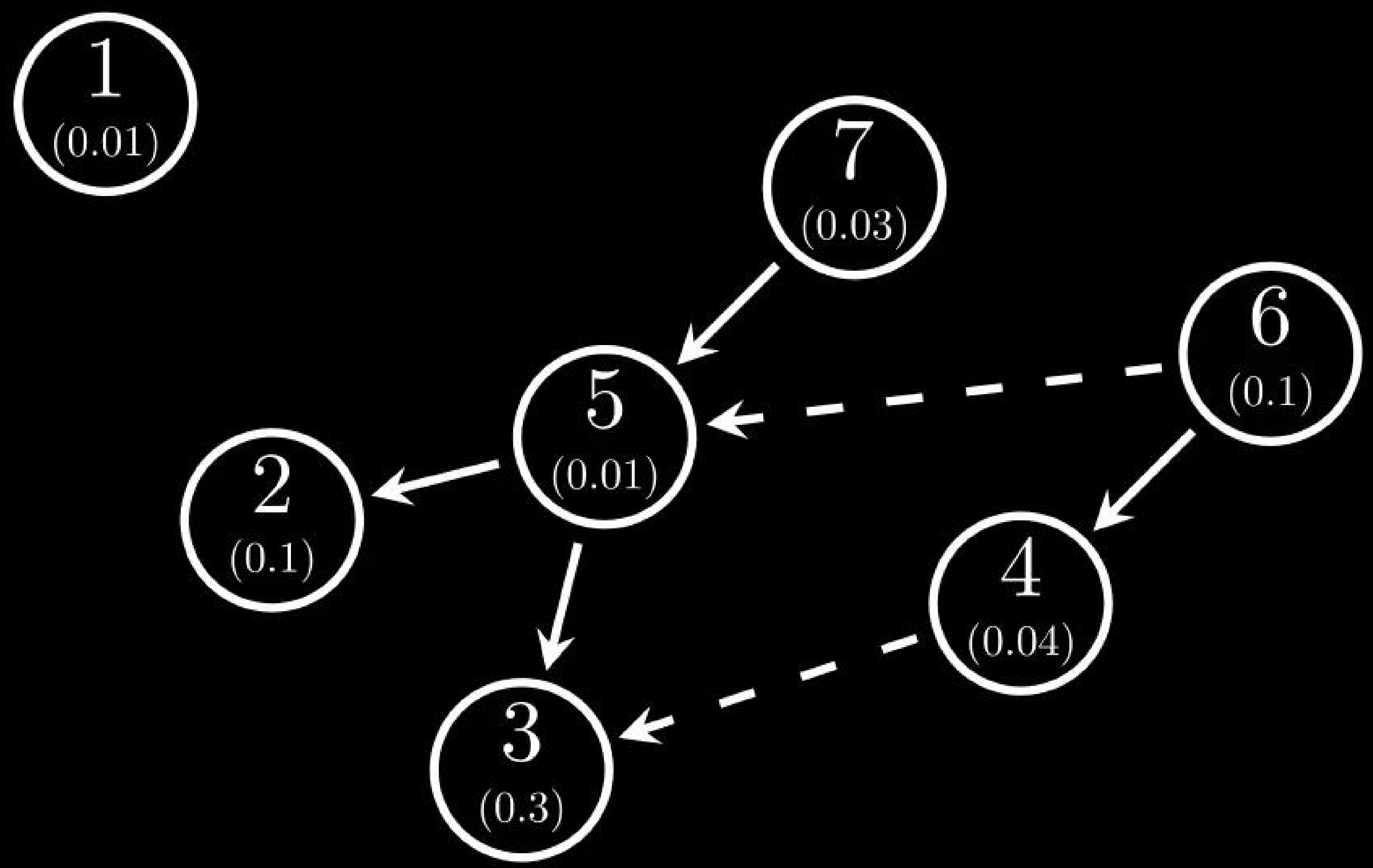

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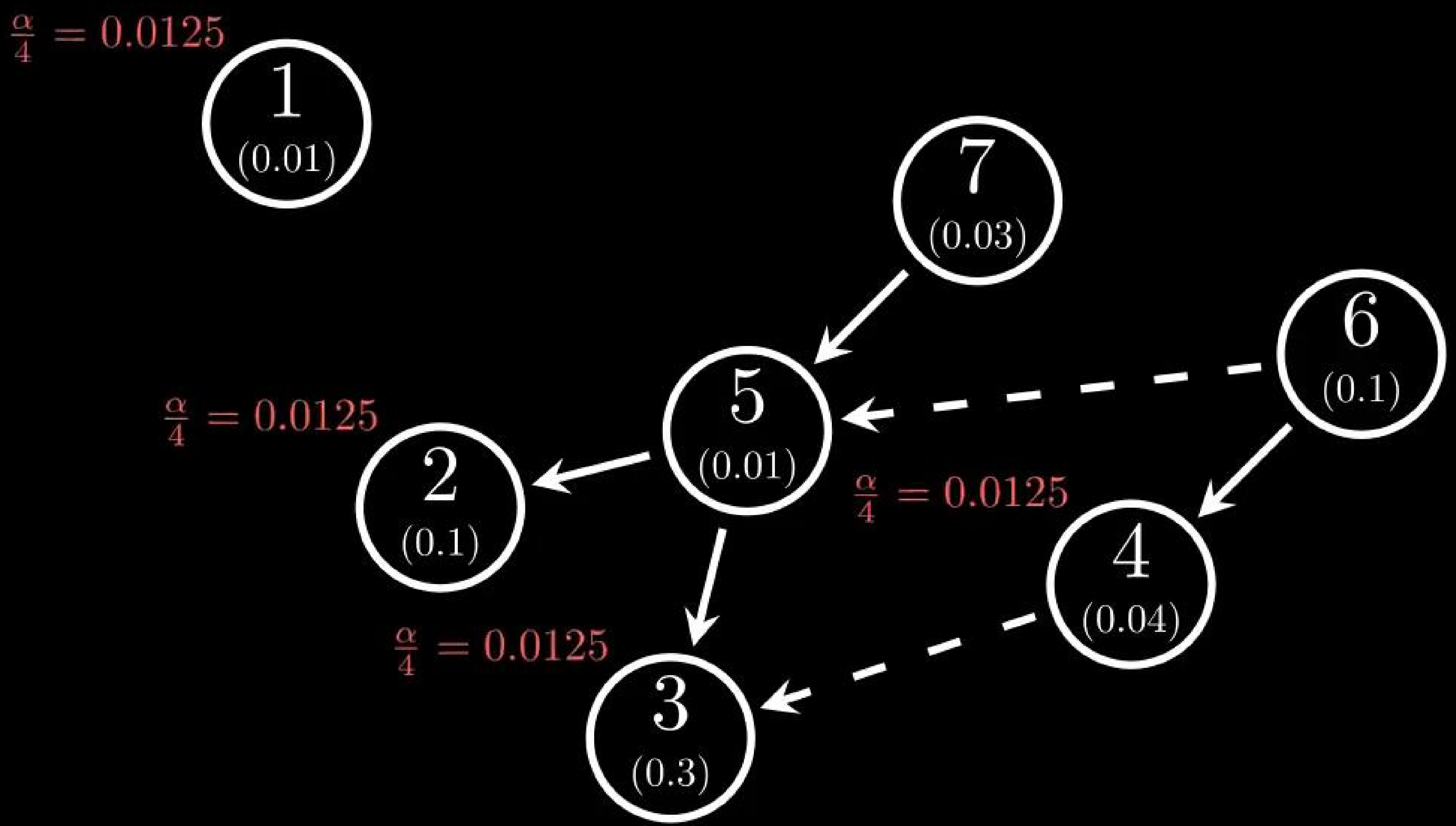

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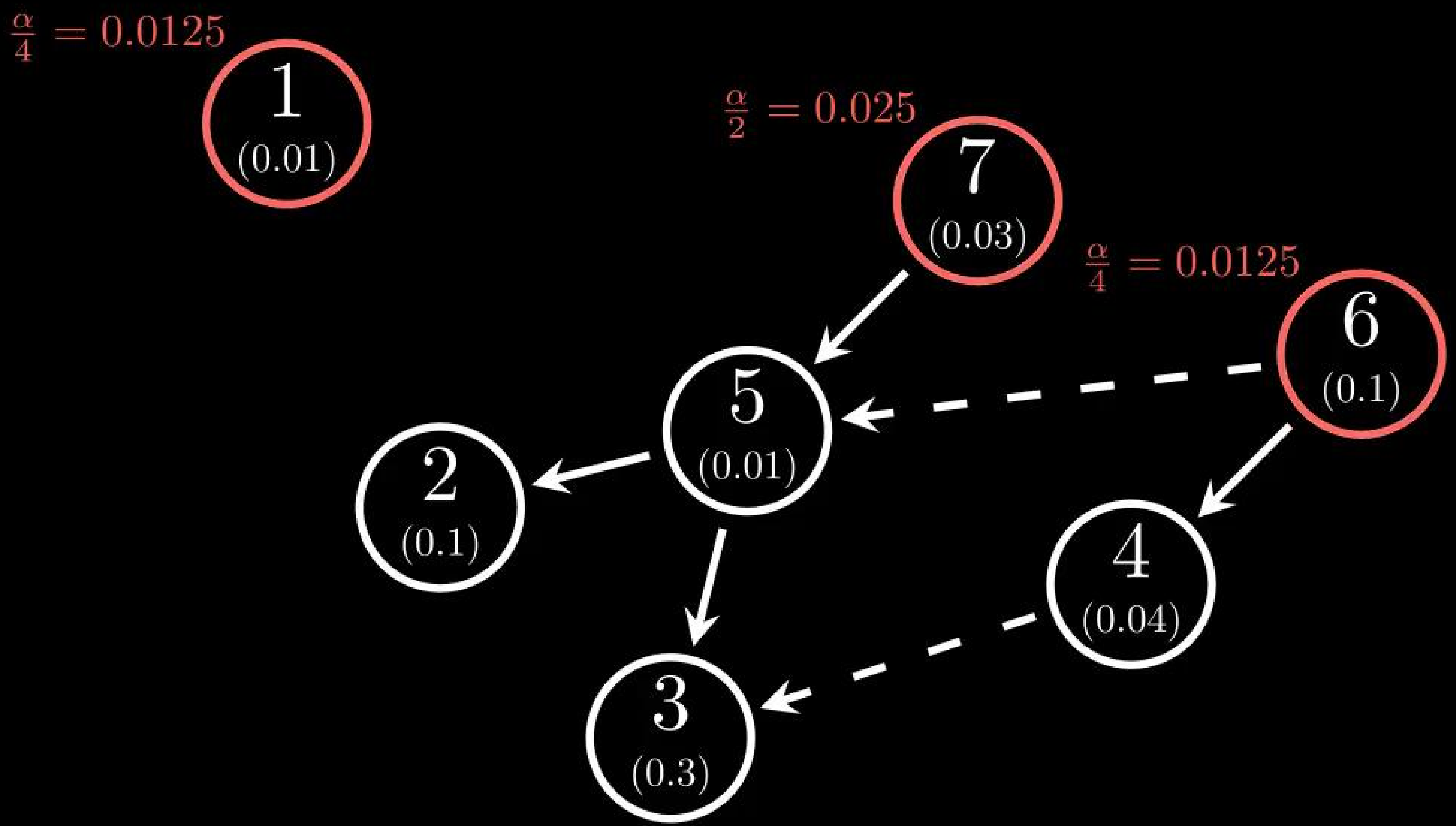

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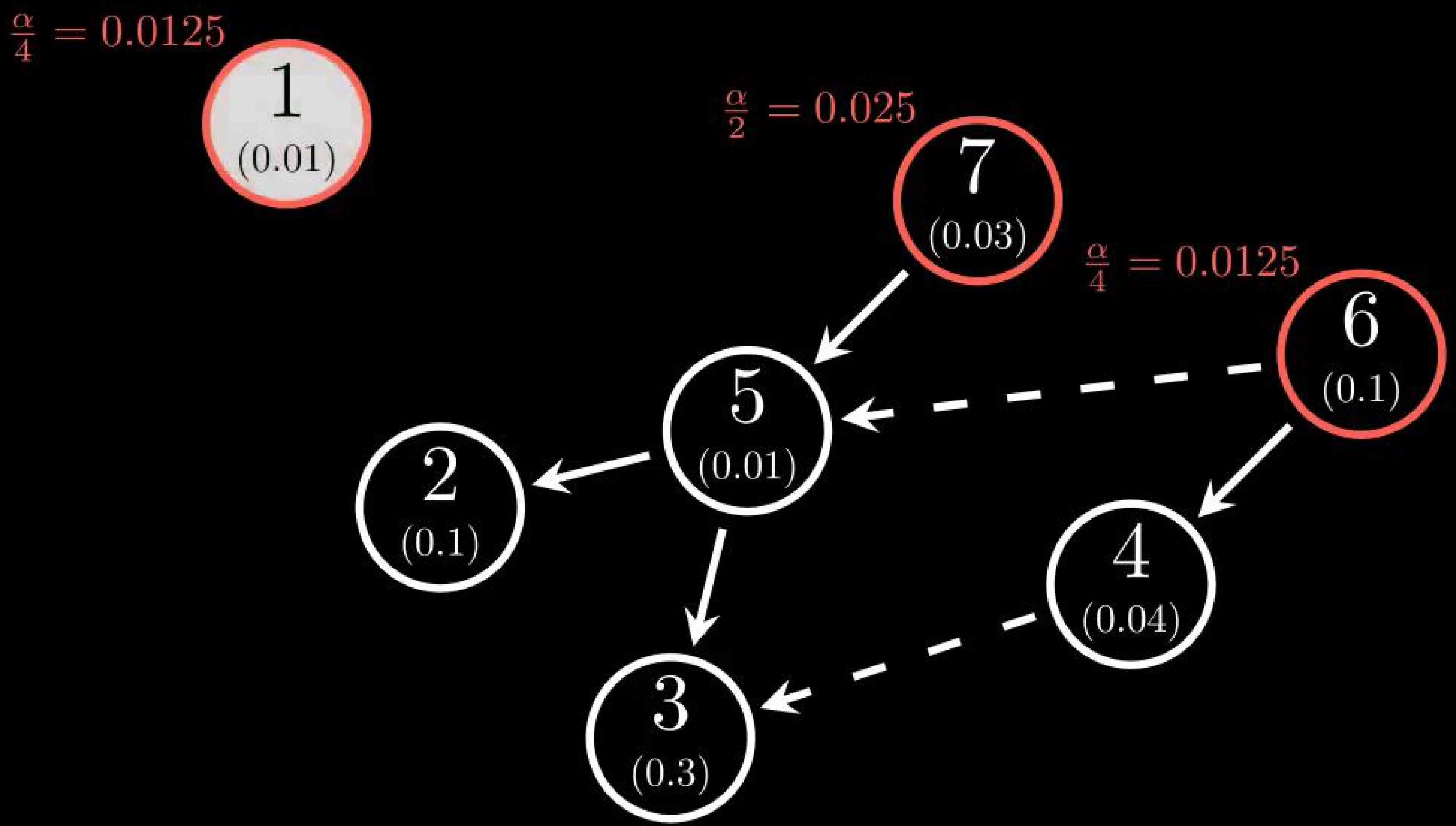

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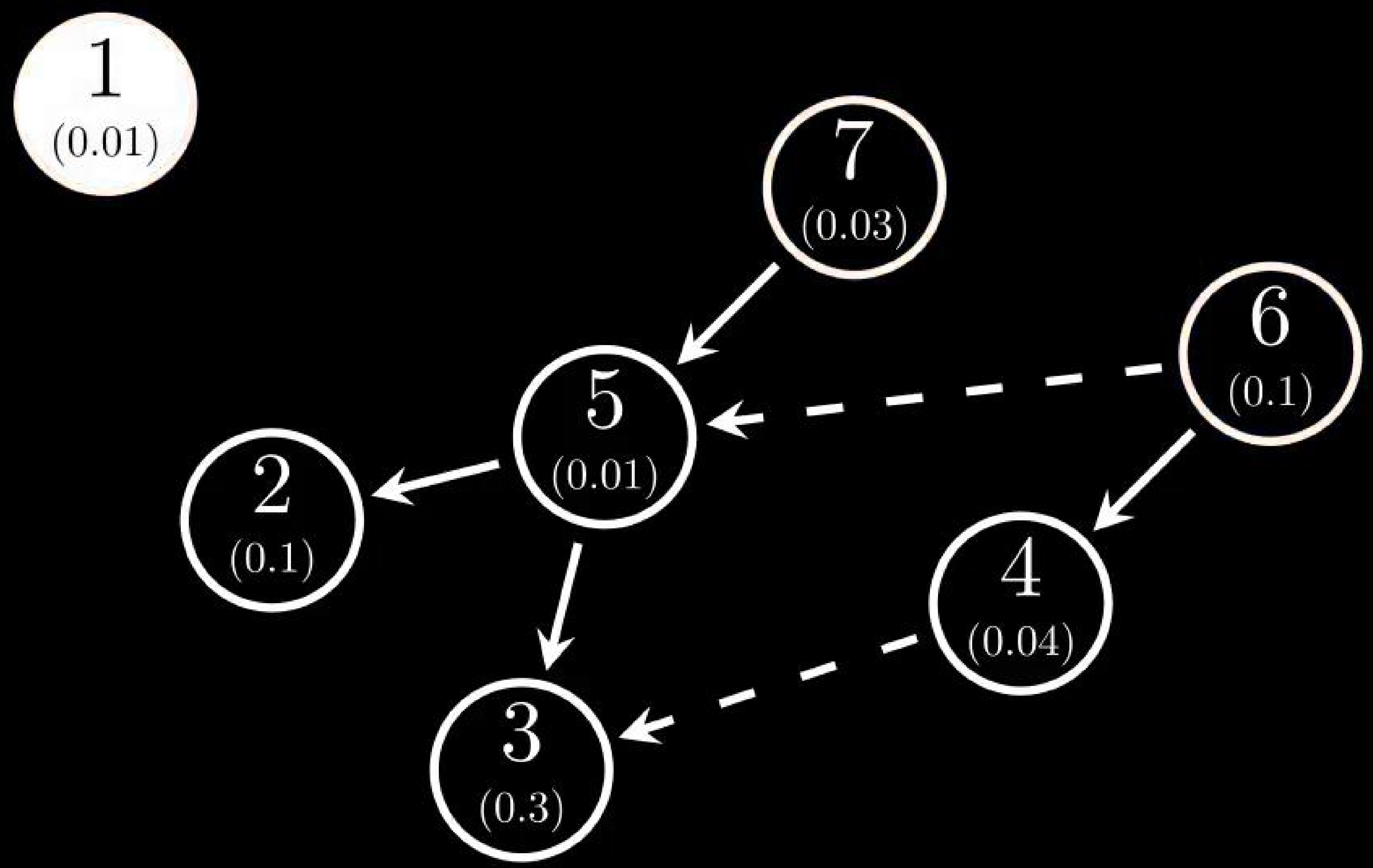

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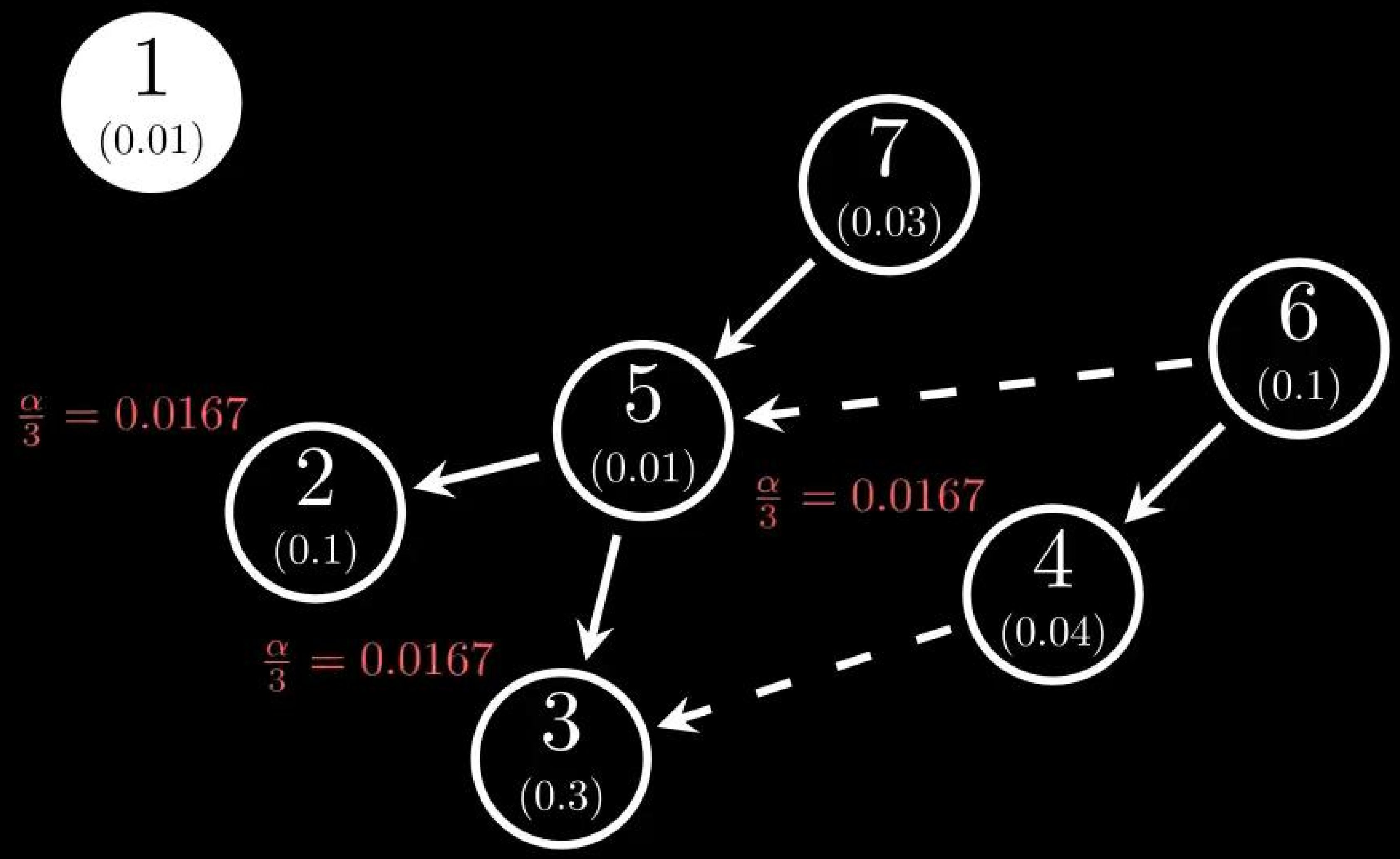

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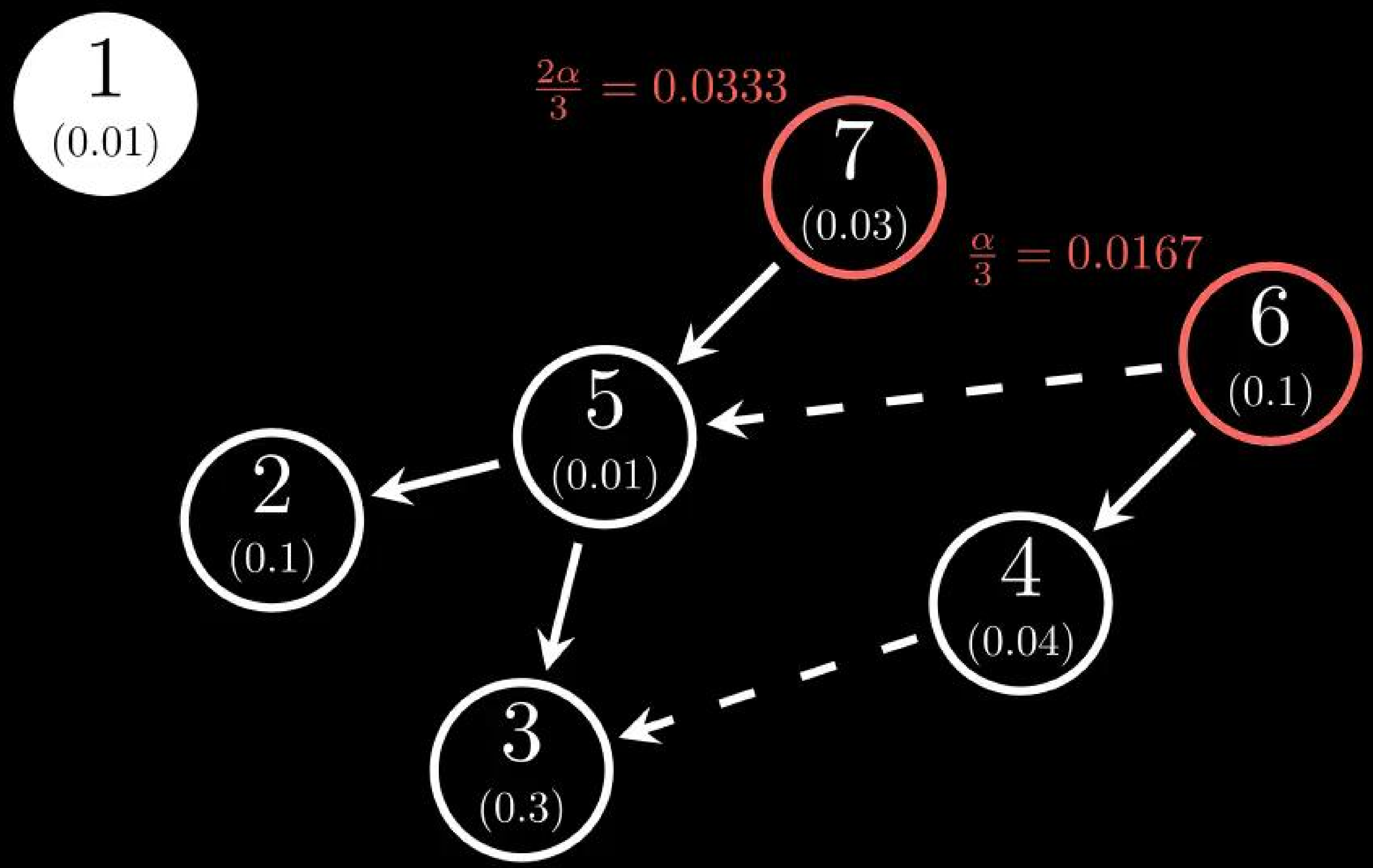

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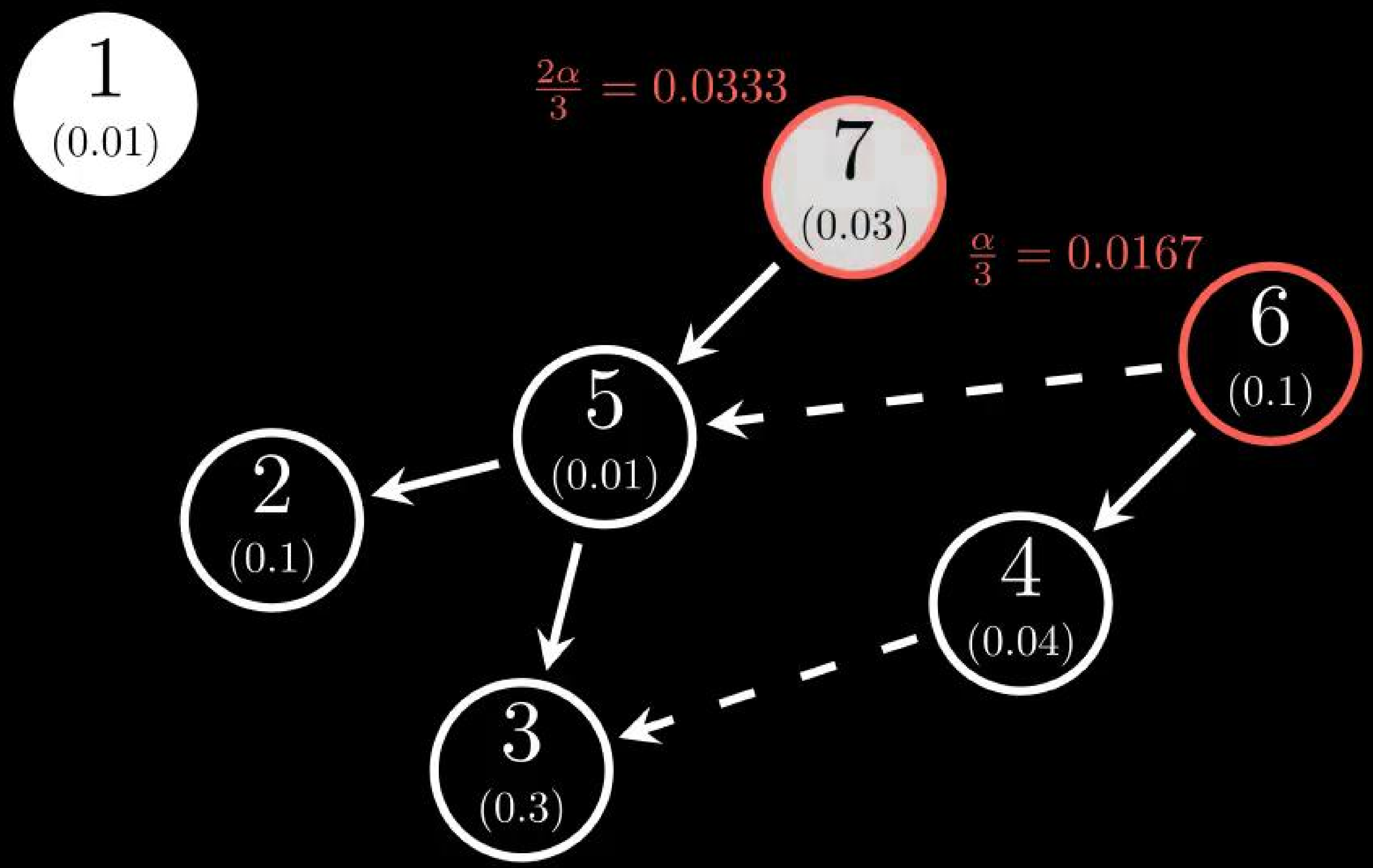

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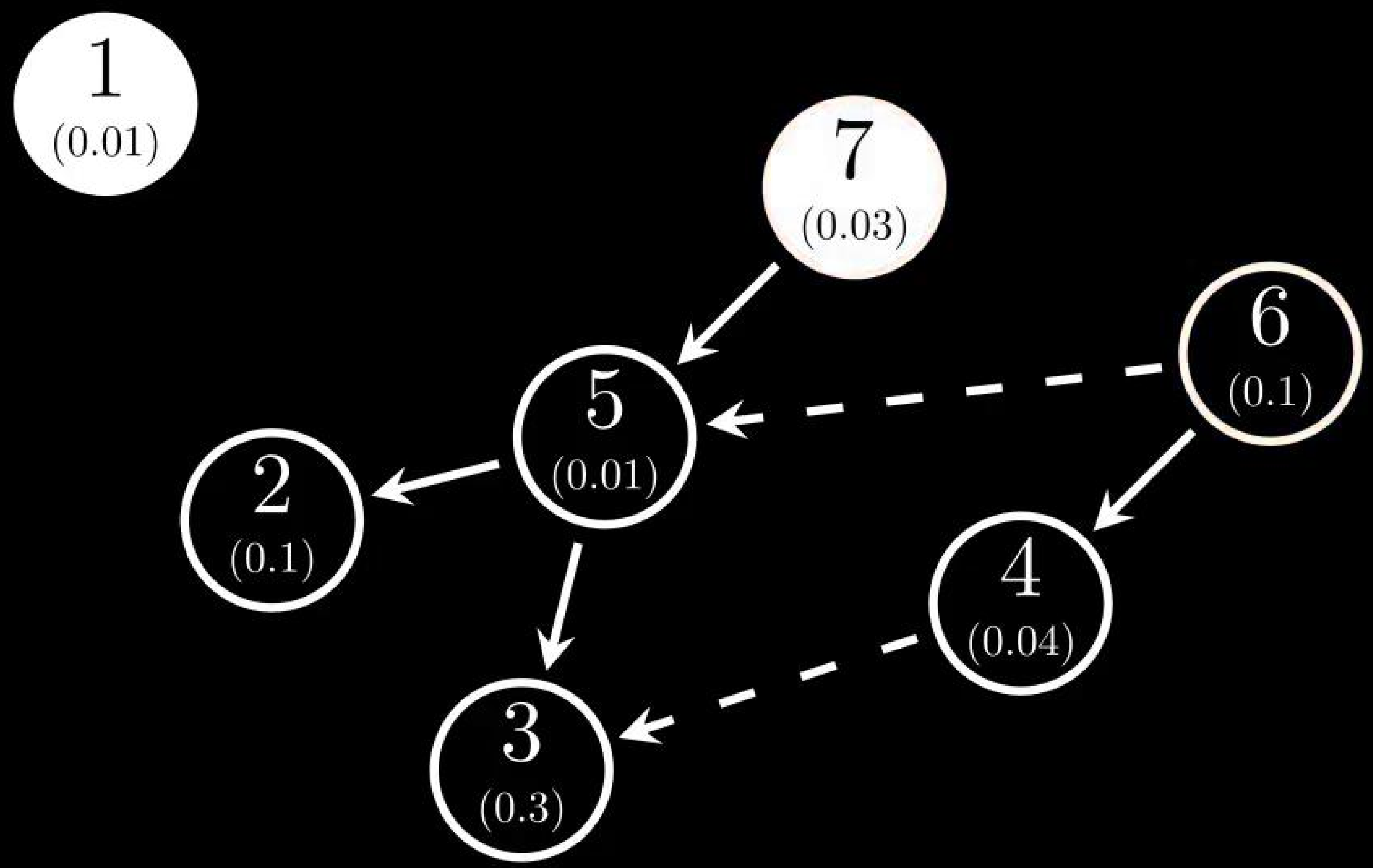

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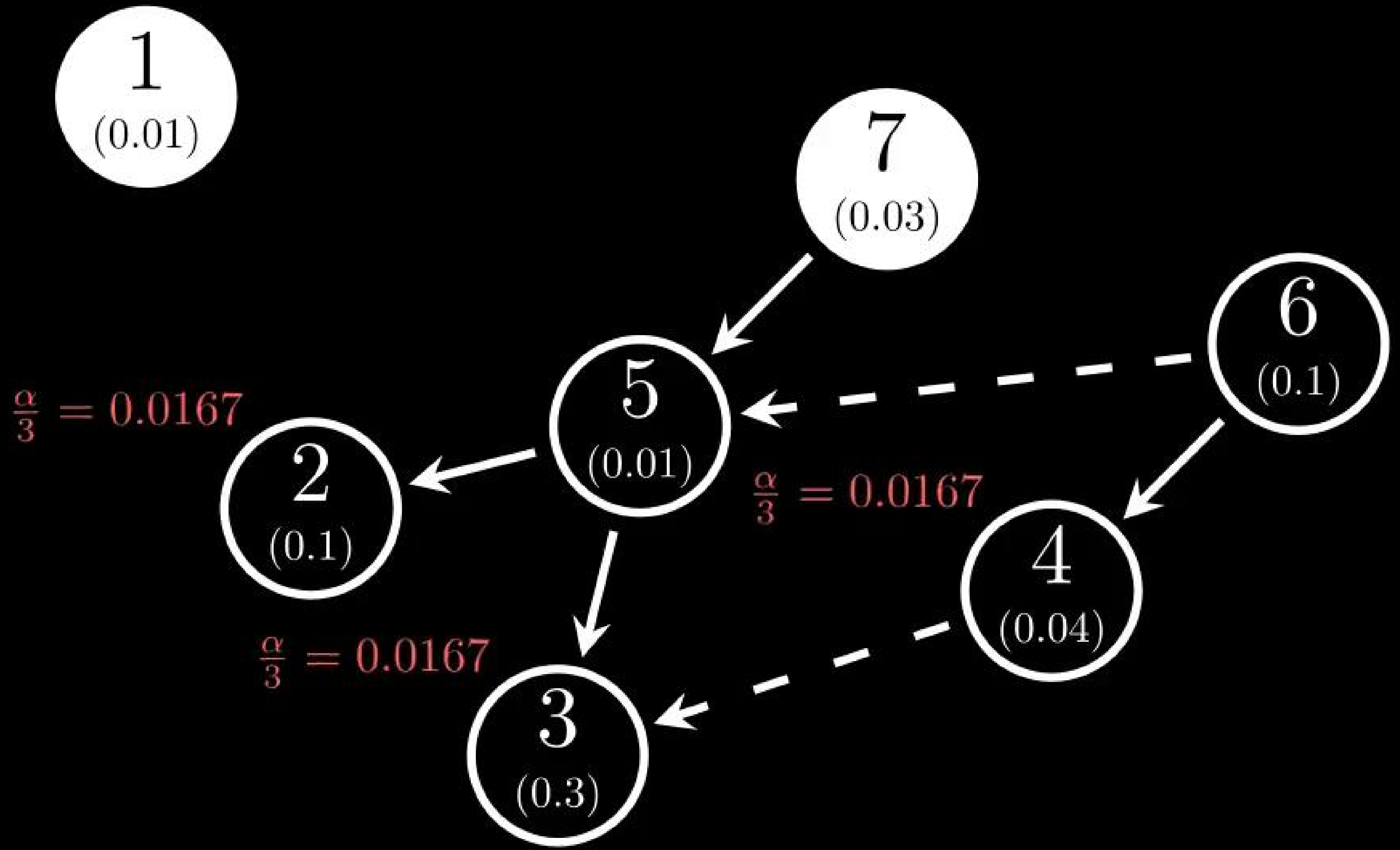

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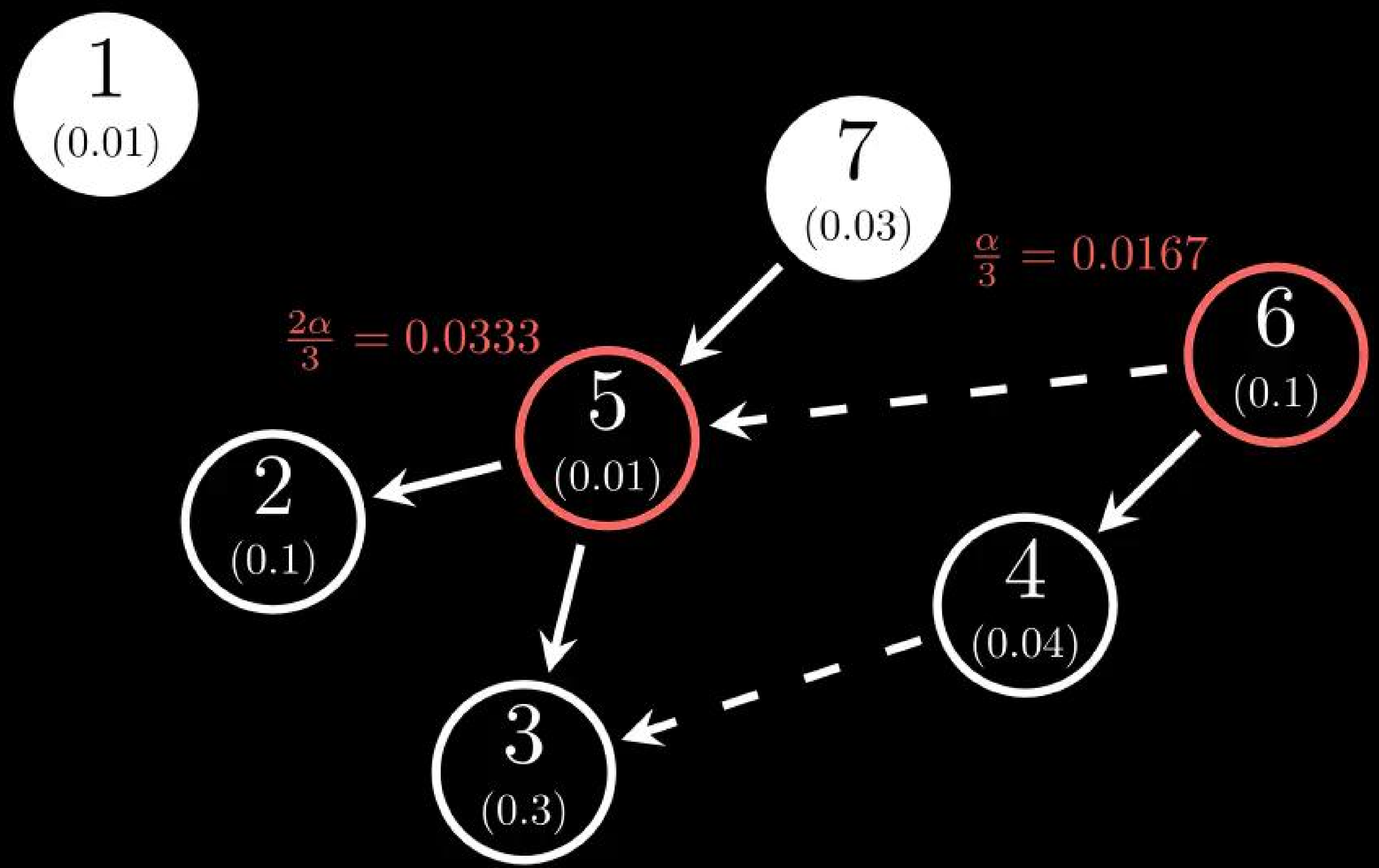

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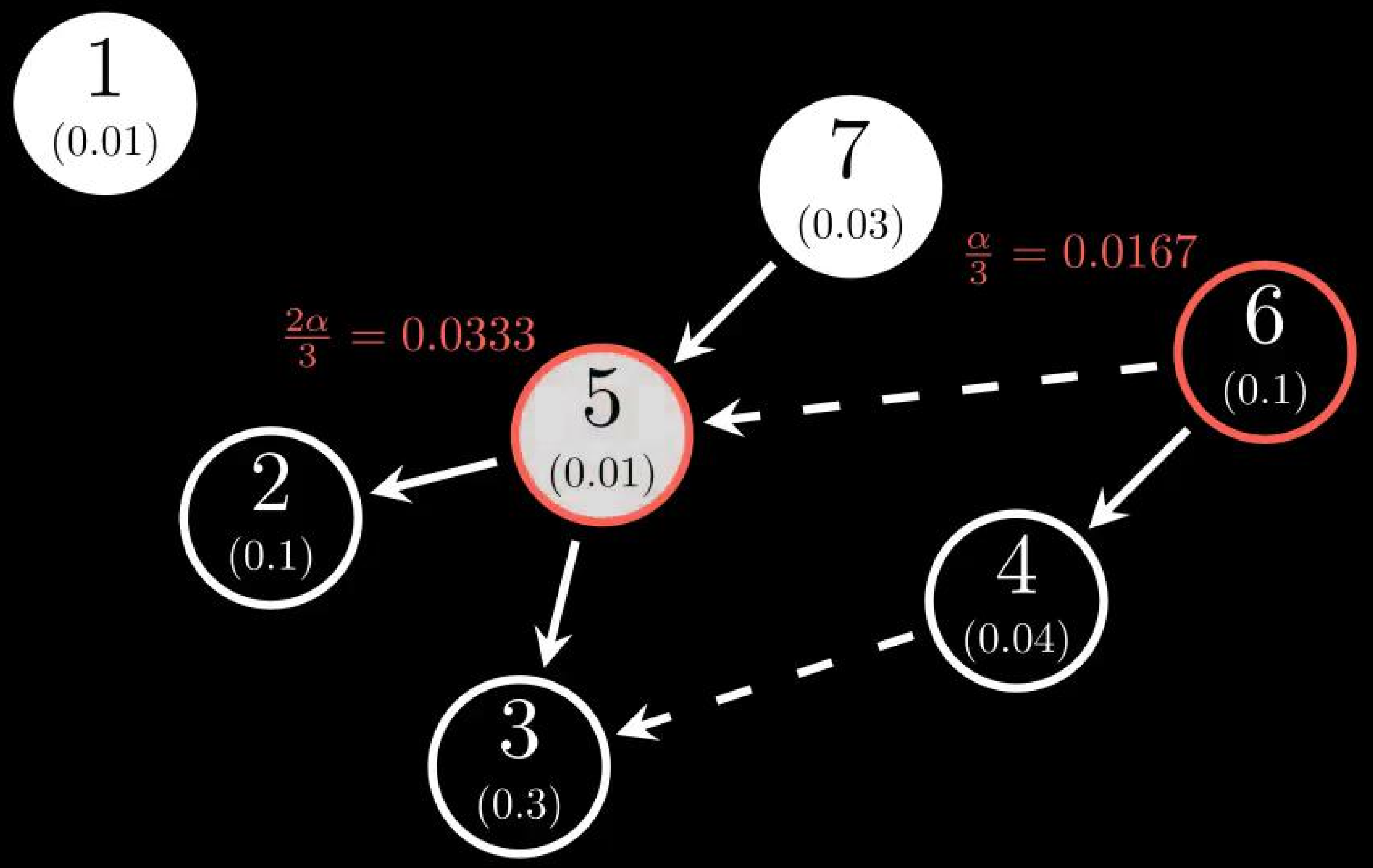

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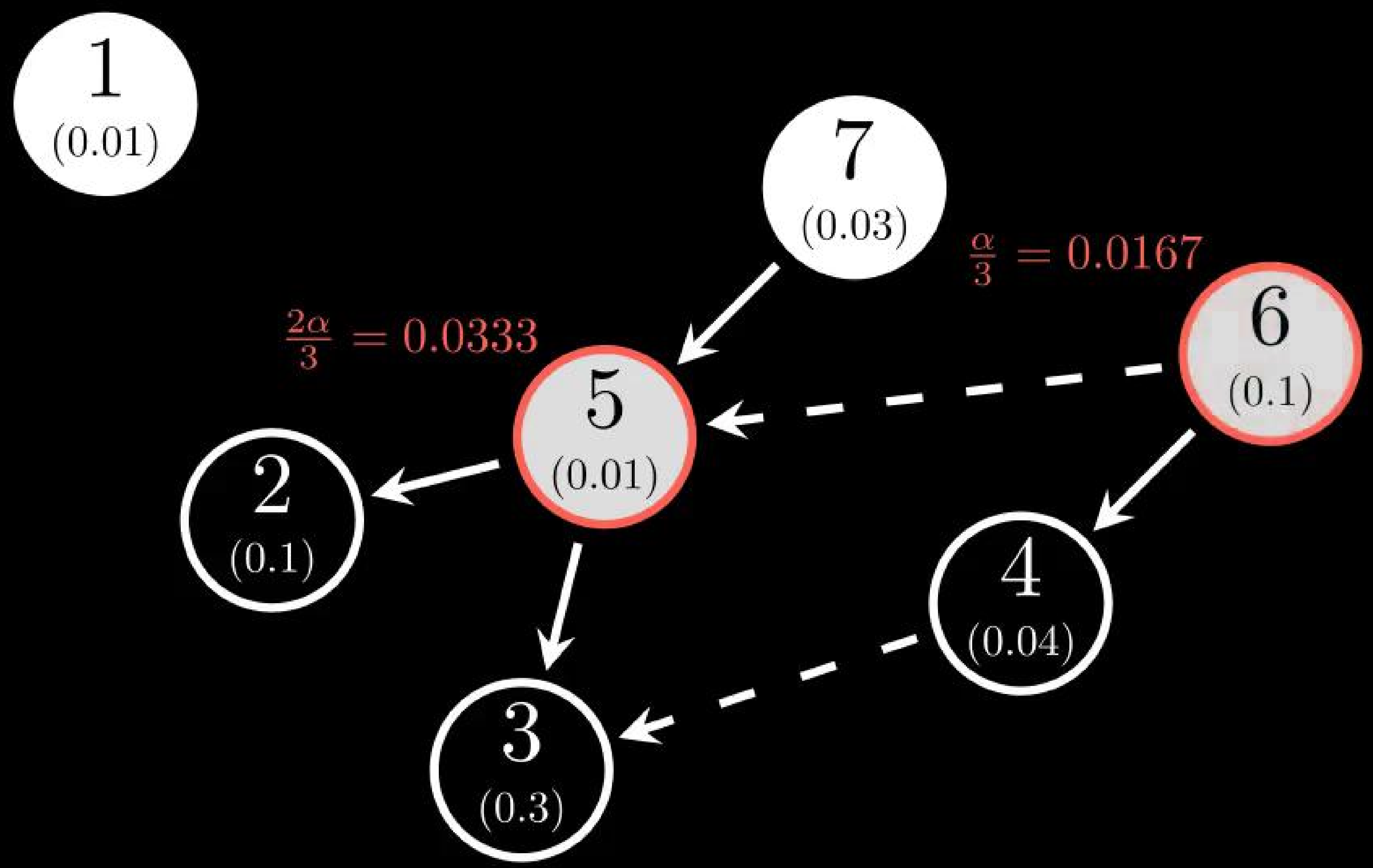

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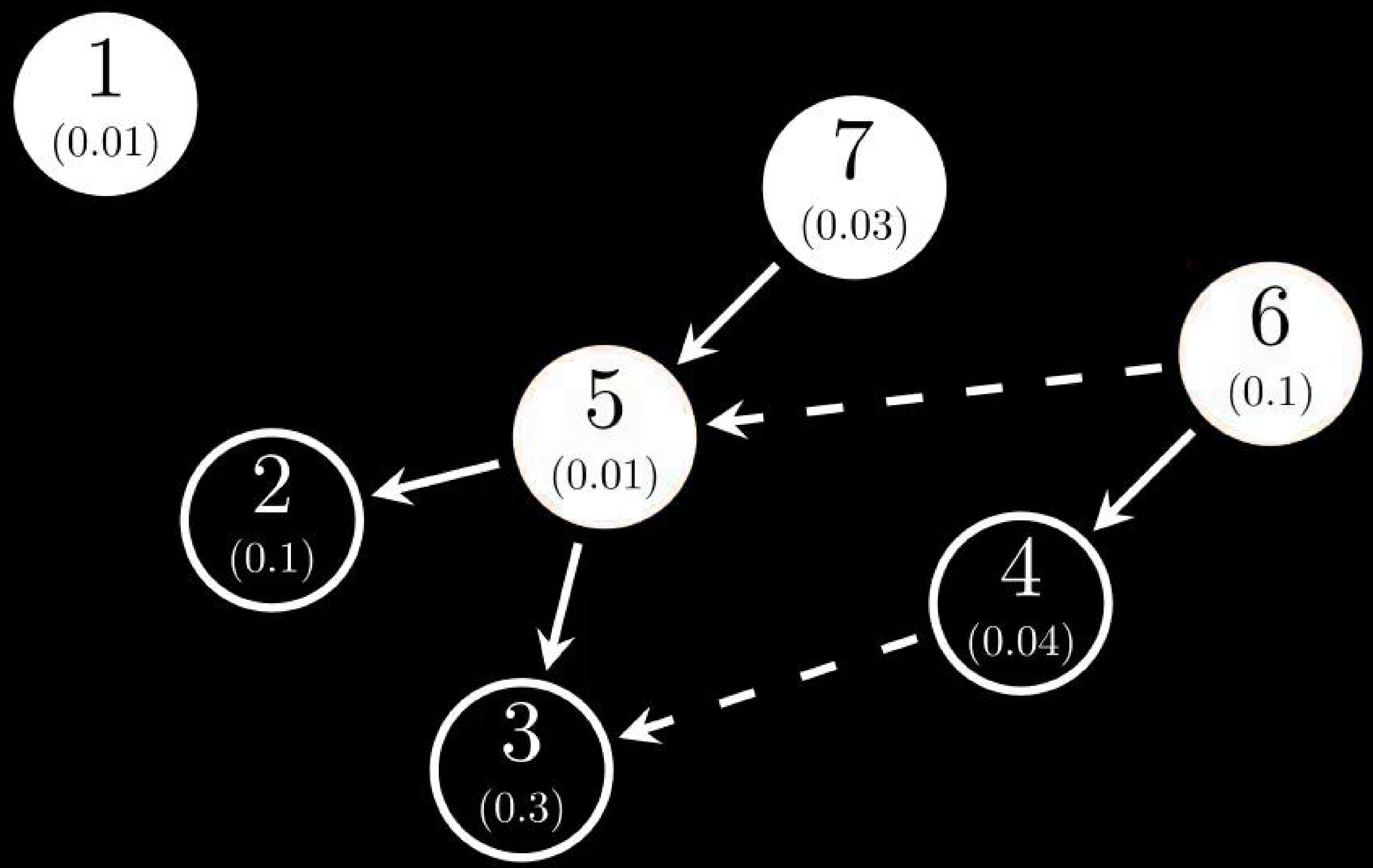

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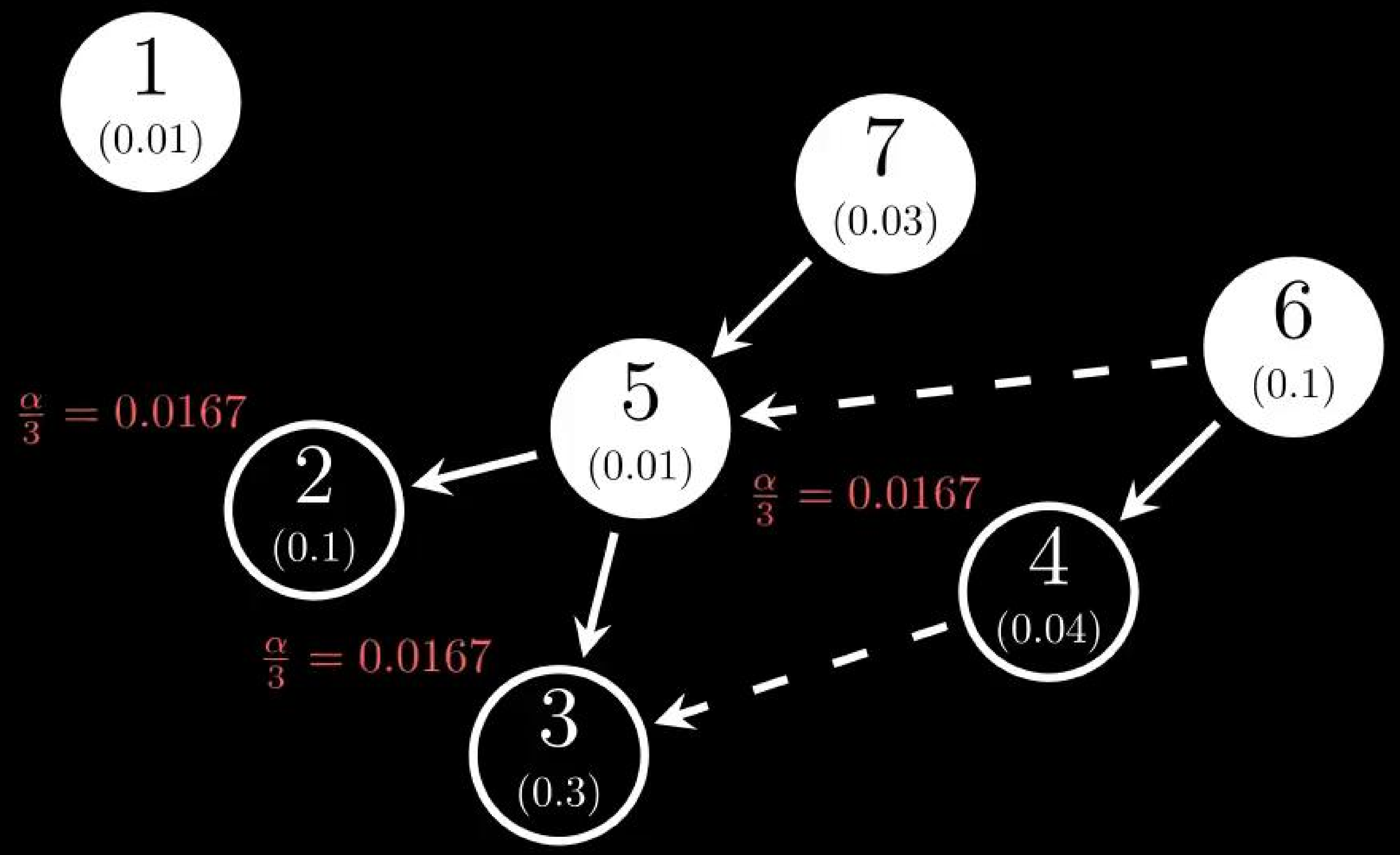

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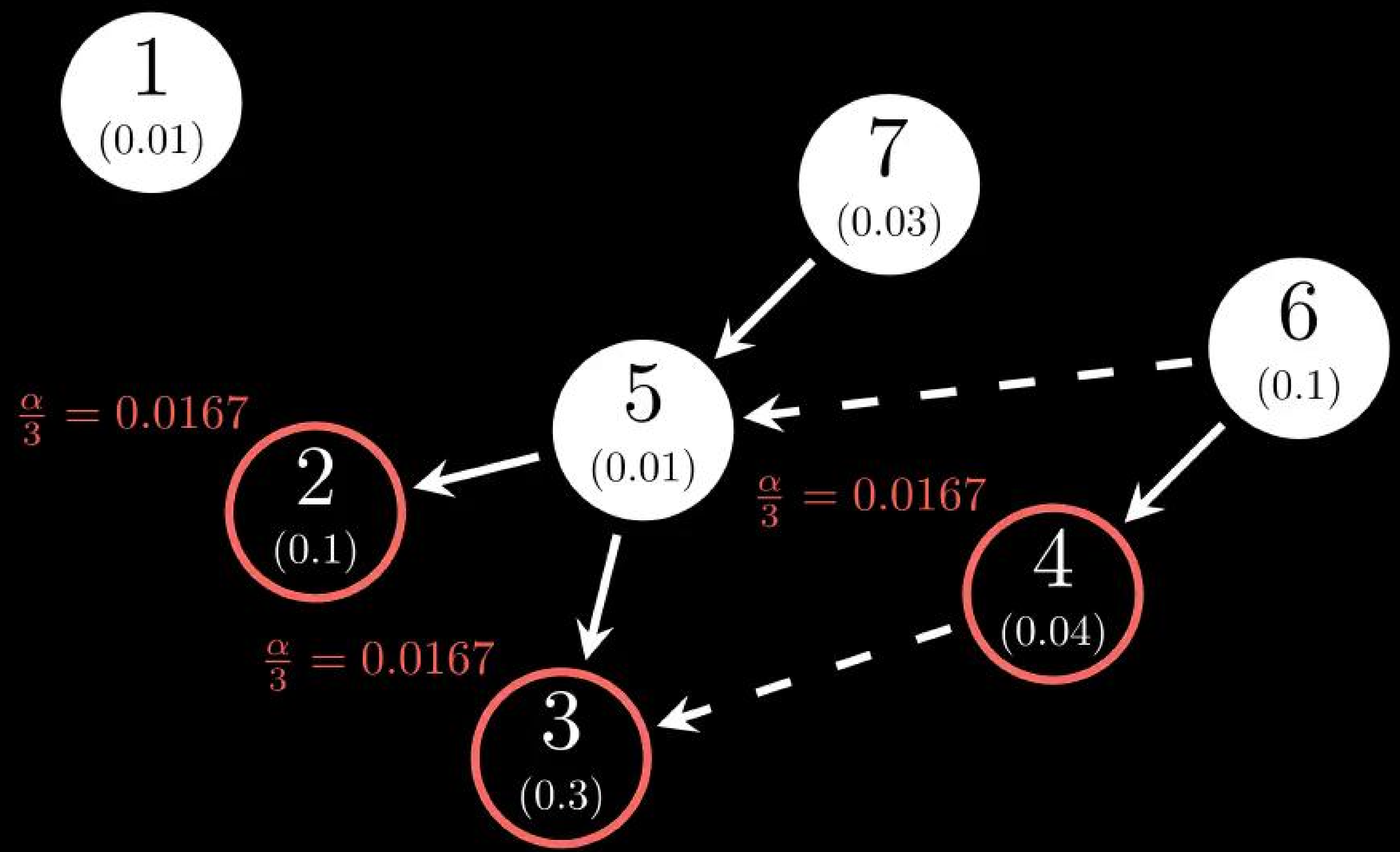

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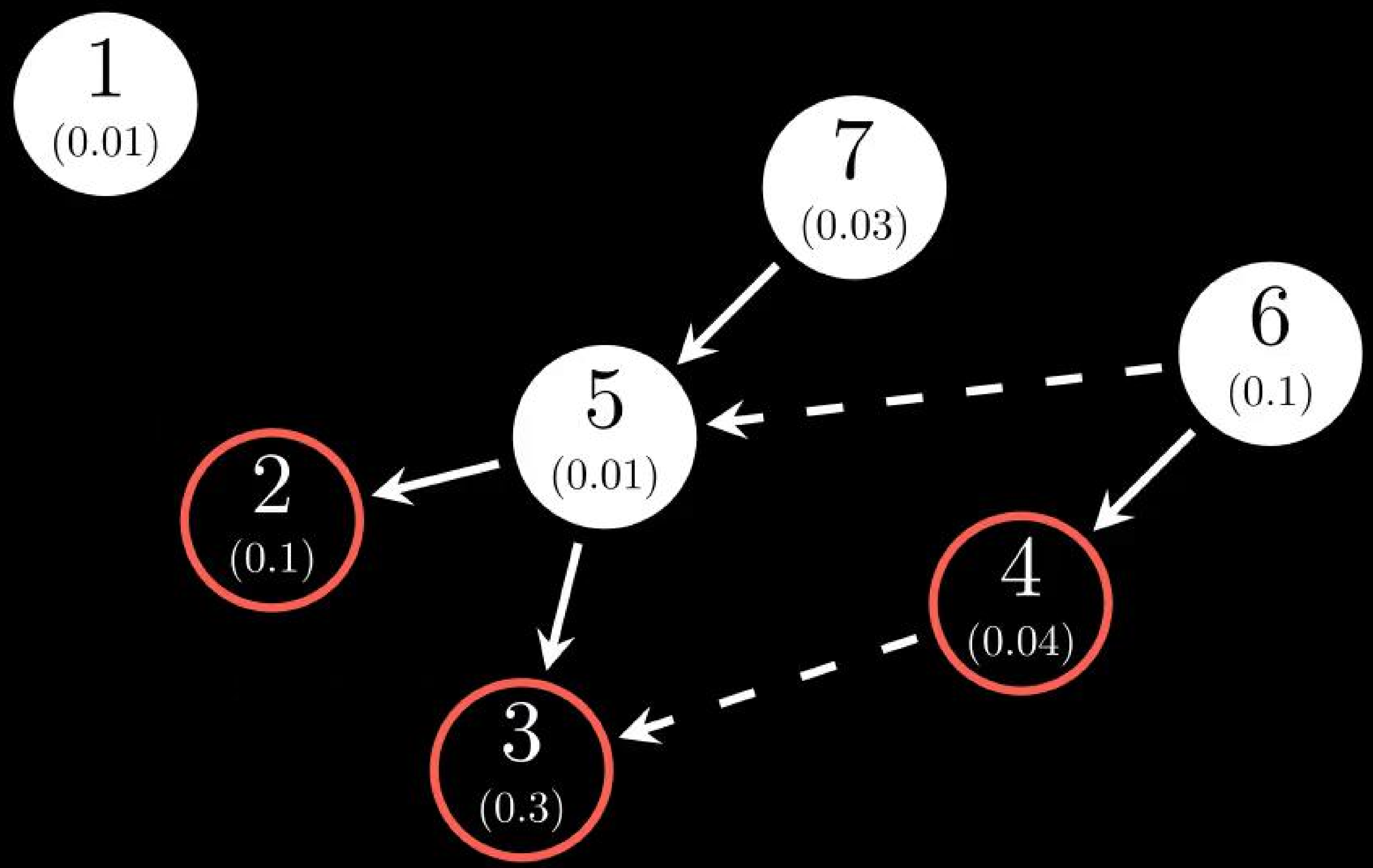

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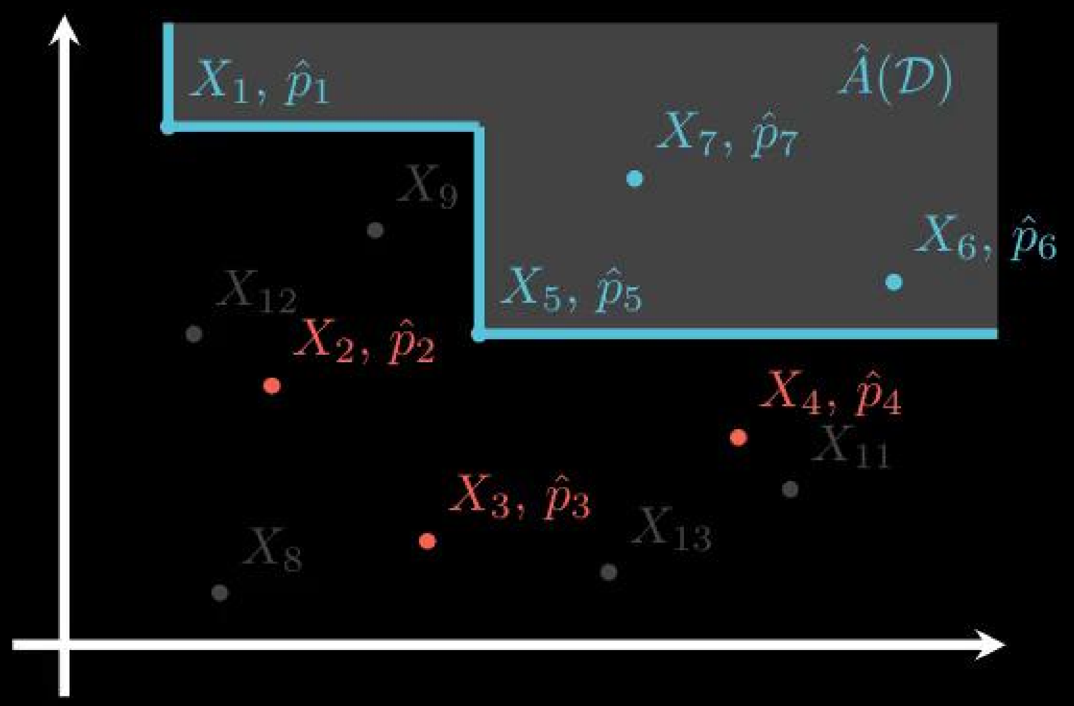

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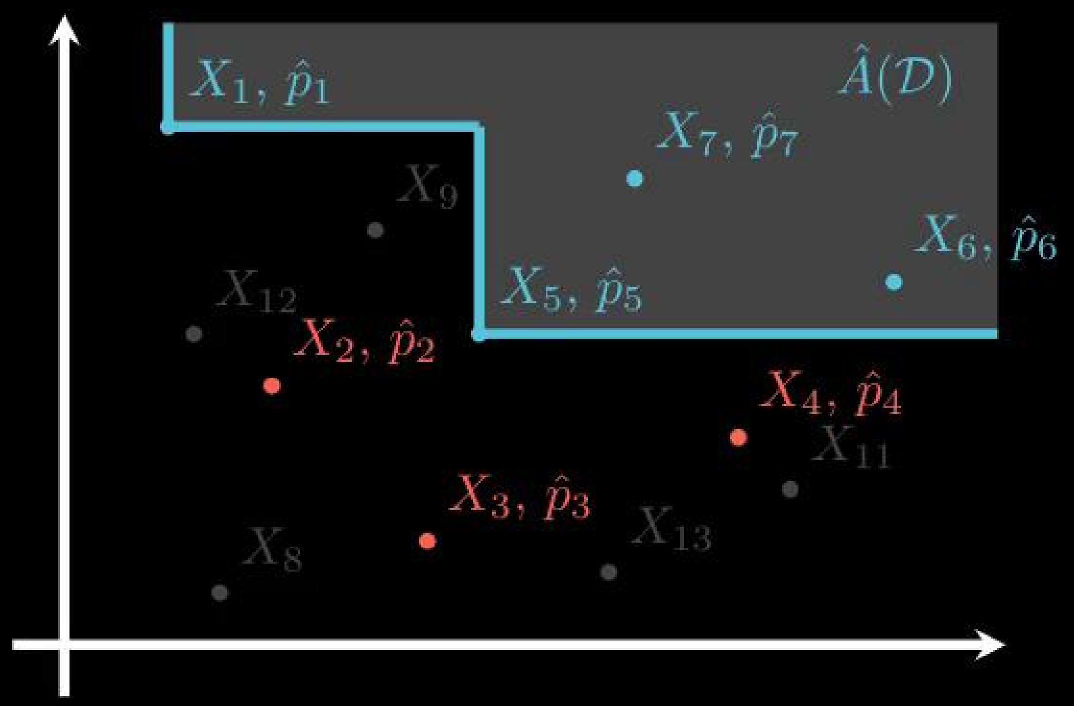

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Theorem. For any $n \geq 1$, $m \in [n]$, $\alpha \in (0,1)$, $\sigma > 0$, we have

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Further conditions are needed for power

Let $\hat{\mathcal{A}}_n(\tau, \alpha, \mathcal{P})$ denote the set of *data-dependent selection sets* controlling Type I error over $\mathcal{P}$.
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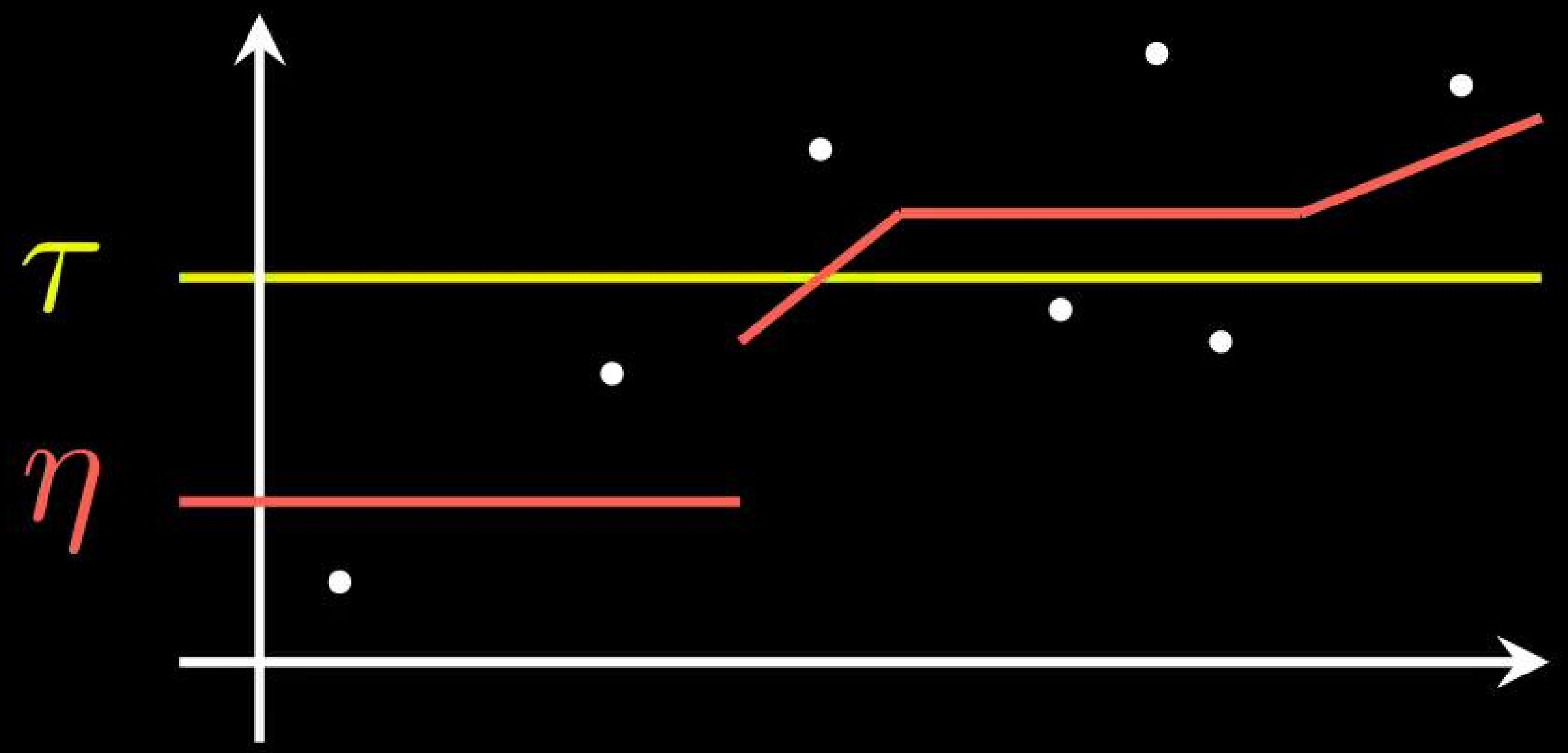

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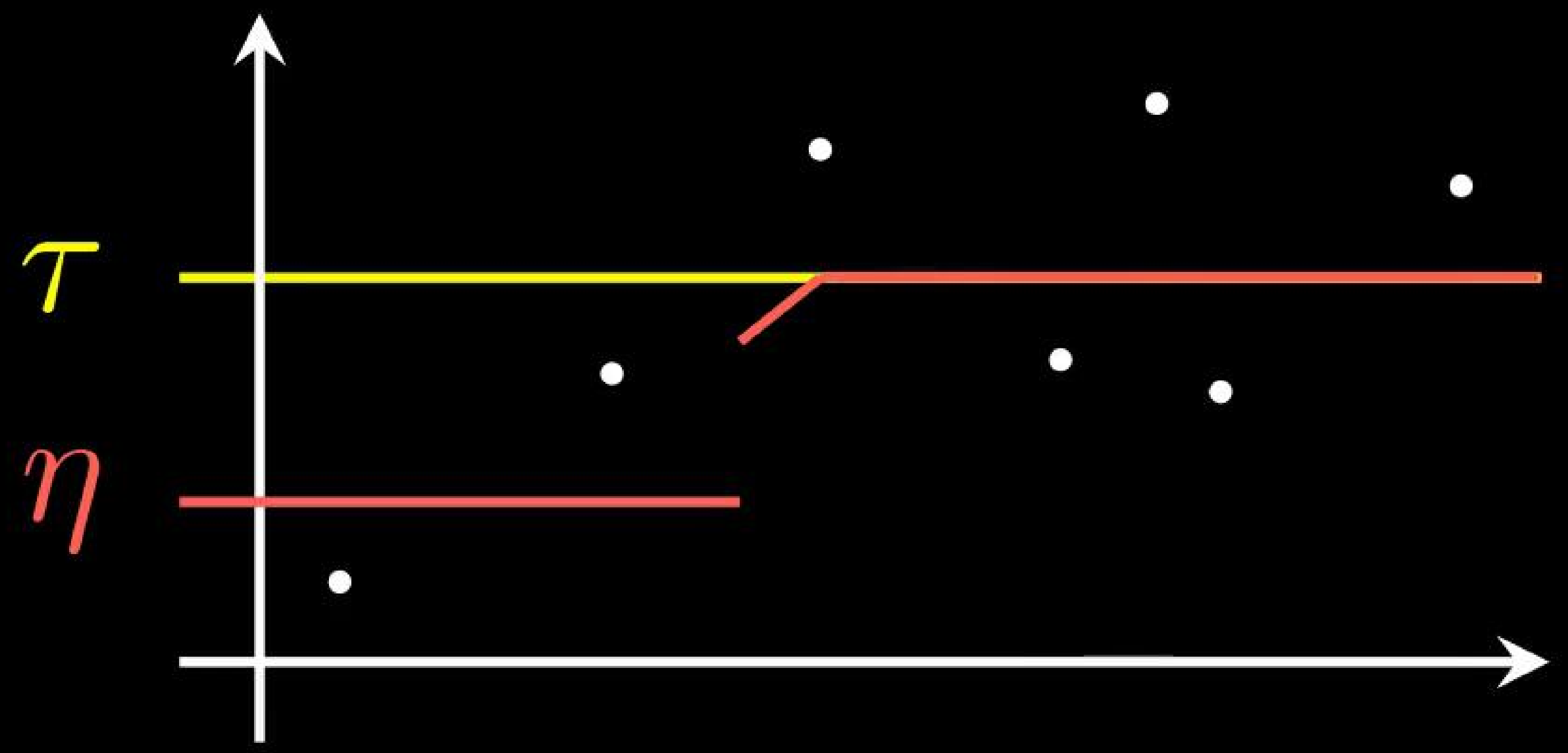

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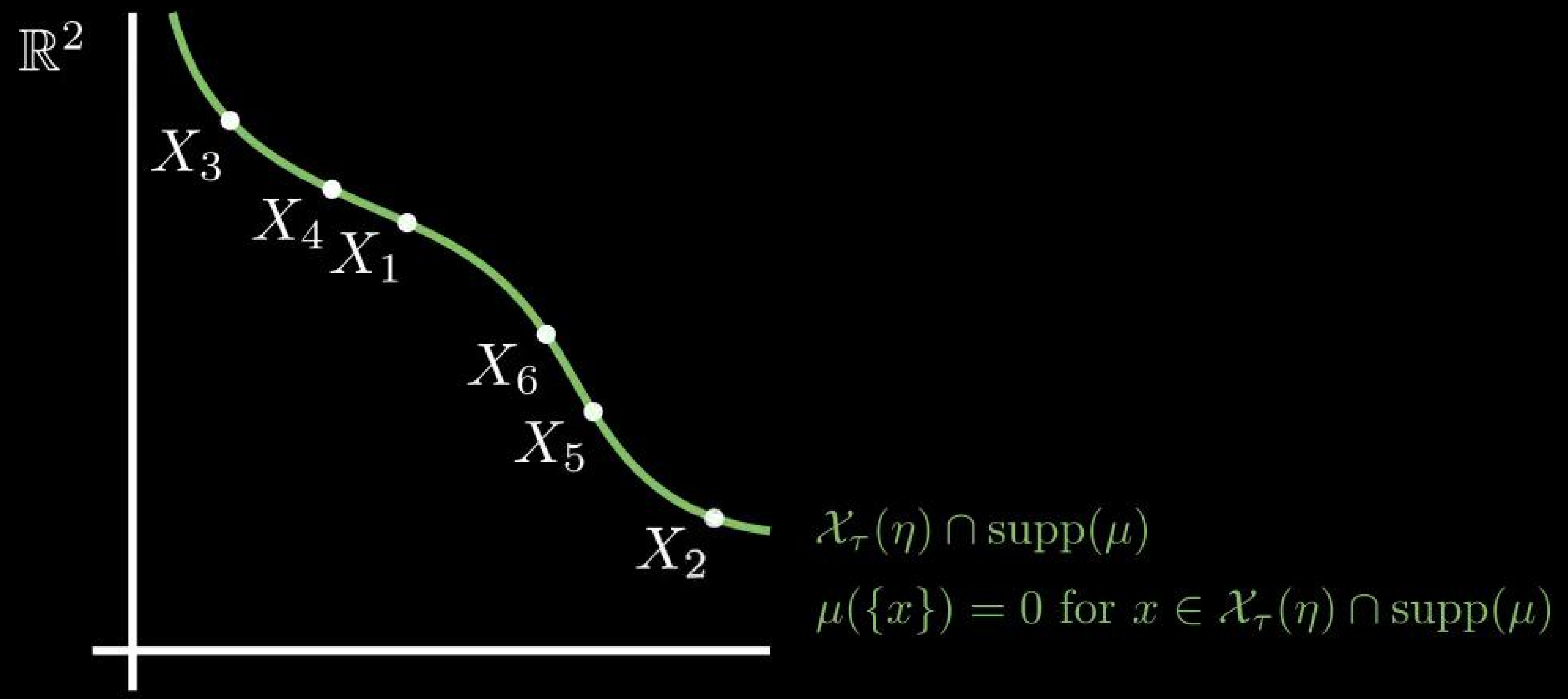

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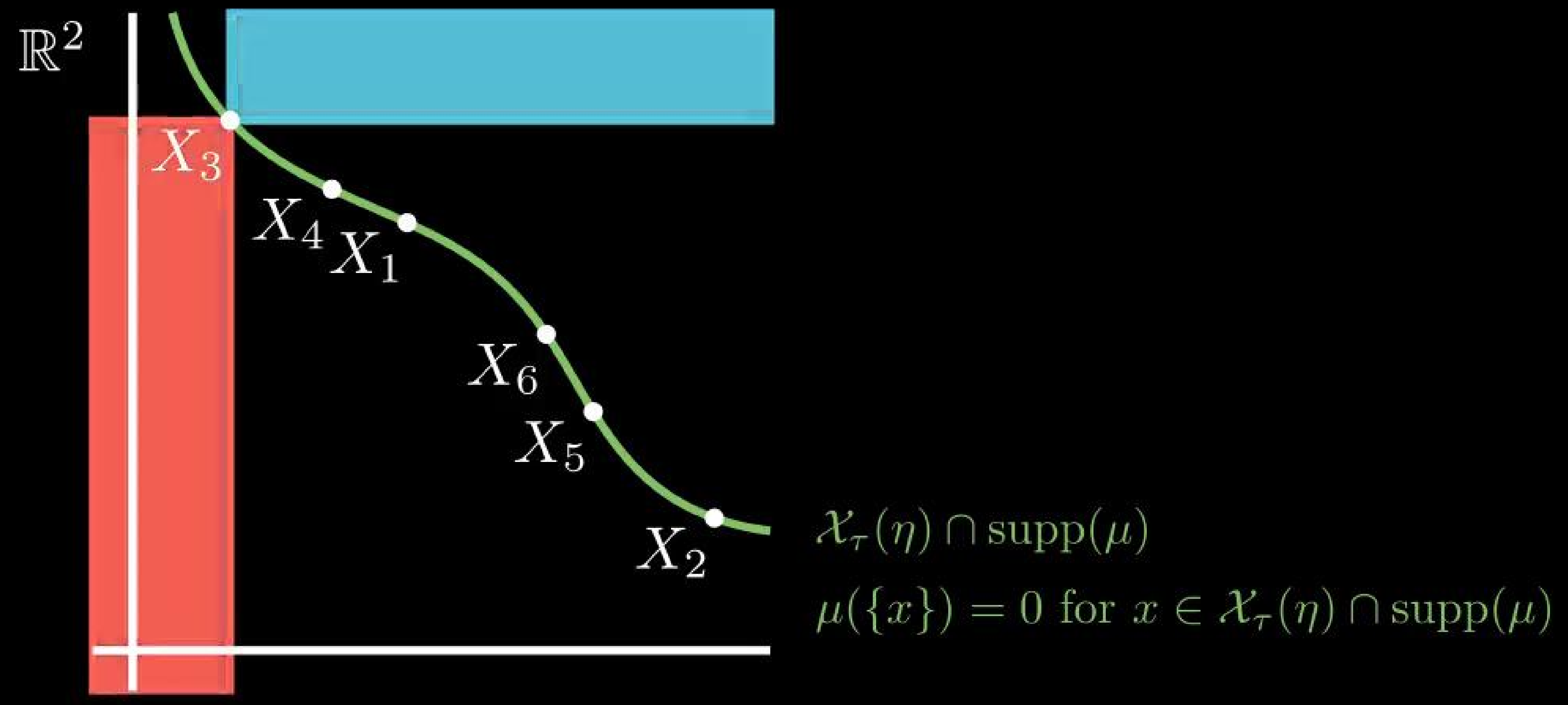
$$\sup_{P \in \mathcal{P}_{\mathrm{Mon},d}(\sigma)} \inf_{\hat{A} \in \hat{\mathcal{A}}_n(\tau, \alpha, \mathcal{P}_{\mathrm{Mon},d}(\sigma))} R_\tau(\hat{A}) \geq 1 - \alpha.$$



Further conditions are needed for power

Let $\hat{\mathcal{A}}_n(\tau, \alpha, \mathcal{P})$ denote the set of *data-dependent selection sets* controlling Type I error over $\mathcal{P}$.
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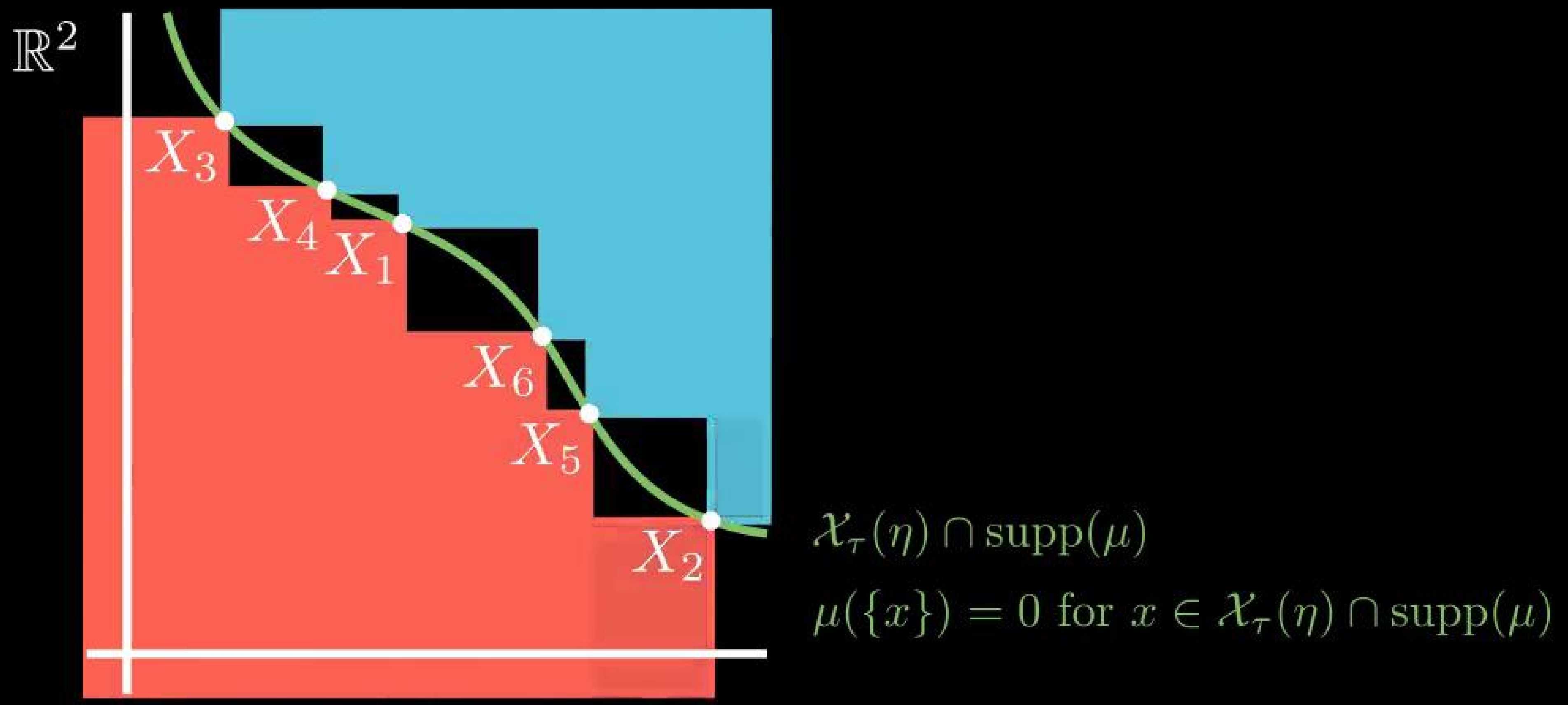

Power

Definition. Let $\sigma, \gamma, \lambda > 0$ and $\theta > 1$. $\mathcal{P}_{\mathrm{MonReg}} \equiv \mathcal{P}_{\mathrm{MonReg},d}(\sigma, \tau, \gamma, \lambda, \theta)$ denotes the set of distributions $P \in \mathcal{P}_{\mathrm{Mon},d}(\sigma)$ for which additionally

1. $\eta\big(x + r(1, \ldots, 1)^\top\big) \geq \tau + \lambda \cdot r^\gamma$ for all $x \in \mathcal{X}_\tau(\eta) \cap \mathrm{supp}(\mu)$ and $r \in (0, 1]$;
2. $\theta^{-1} \cdot r^d \leq \mu\big(\{y \in \mathbb{R}^d : \|y - x\|_\infty \leq r\}\big) \leq \theta \cdot (2r)^d$ for all $x \in \mathcal{X}_\tau(\eta) \cap \mathrm{supp}(\mu)$, $r \in (0, 1]$.

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Theorem. $\exists C(d, \theta) \geq 1$, such that for any $n \geq 1$, $m \in [n]$ and $\alpha \in (0, 1)$,

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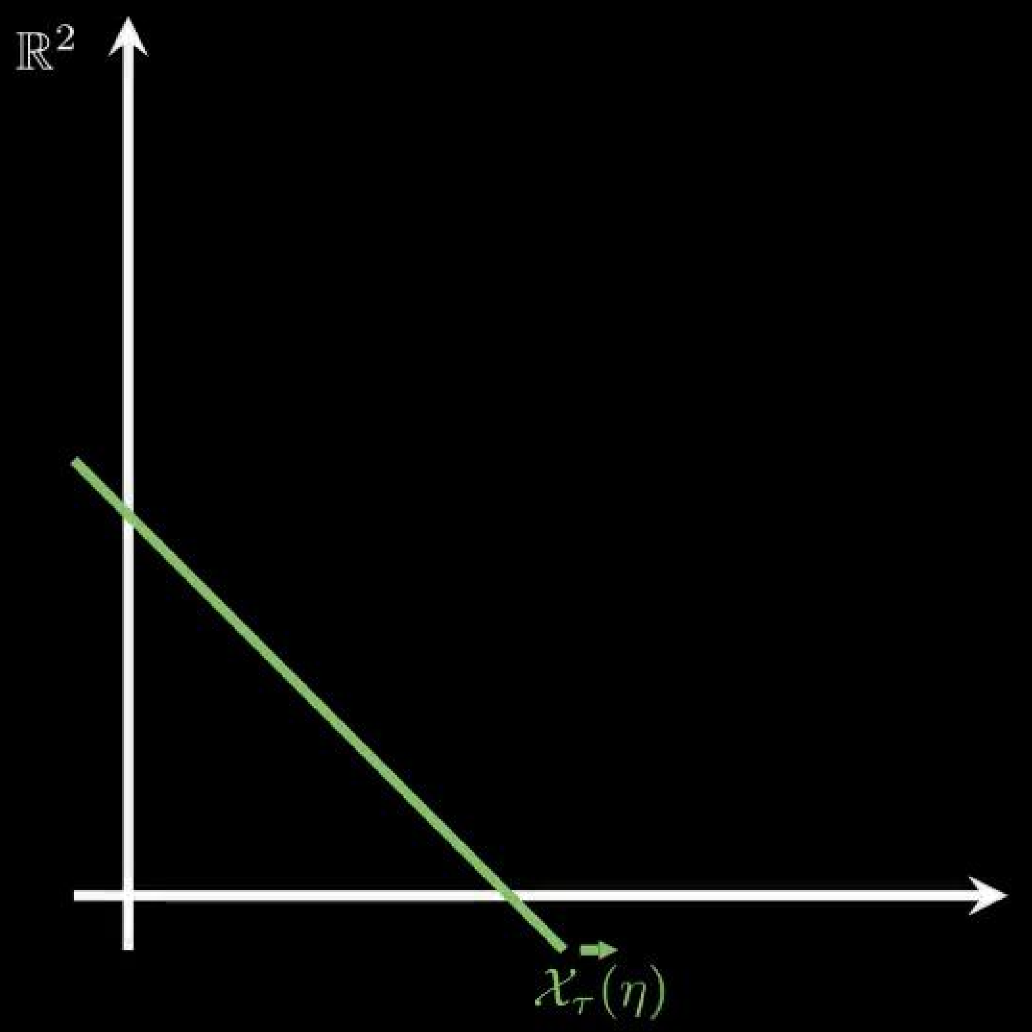

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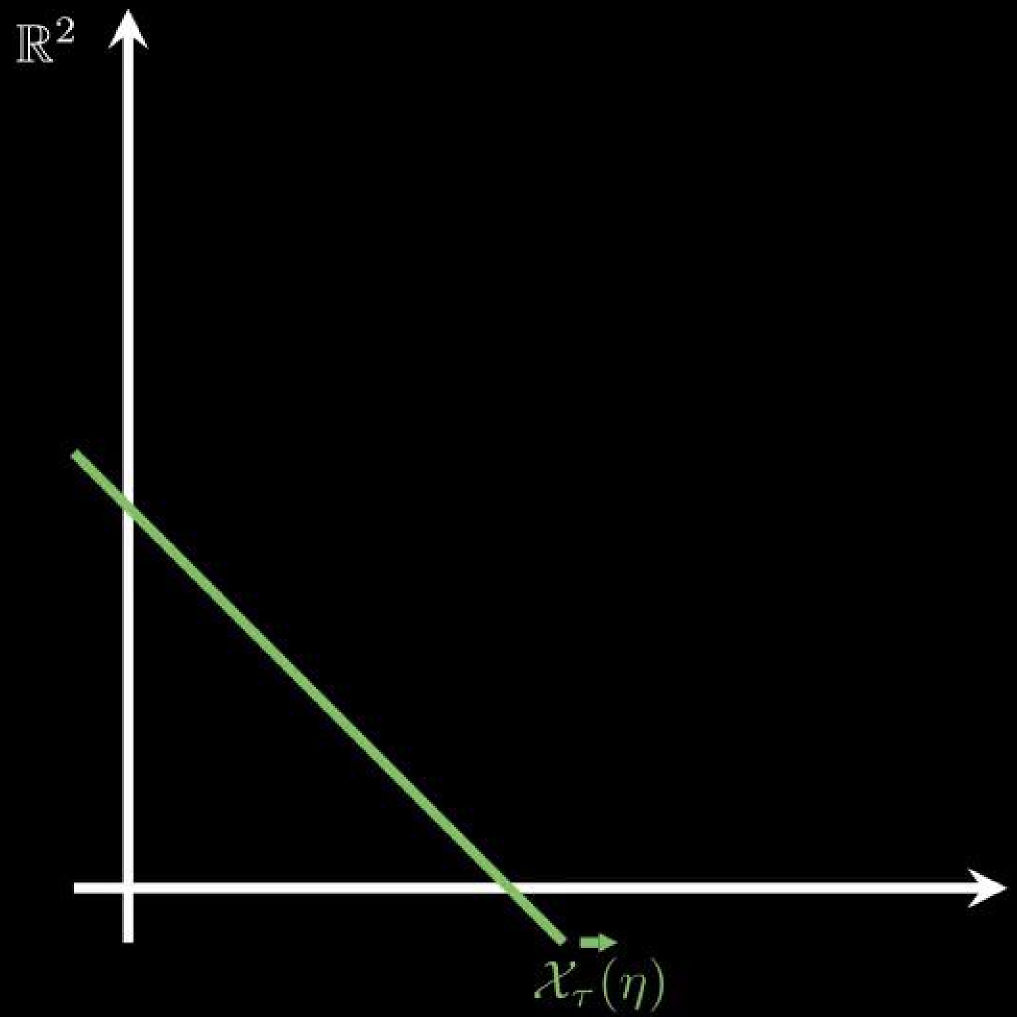

Let $r > 0$ be small.

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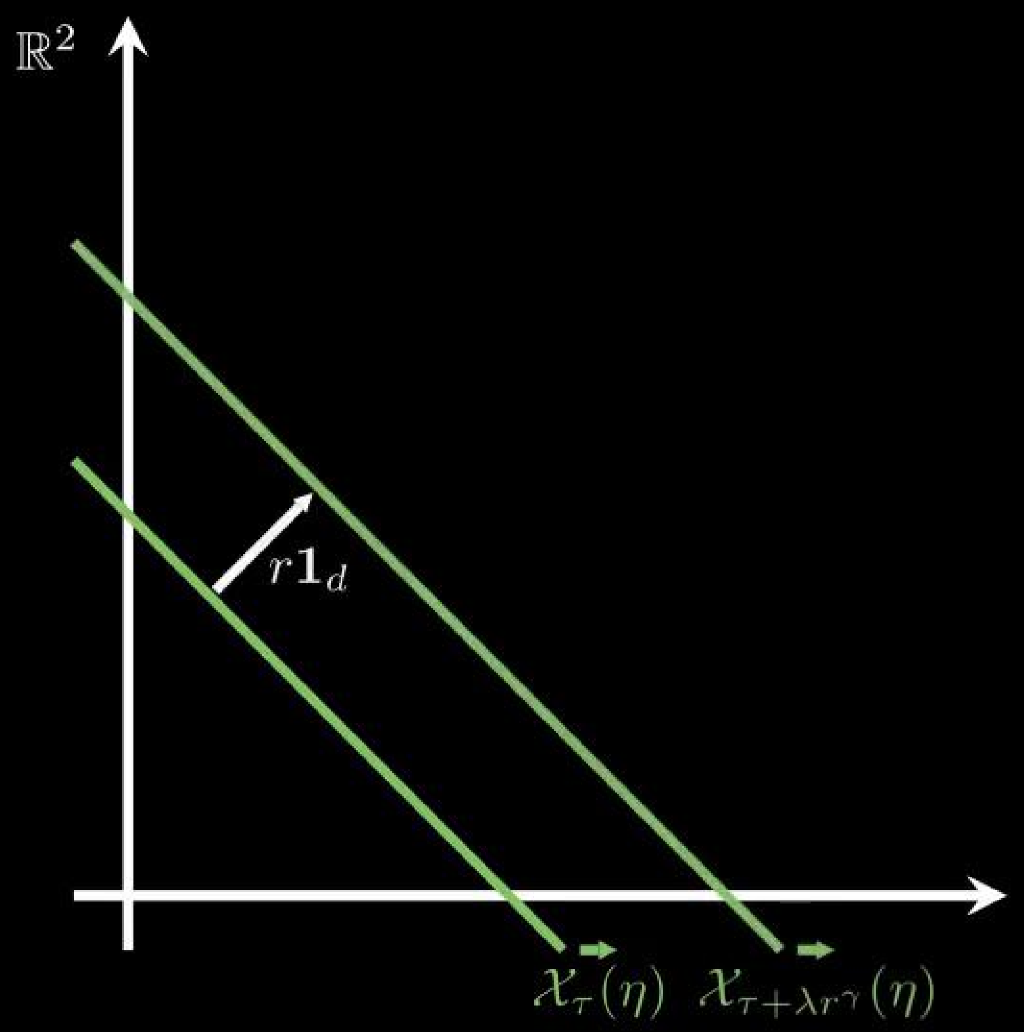

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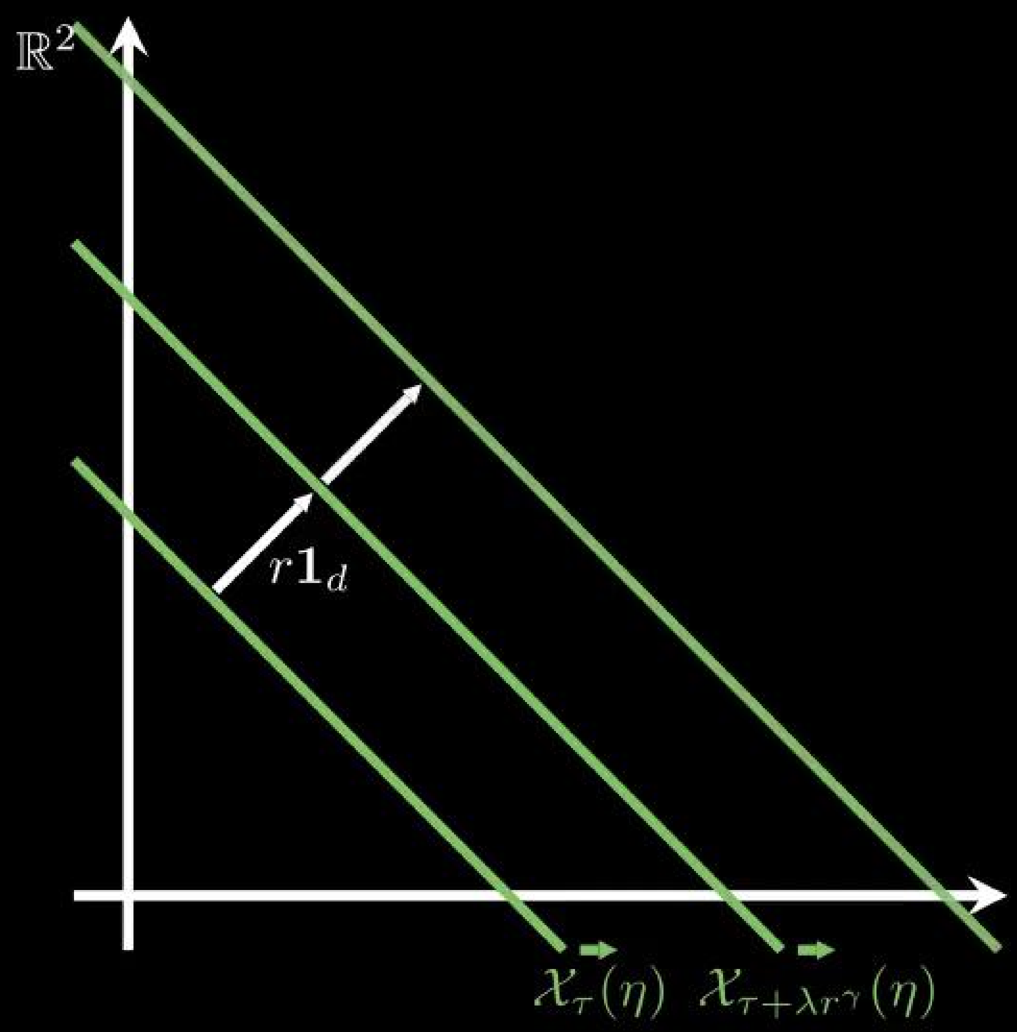

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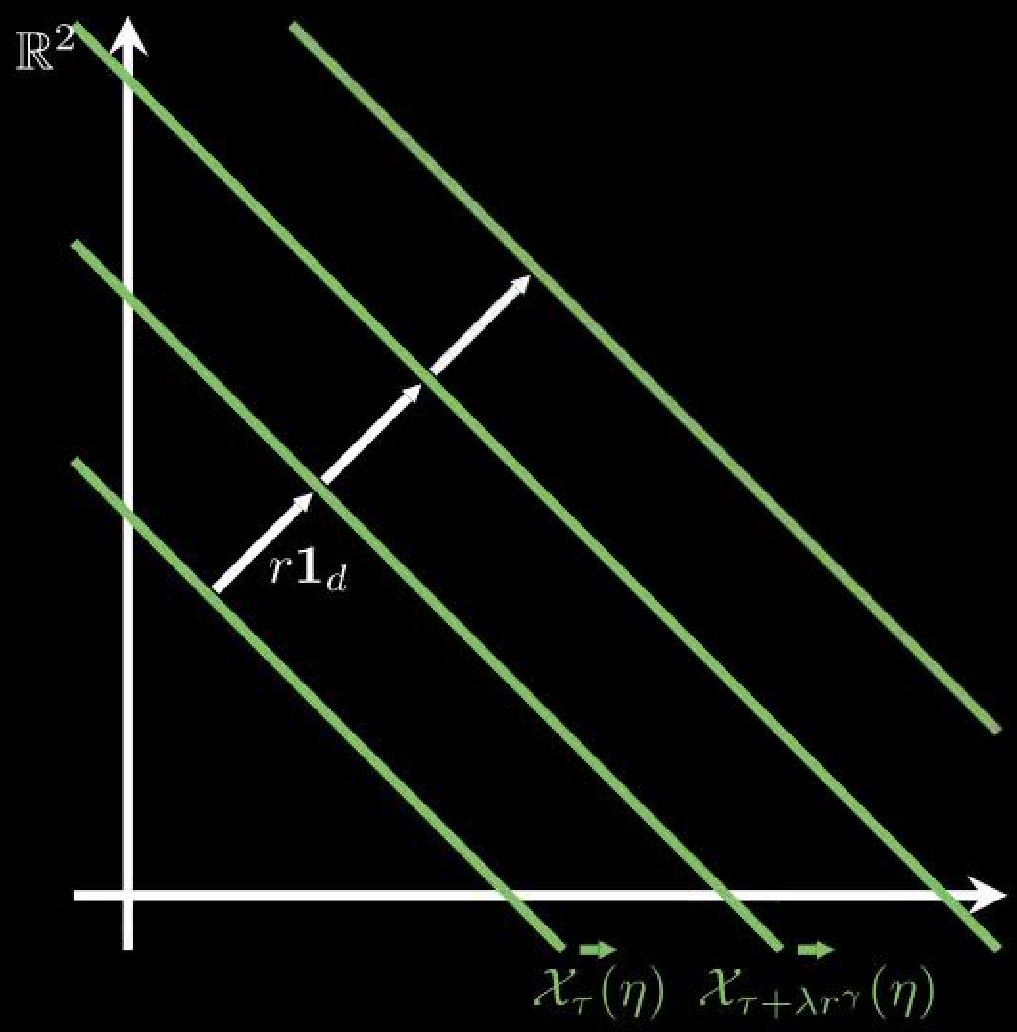

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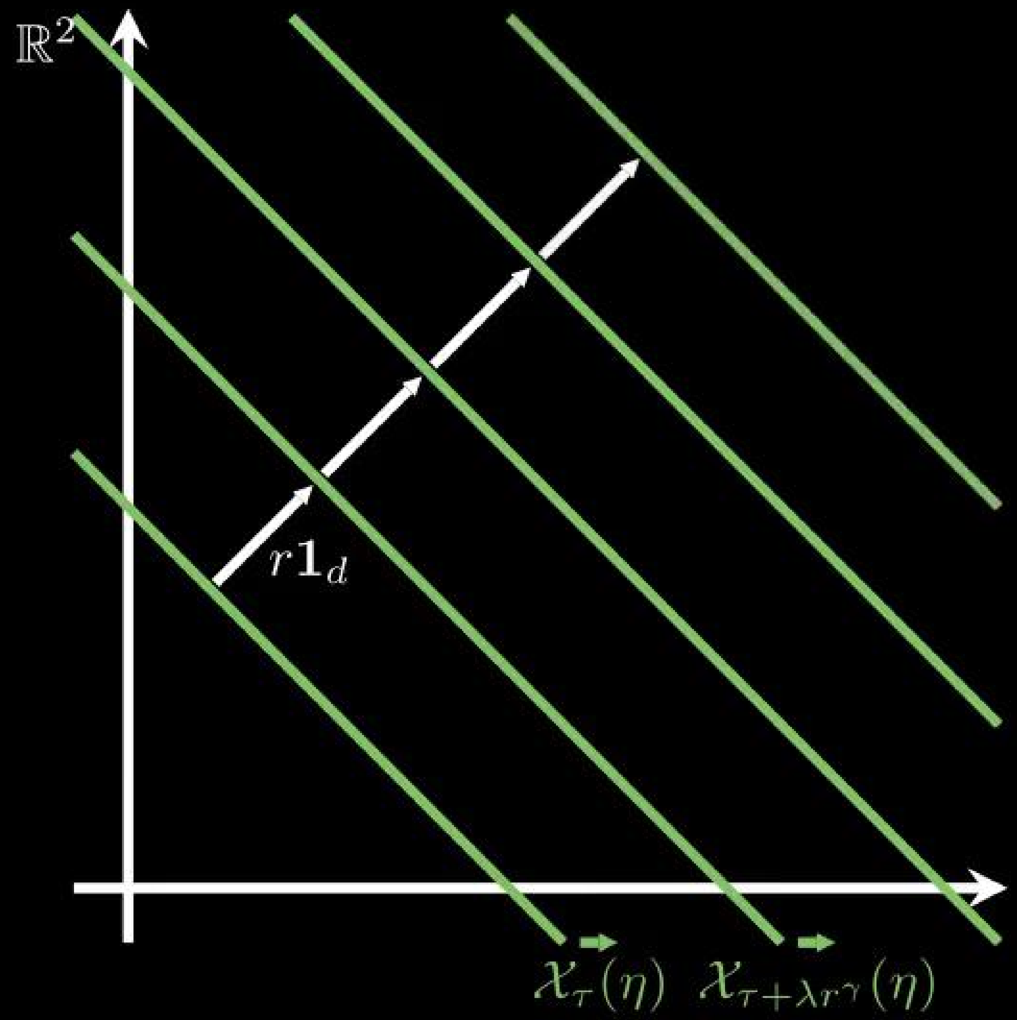

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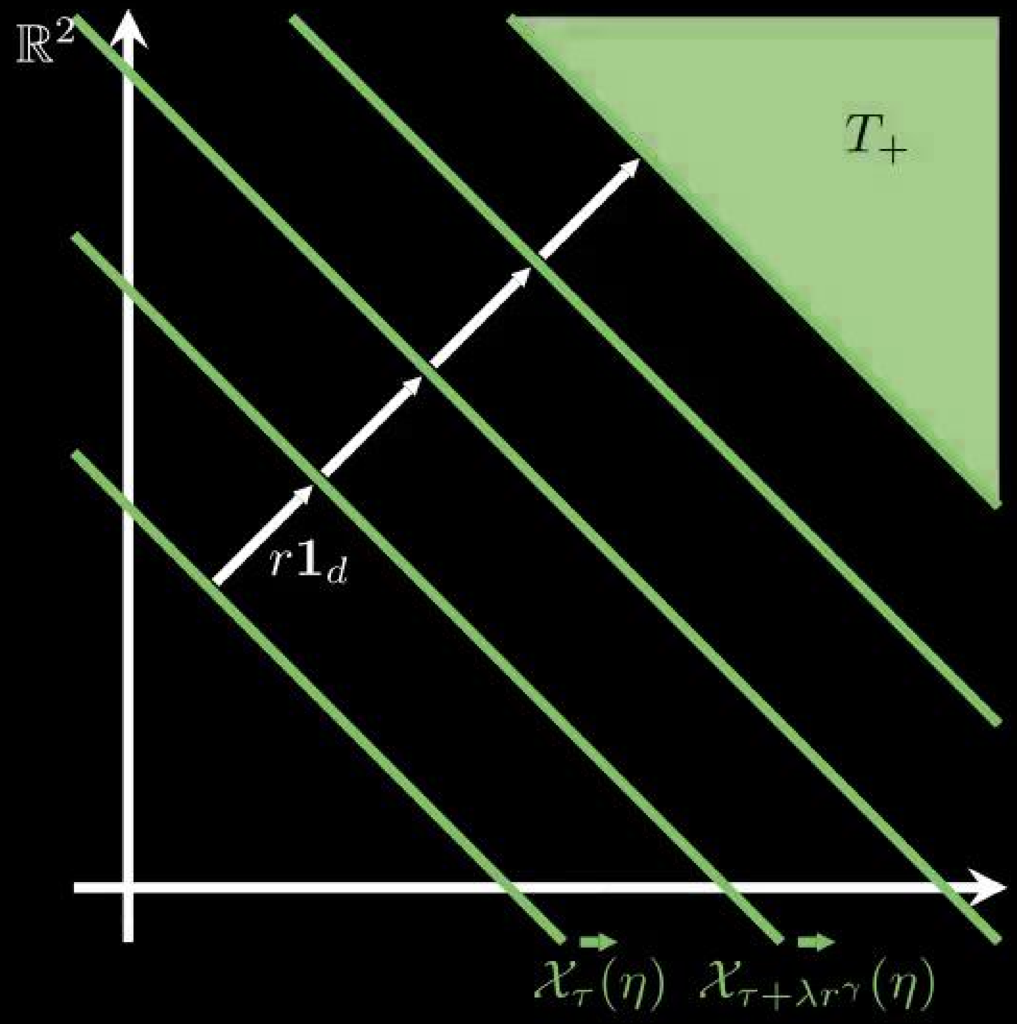

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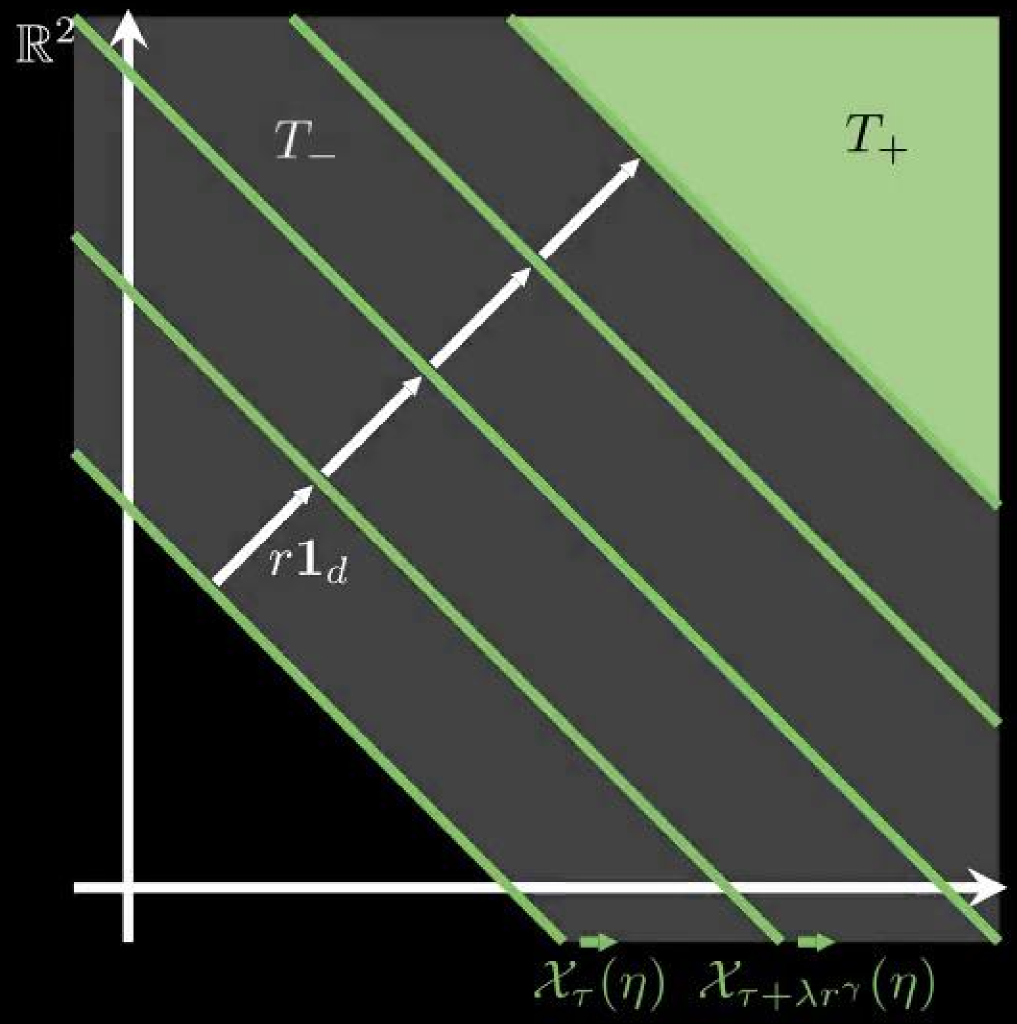

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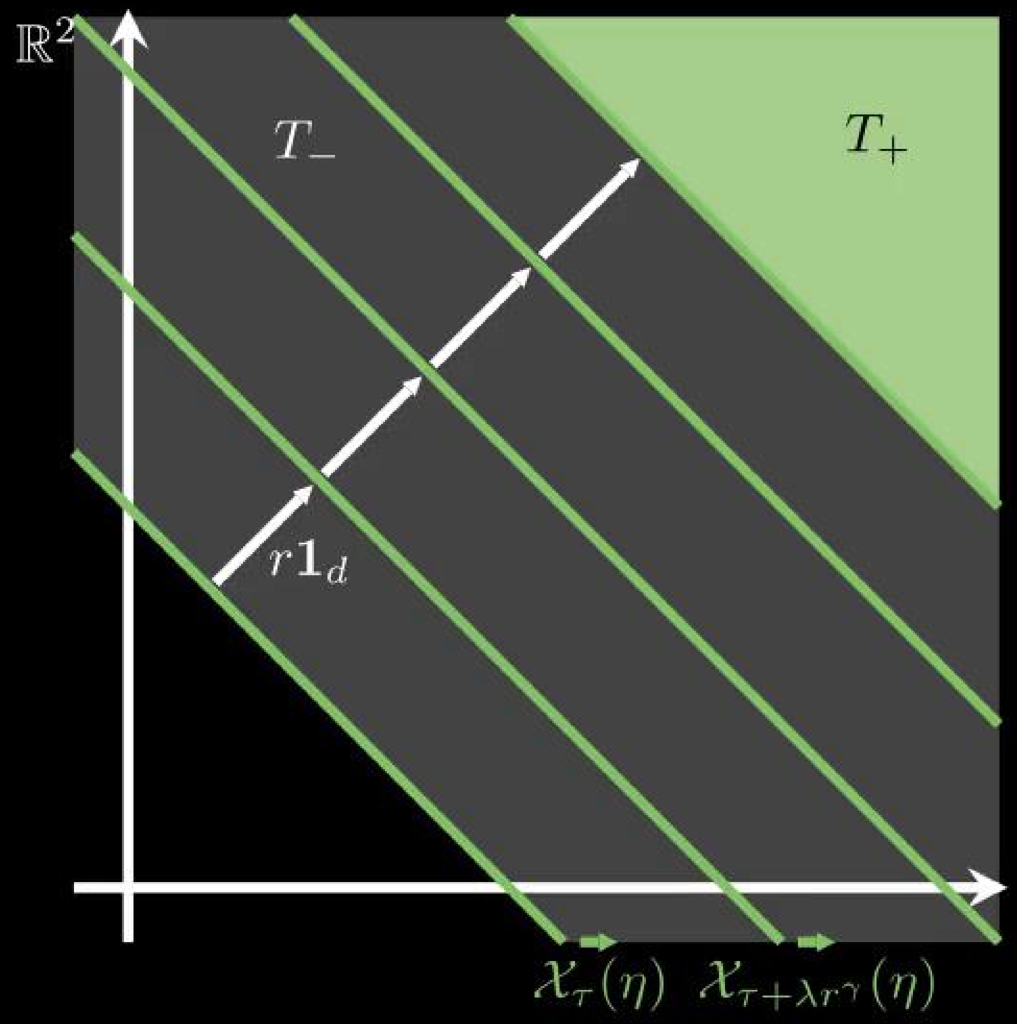

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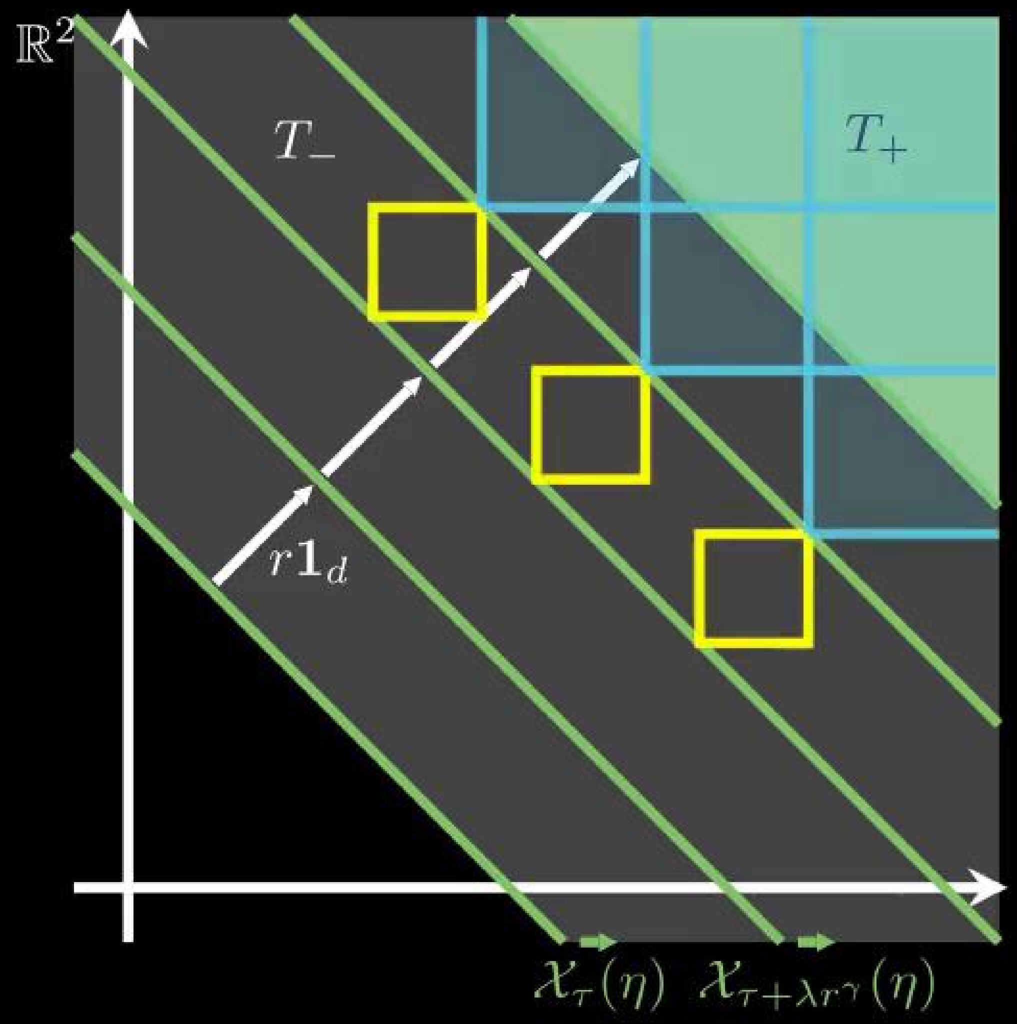

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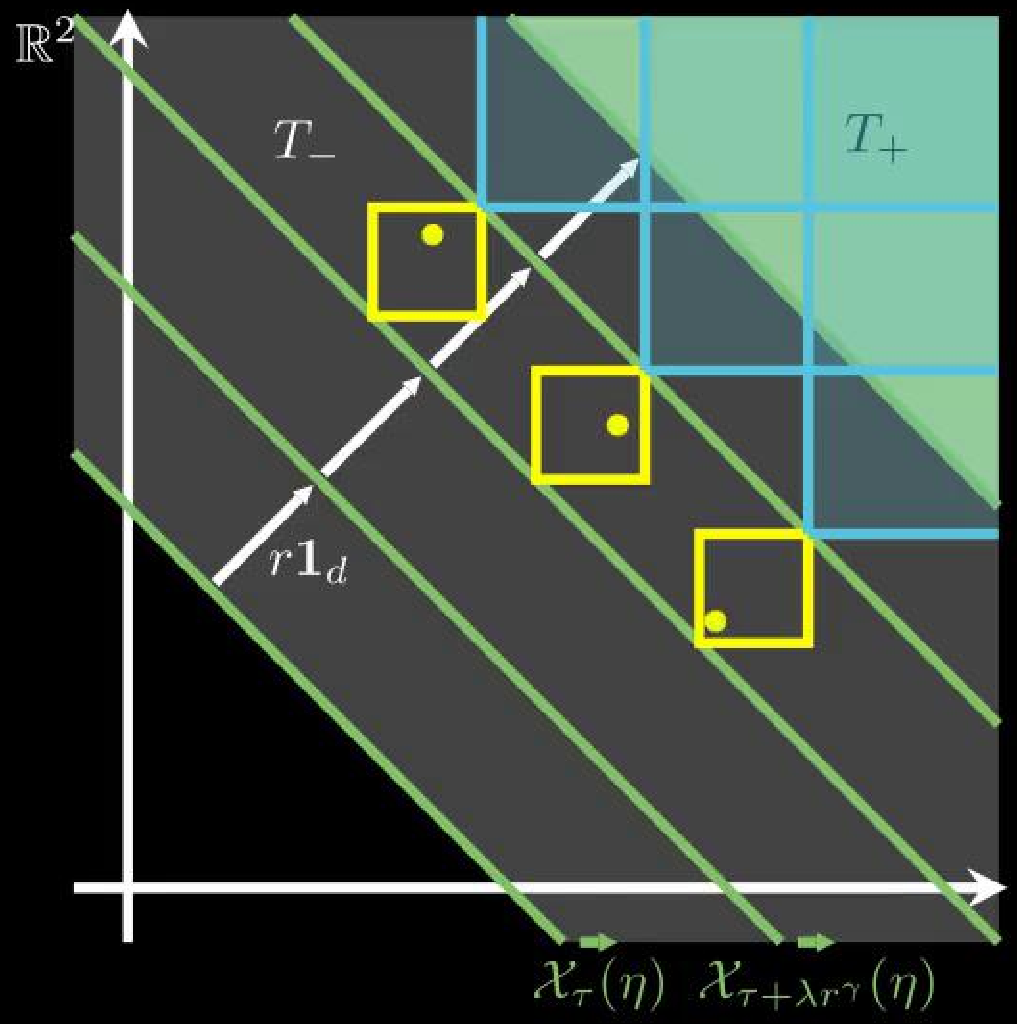

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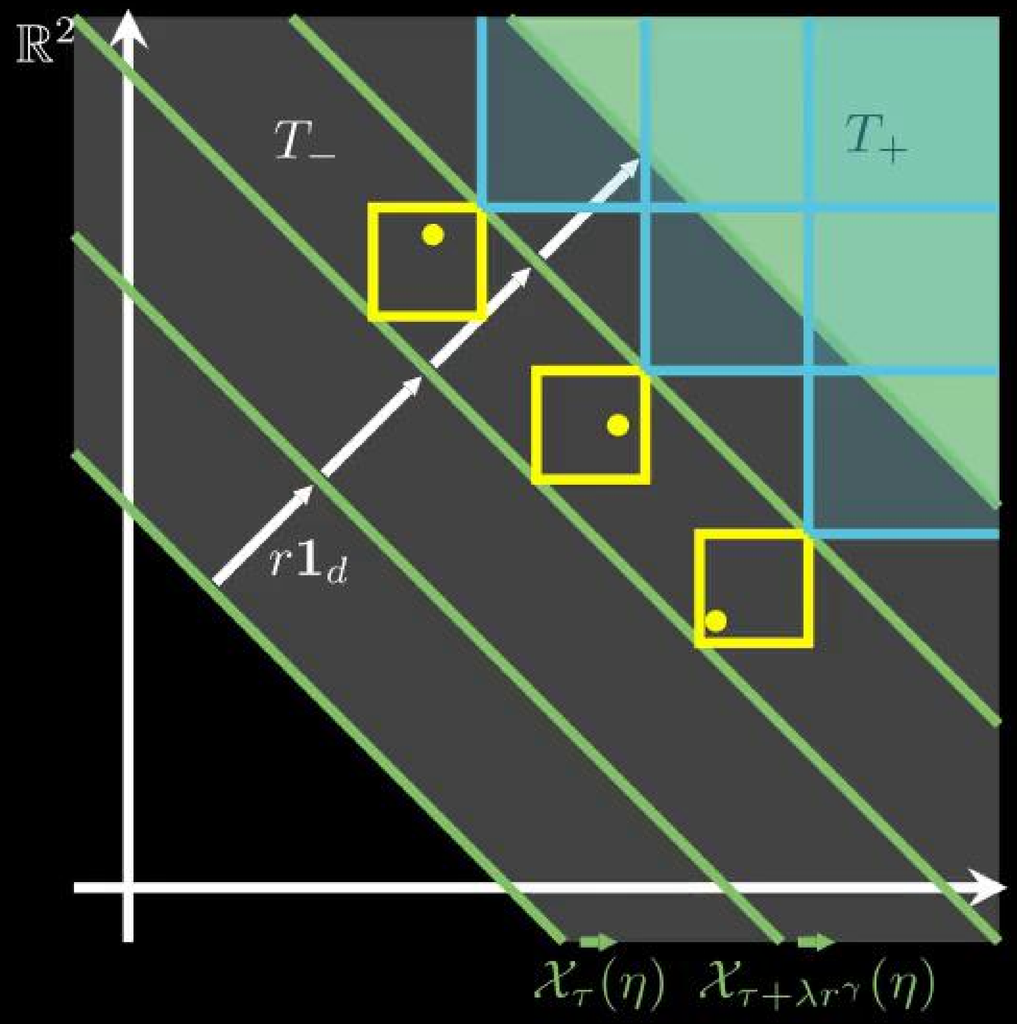

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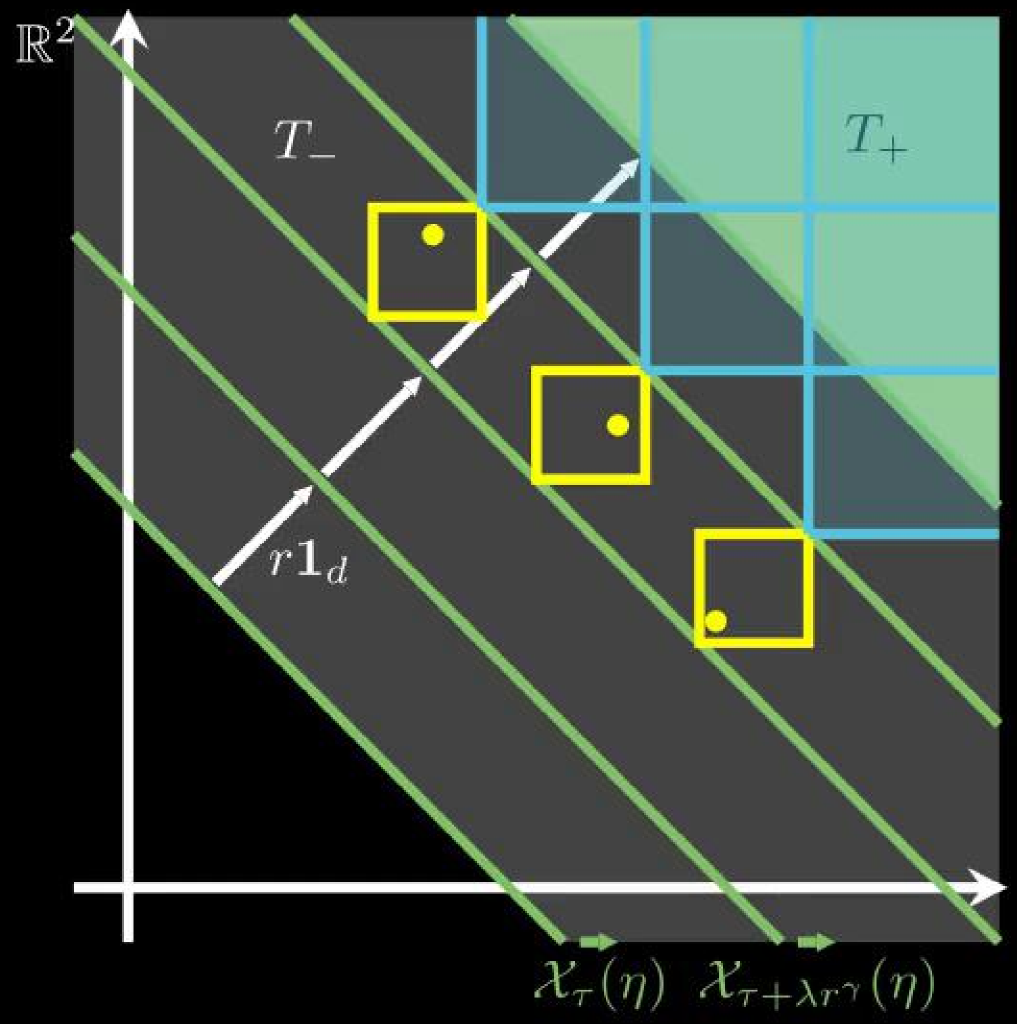

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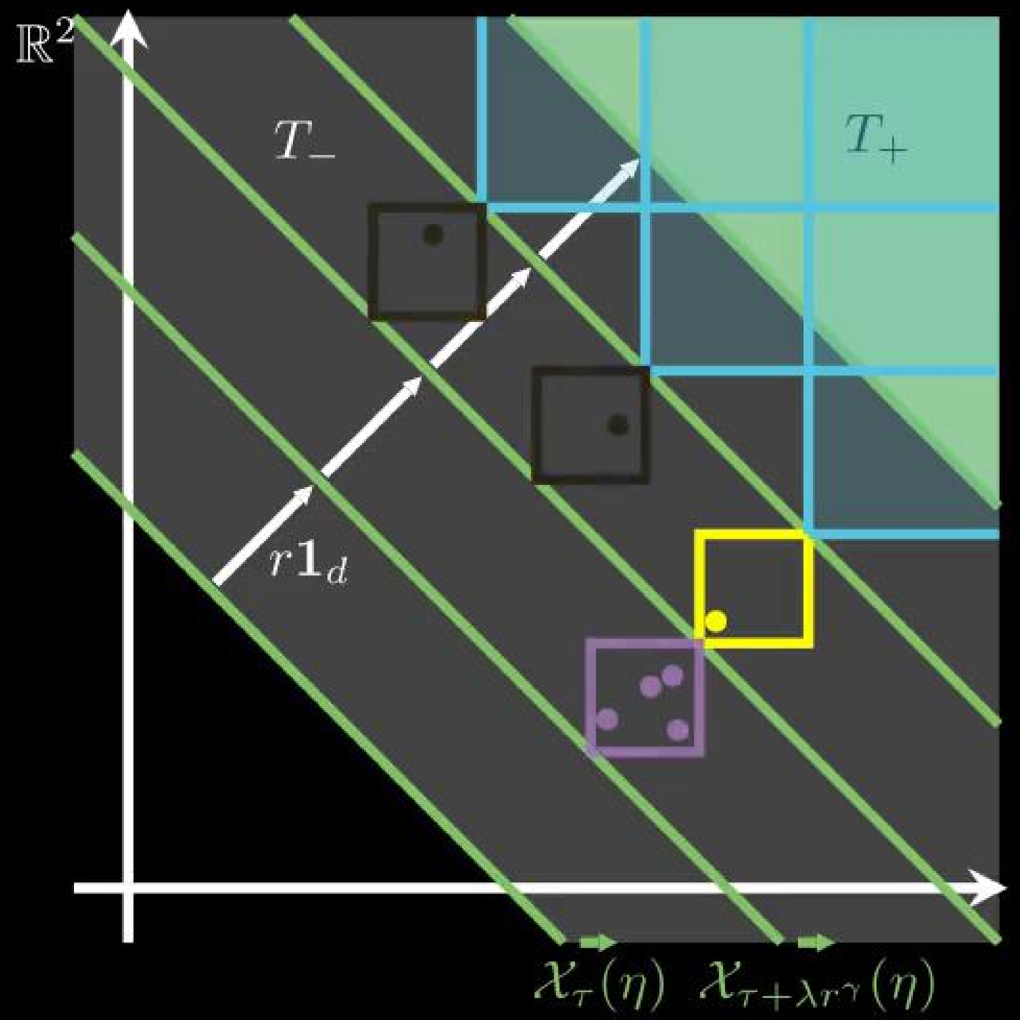

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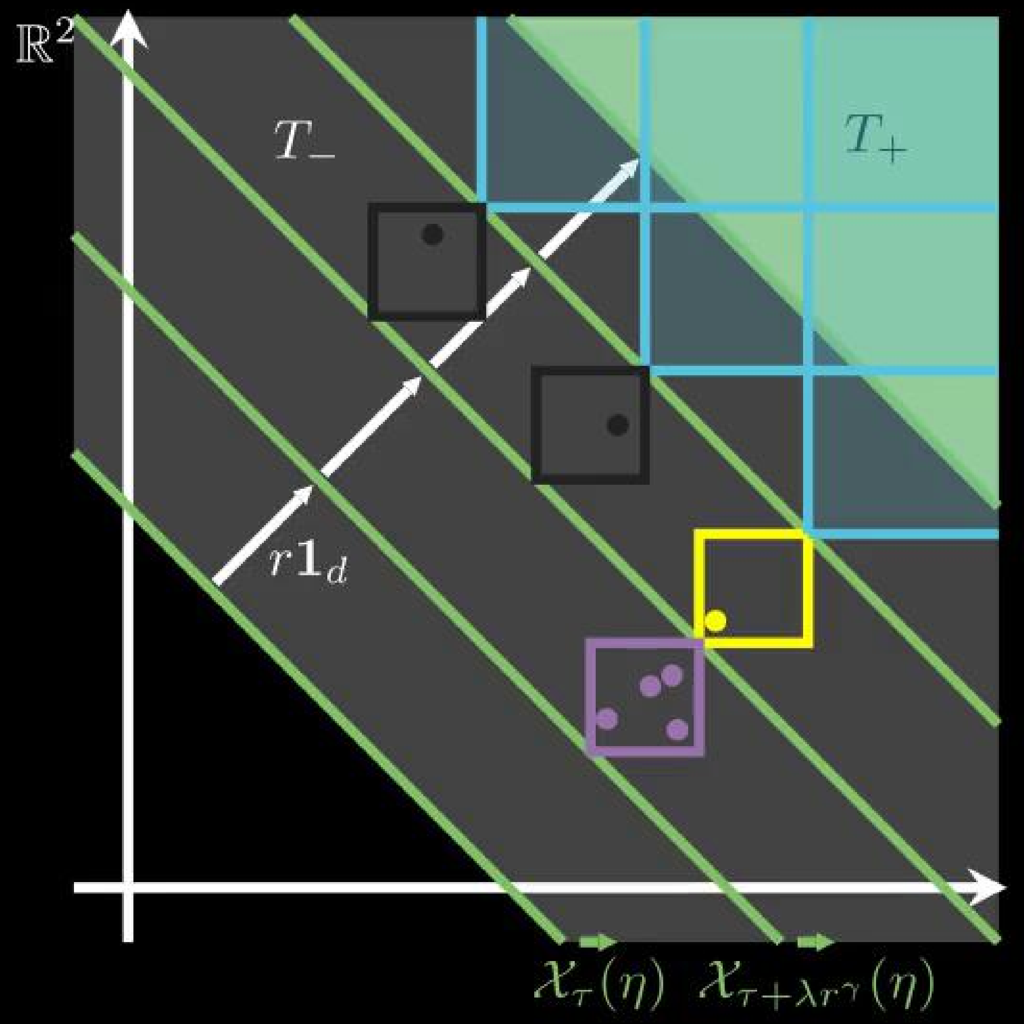

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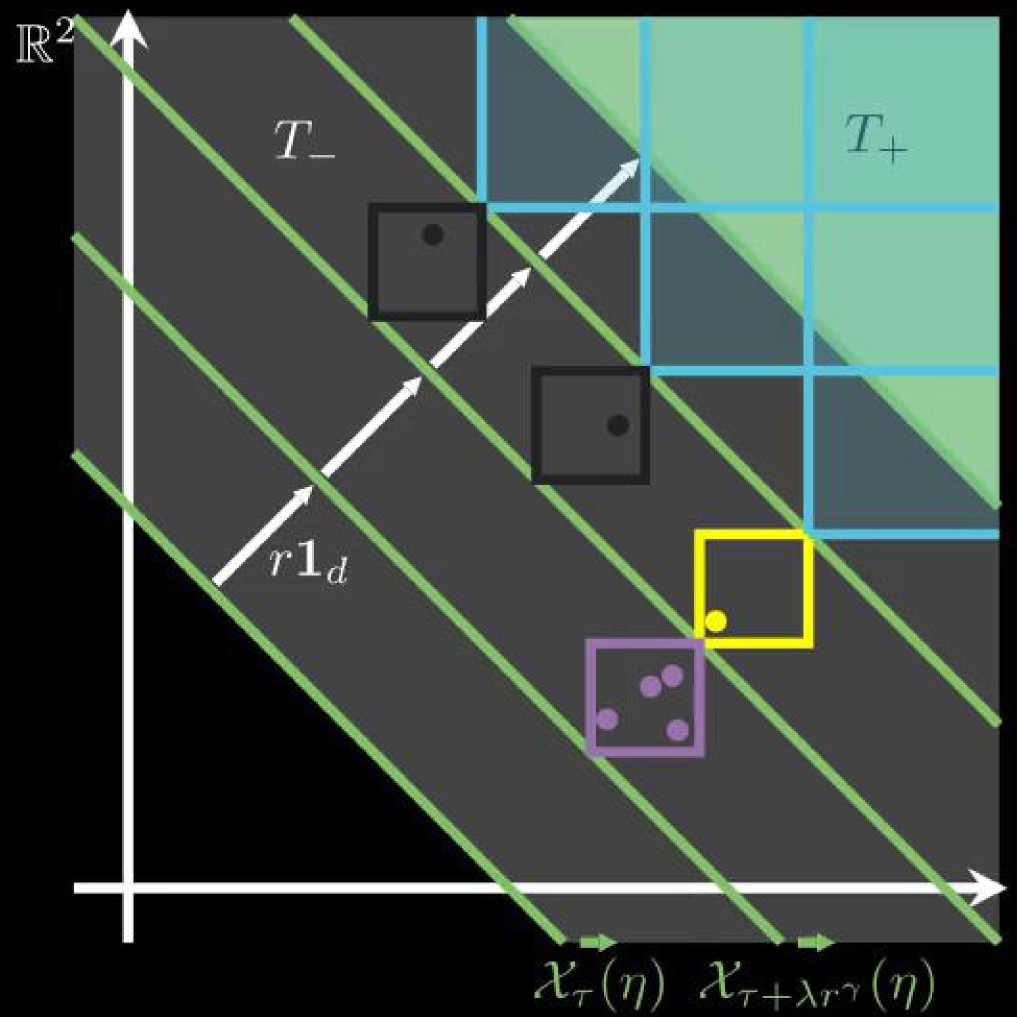

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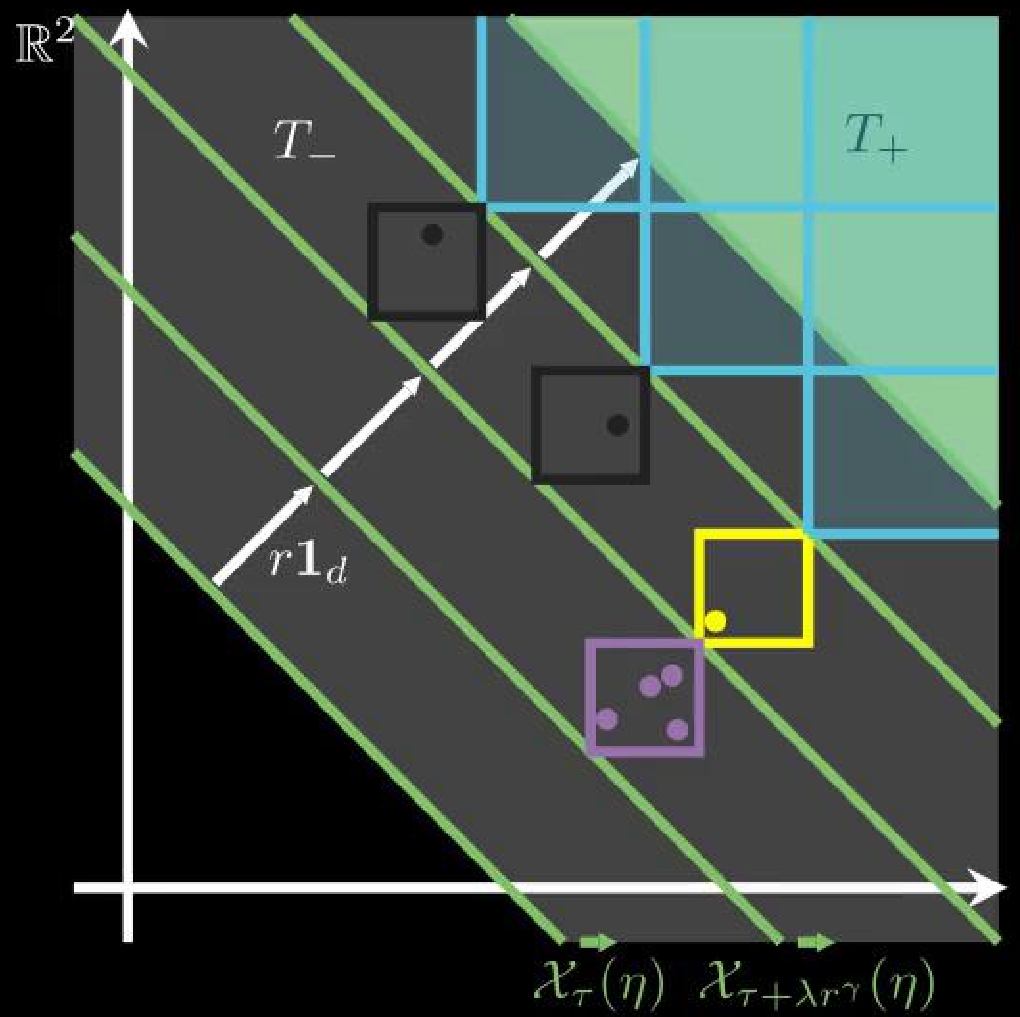

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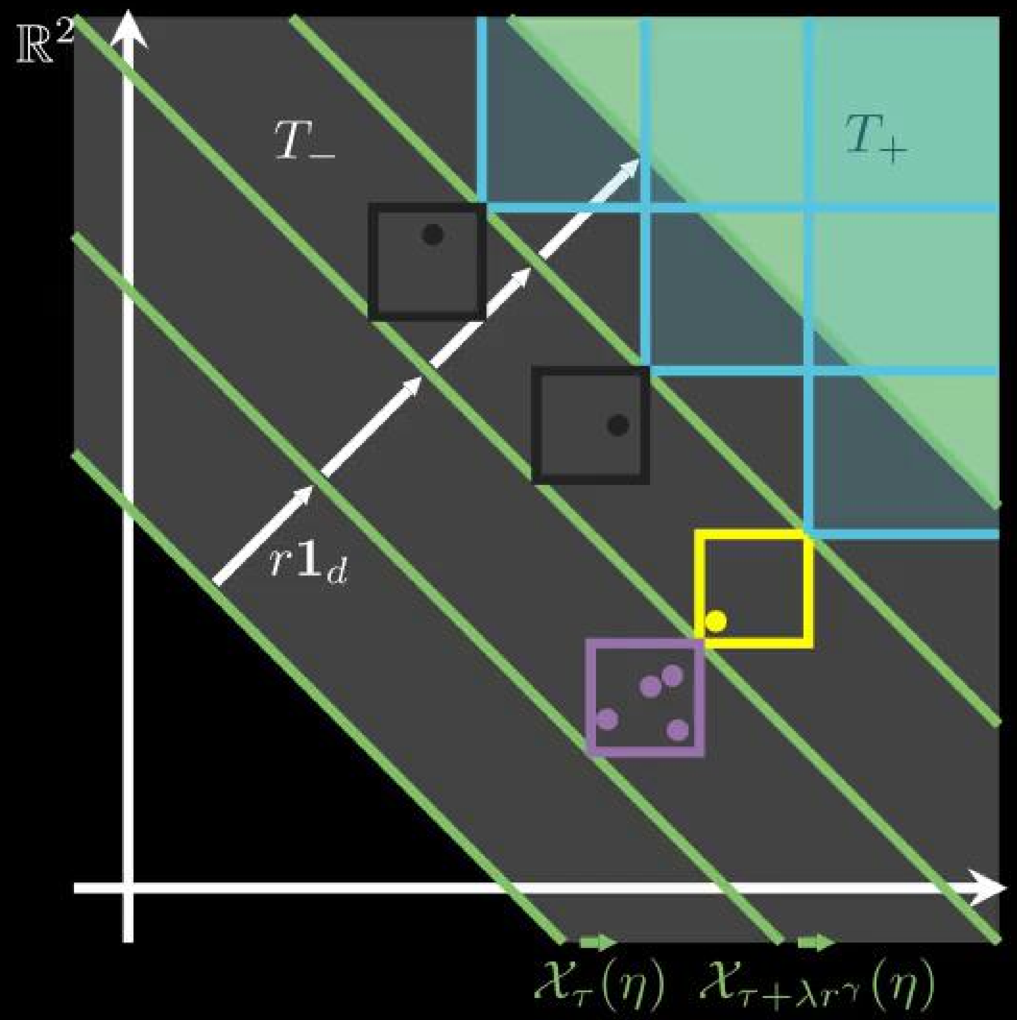

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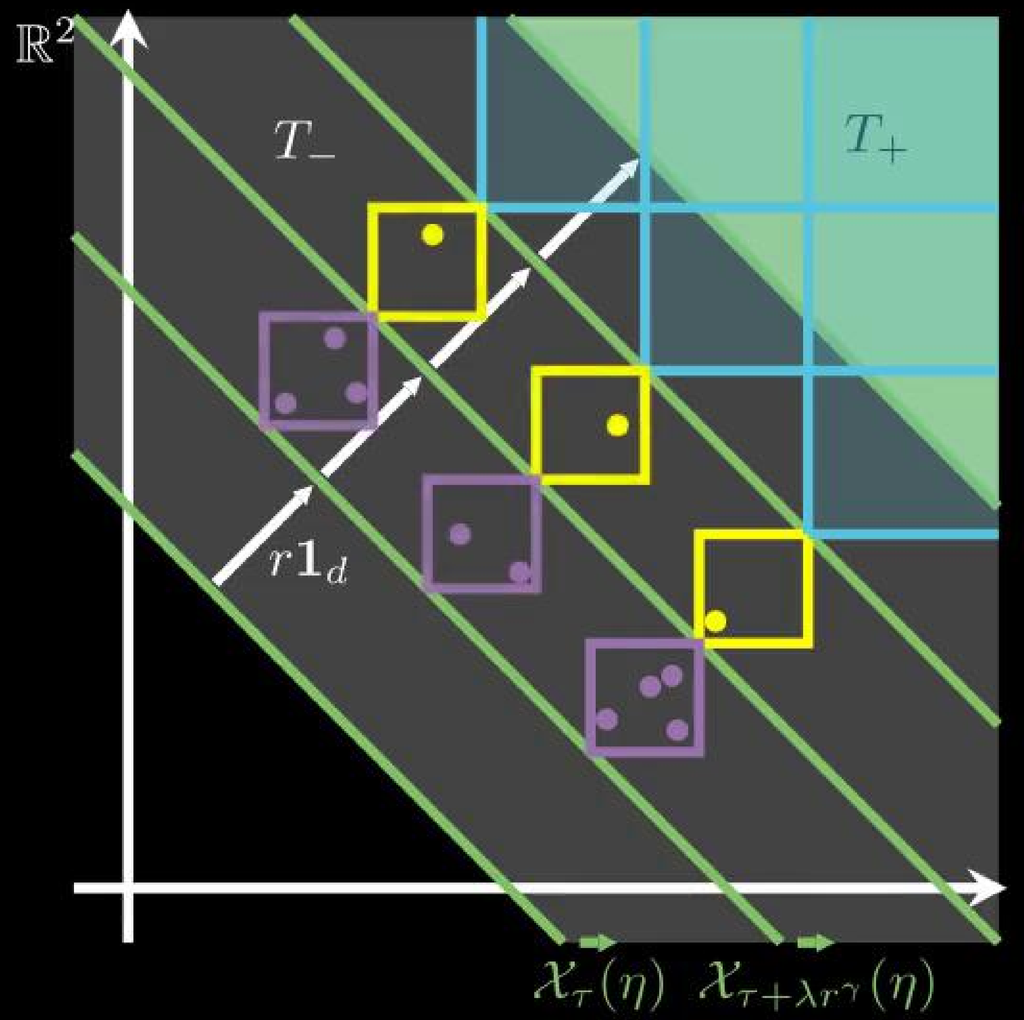
$$\sup_{P \in \mathcal{P}_{\mathrm{MonReg}}} R_\tau(\hat{A}^{\mathrm{ISS}}) \leq 1 \wedge C(d,\theta)\biggl\{\biggl(\frac{\sigma^2}{n\lambda^2}\log_+\Bigl(\frac{m\log_+ n}{\alpha}\Bigr)\biggr)^{1/(2\gamma+d)} + \Bigl(\frac{\log_+ m}{m}\Bigr)^{1/d}\biggr\},$$

where $\log_+ x := \log(x \vee e)$ for $x \in \mathbb{R}$.



Let $r > 0$ be small.
$\mu\{\mathcal{X}_\tau(\eta) \setminus T_+\} = \mu(T_-) \approx 4r \approx r$.
Need $q :\approx 1/r^{d-1}$ boxes to cover T_+.
Out of $(X_i)_{i\in[m]}$ roughly mr^d in each box.
At least one per box if $mr^d \gtrsim \log q \Longleftarrow \boxed{r \overset{!}{\gtrsim} \bigl(\frac{\log m}{m}\bigr)^{1/d}}$.
Have $\hat{p} \leq \alpha$ if $S_k \gtrsim \sqrt{k\{\log((\log n)/\alpha)\}}$ (Howard et al, 2021).
Box contains roughly nr^d points with expected response $\geq \tau + \lambda r^\gamma$.
For $k \approx nr^d$, have $S_k \gtrsim nr^d \cdot \frac{\lambda r^\gamma}{\sigma} \overset{!}{\gtrsim} \sqrt{nr^d\{\log((\log n)/\alpha)\}}$.
Sufficient: $\boxed{r \overset{!}{\gtrsim} \Bigl\{\frac{\sigma^2}{n\lambda^2}\log\Bigl(\frac{m\log n}{\alpha}\Bigr)\Bigr\}^{1/(2\gamma+d)}}$.

Lower bound

Theorem. $\exists C(d,\theta) \geq 1$, such that for any $n \geq 1$, $m \in [n]$ and $\alpha \in (0,1)$,

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Theorem. $\exists C(d,\theta) \geq 1$, such that for any $n \geq 1$, $m = n$ and $\alpha \in (0,1)$,

$$\sup_{P \in \mathcal{P}_{\mathrm{MonReg}}} R_\tau(\hat{A}^{\mathrm{ISS}}) \leq 1 \wedge C(d,\theta) \left\{ \left(\frac{\sigma^2}{n\lambda^2} \log_+\left(\frac{n \log_+ n}{\alpha} \right) \right)^{1/(2\gamma+d)} + \left(\frac{\log_+ n}{n} \right)^{1/d} \right\},$$

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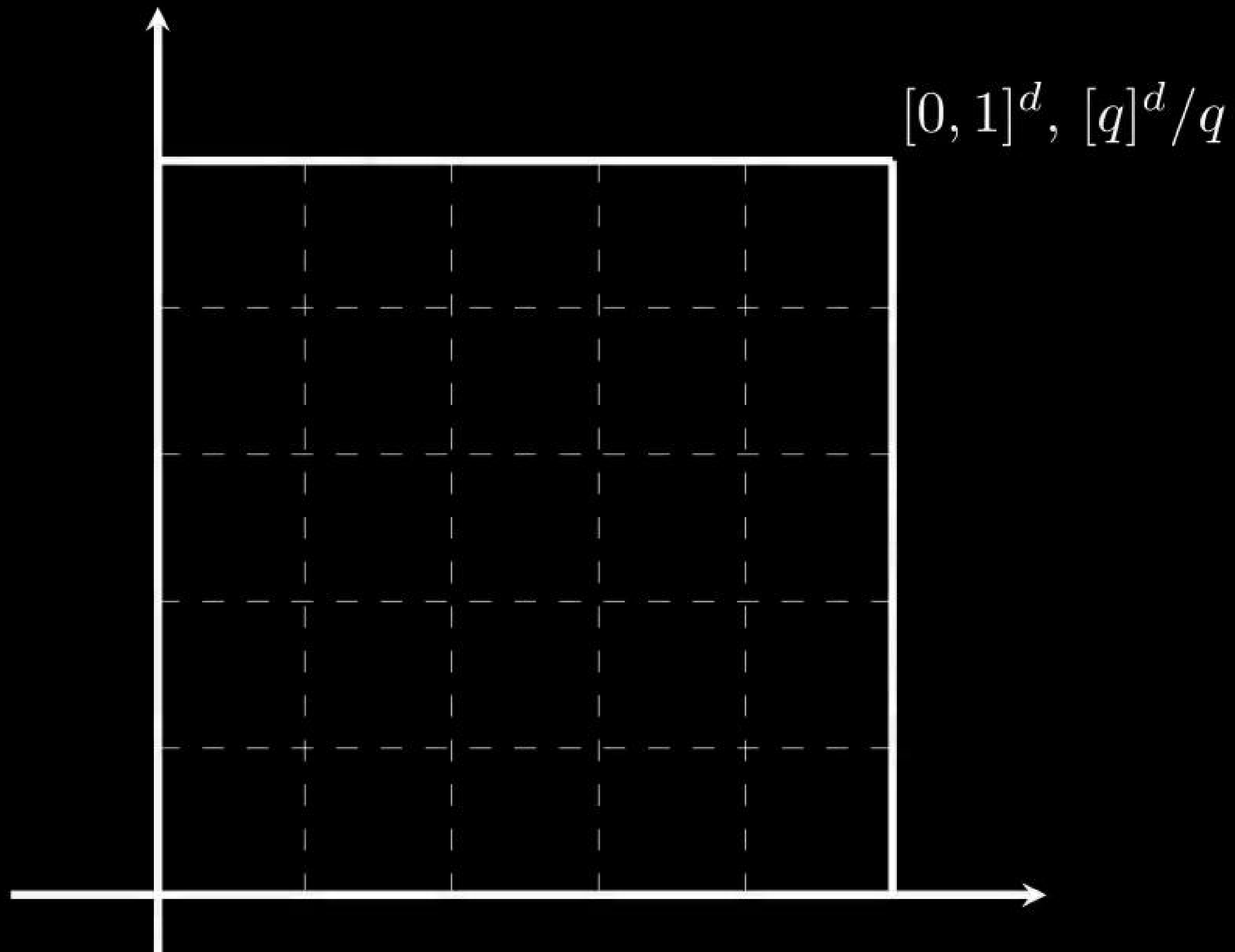

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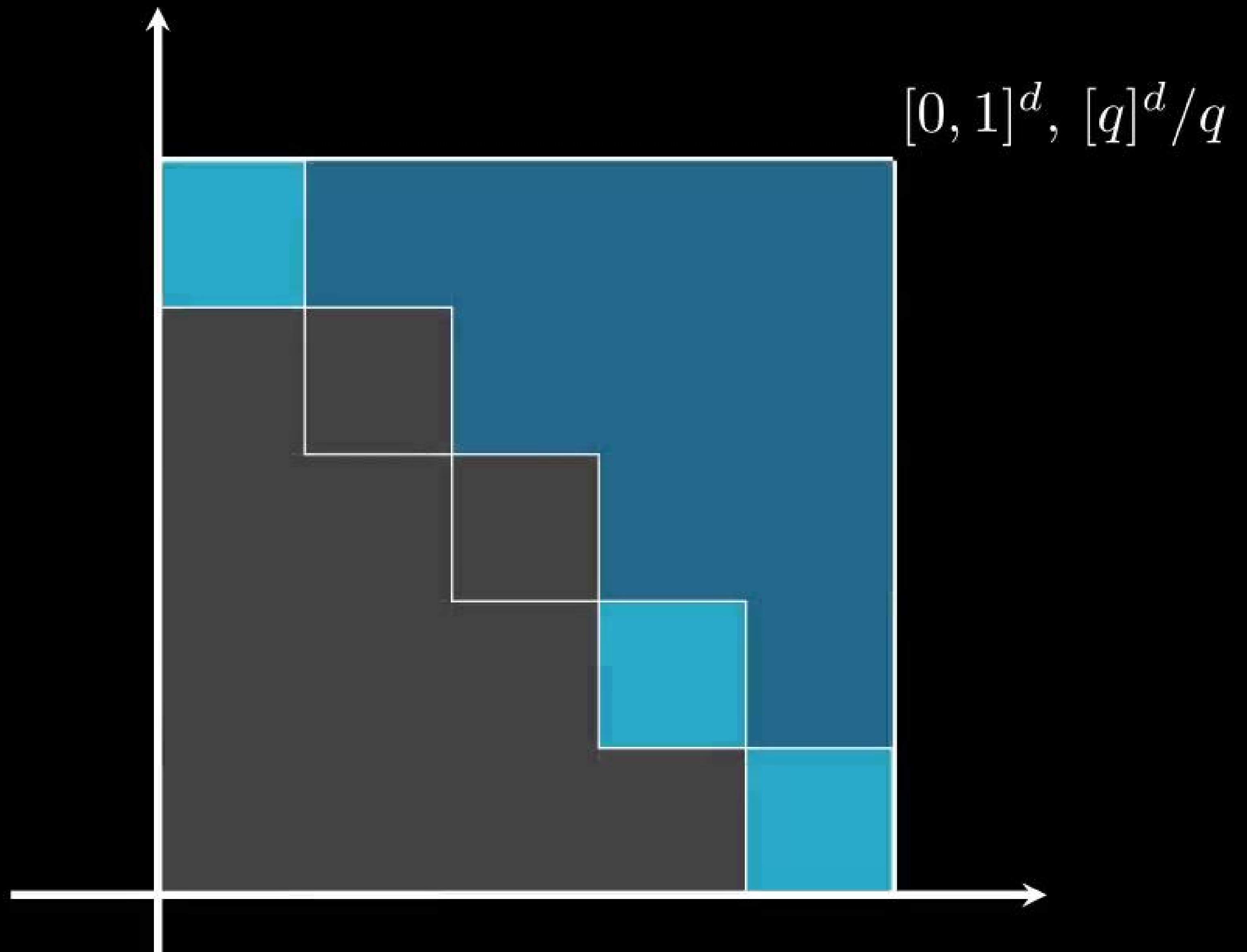

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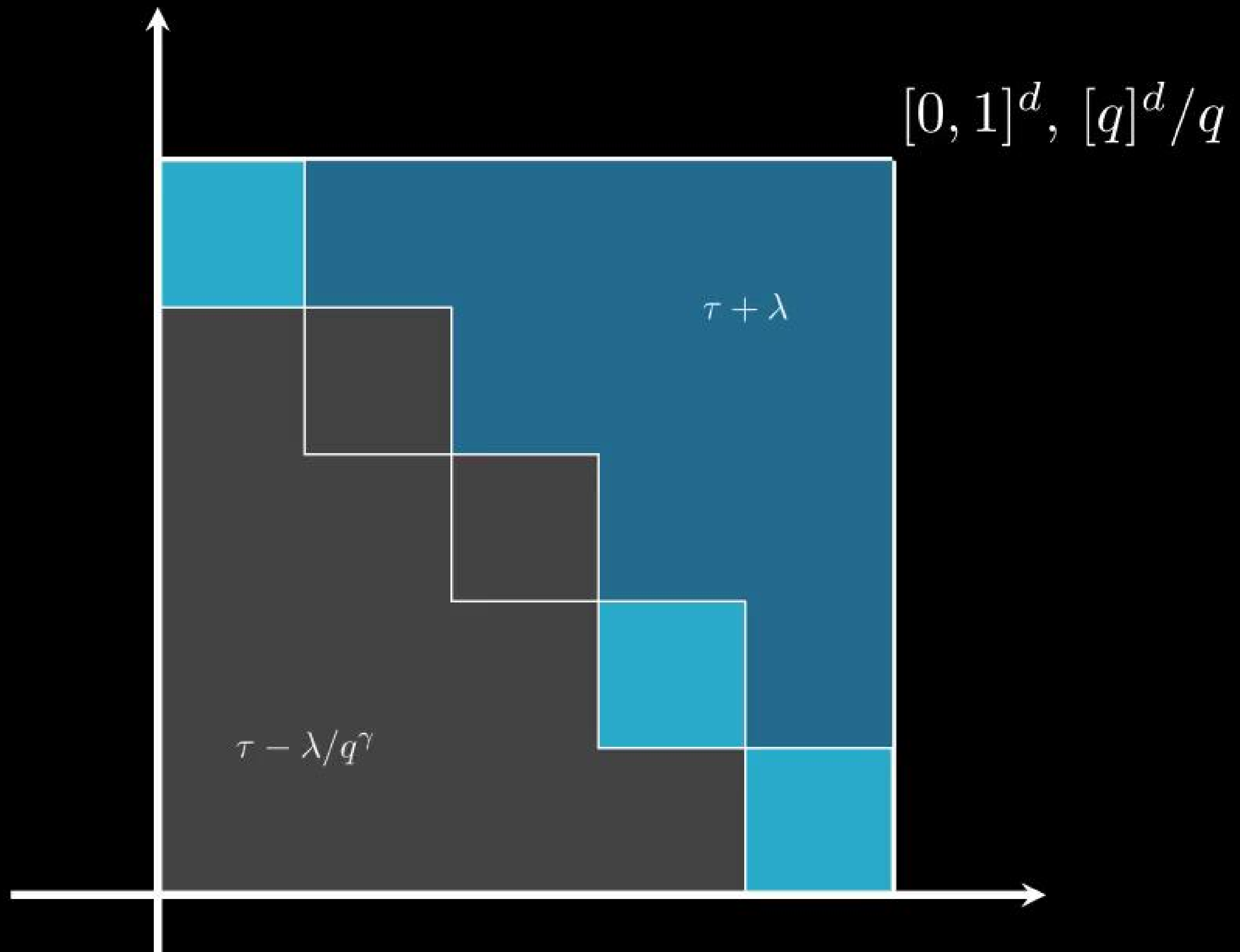

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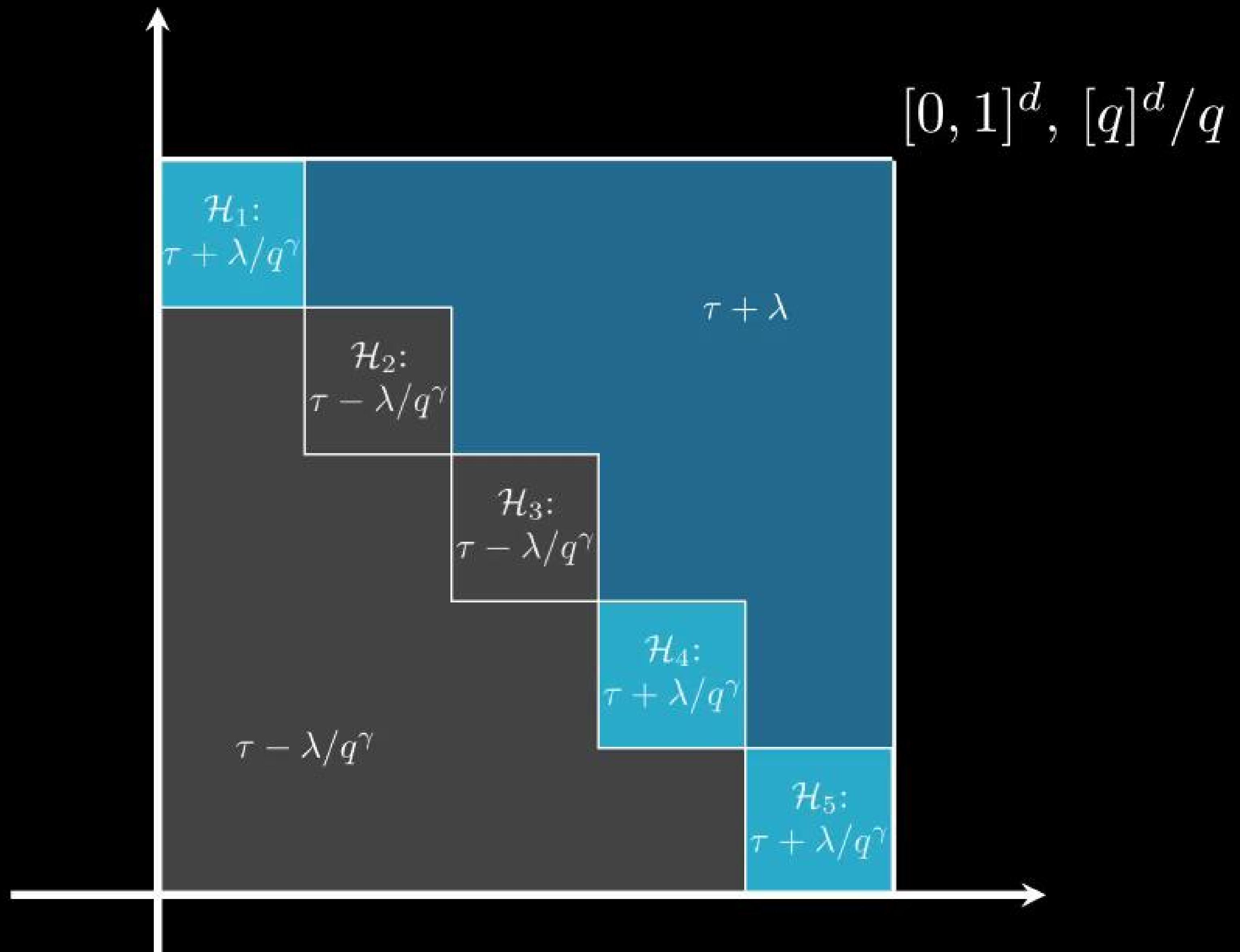

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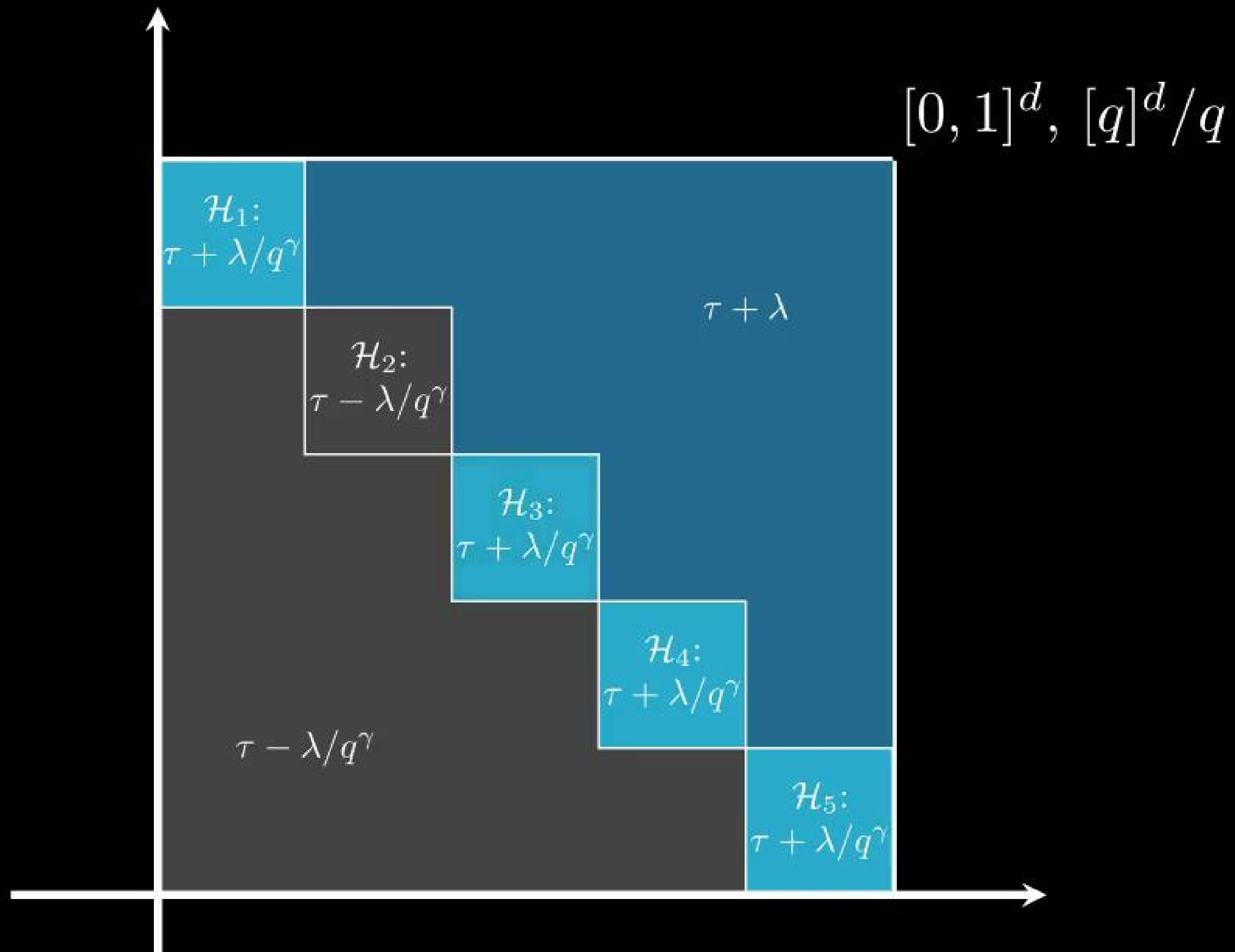

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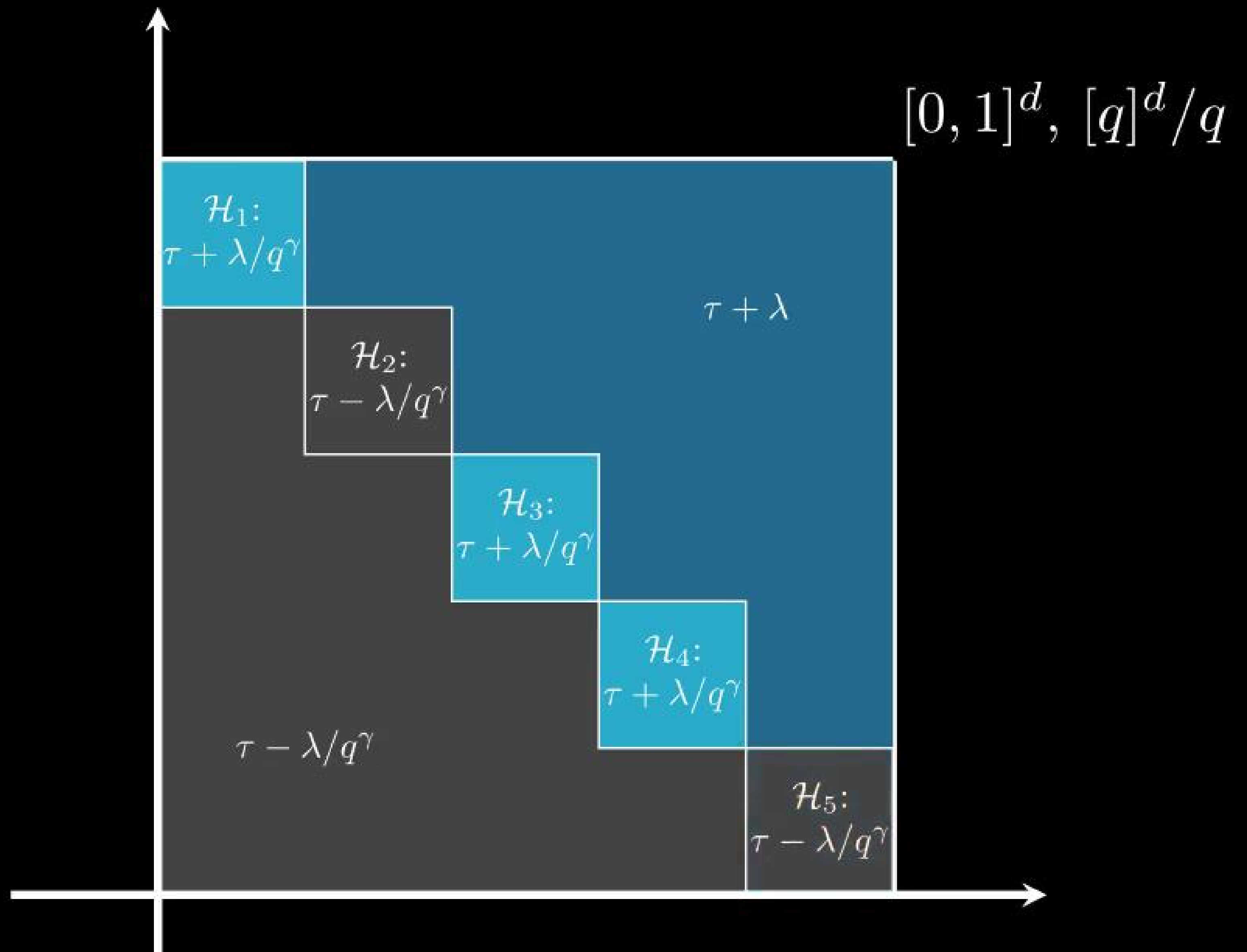

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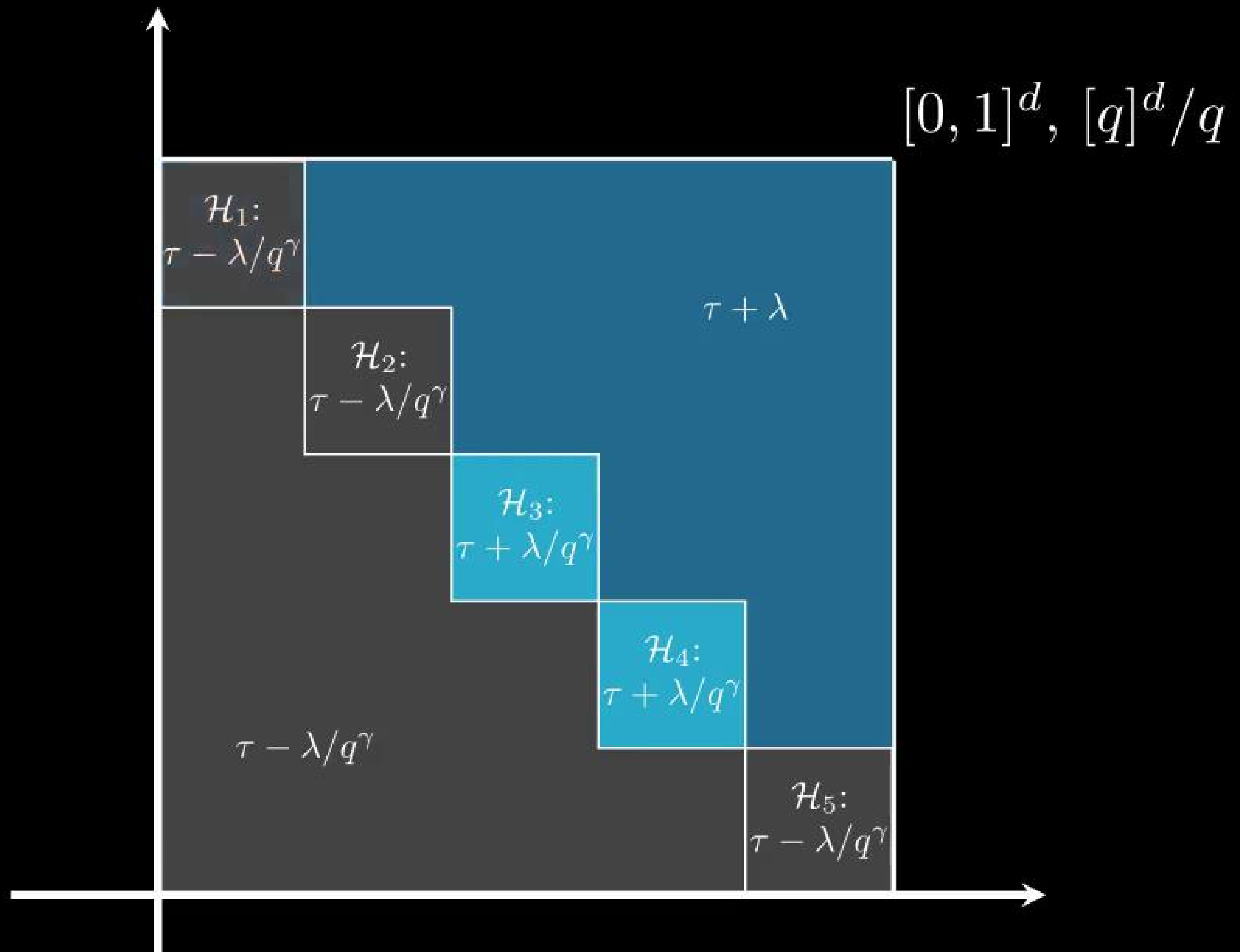

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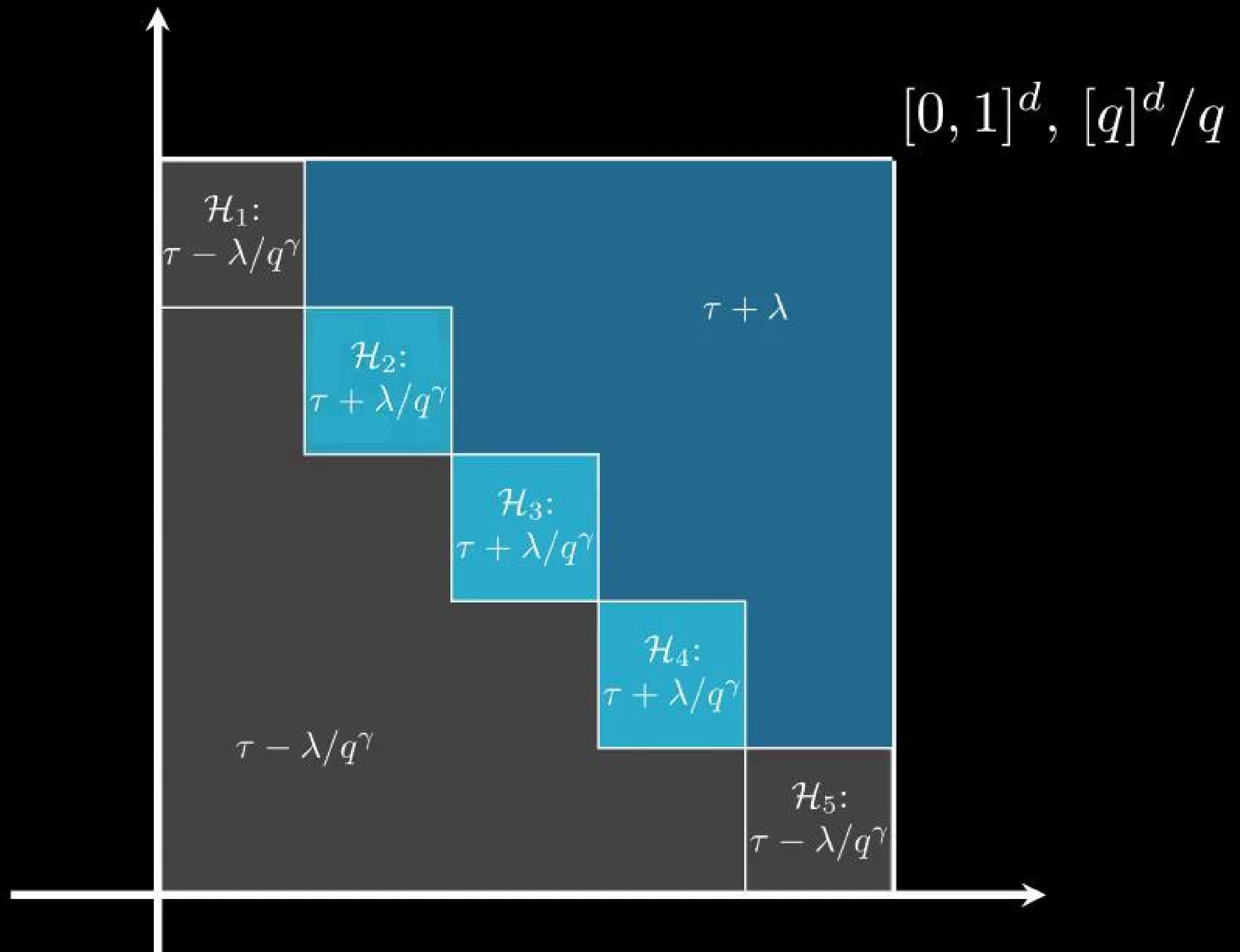

Heterogeneous treatment effects

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Suppose we observe n independent copies of $(X, T, \tilde{Y})$, where $T \in \{0, 1\}$ is a treatment indicator and $\tilde{Y}$ is the response.

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For $\ell \in \{0, 1\}$, let $\tilde{\eta}^{\ell}(x) := \mathbb{E}(\tilde{Y}|X = x, T = \ell)$, and define the *heterogeneous treatment effect* $\eta(x) := \tilde{\eta}^1(x) - \tilde{\eta}^0(x)$.

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Write $\pi(x) := \mathbb{P}(T = 1|X = x)$ for the *propensity score*, and consider the *inverse propensity weighted response*

$$Y := \frac{T - \pi(X)}{\pi(X)\bigl(1 - \pi(X)\bigr)} \cdot \tilde{Y},$$

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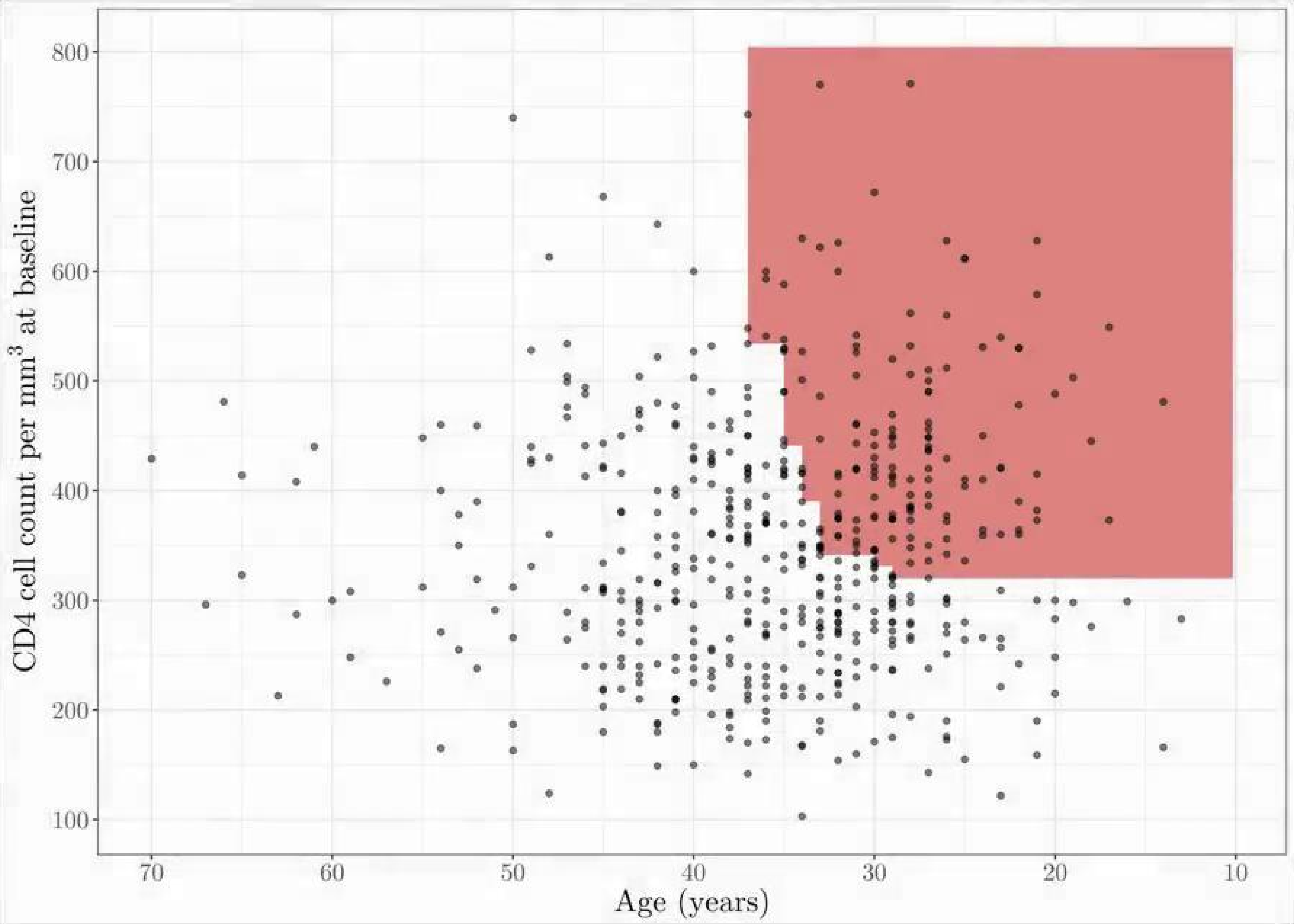
so that $\mathbb{E}(Y|X = x) = \eta(x)$ for all $x \in \mathbb{R}^d$.

Hence, if we compute $\mathcal{D} = \big((X_1, Y_1), \ldots, (X_n, Y_n)\big) \sim P^n$, then $\mathbb{P}\big(\hat{A}^{\mathrm{ISS}}(\mathcal{D}) \subseteq \mathcal{X}_\tau(\eta)\big) \geq 1 - \alpha$ whenever $P \in \mathcal{P}_{\mathrm{Mon},d}(\sigma)$.

Application

Primary endpoint: reduction of the CD4 cell count by 50%, development of AIDS, or death, with median follow-up duration 143 weeks (Hammer et al., 1996). Let $\alpha = 0.05$ and $\tau = 1/2$.



Extensions in the paper

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Take-home messages

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In common situations, no smoothing-parameters have to be specified.

References and acknowledgement

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Thank you!

Main reference:

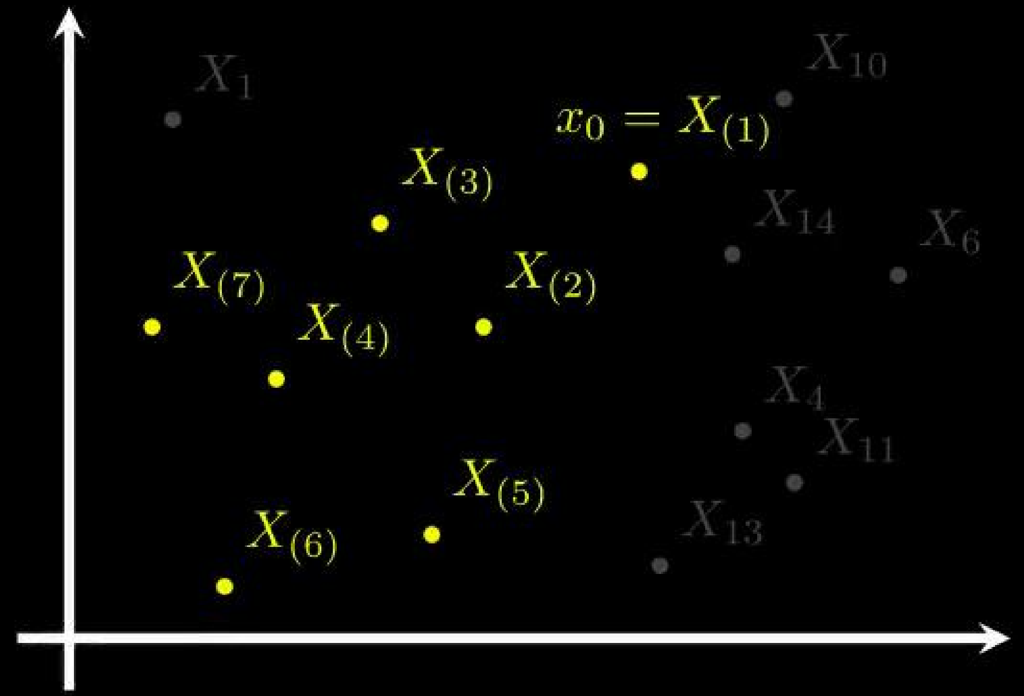
Müller, M. M., Reeve, H. W. J., Cannings, T. I. and Samworth, R. J. (2023) Isotonic subgroup selection. *arXiv preprint arXiv:2305.04852*.

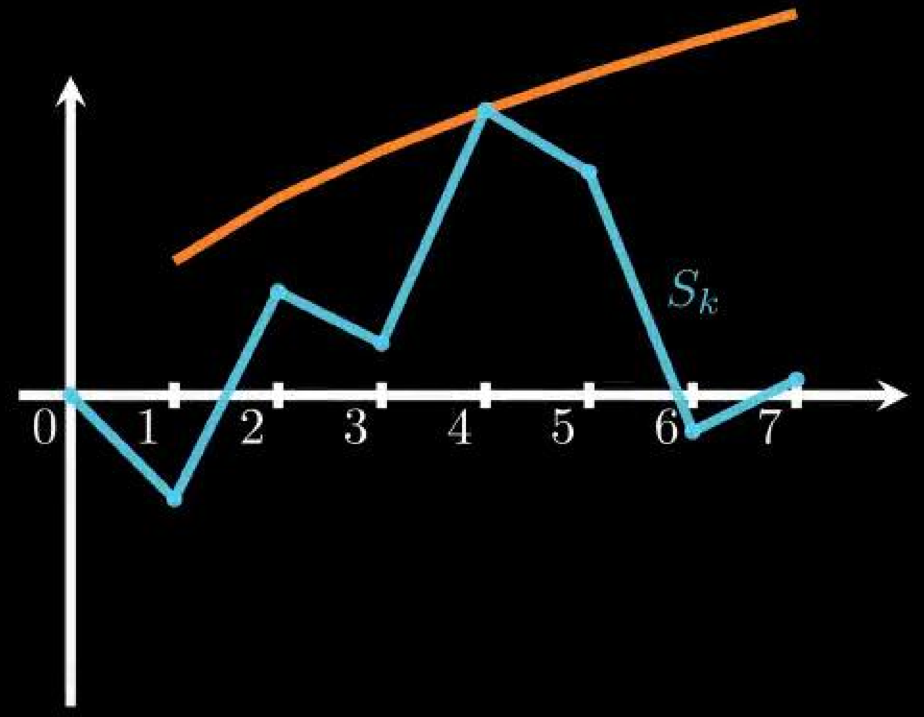
See manuelmmueller.github.io for data and `R`-code.

Appendix

Construct p-values $\hat{p}_i$ for $H_0(X_i)$, $i \in [m]$

Given $x_0 \in \mathbb{R}^d$, we seek a p-value for $H_0(x_0) := \{P \in \mathcal{P}_{\mathrm{Mon},d}(\sigma) : \eta(x_0) < \tau\}$.





Denote $\mathcal{I}(x_0) := \{i \in [n] : X_i \preccurlyeq x_0\}$, $n(x_0) := |\mathcal{I}(x_0)|$.

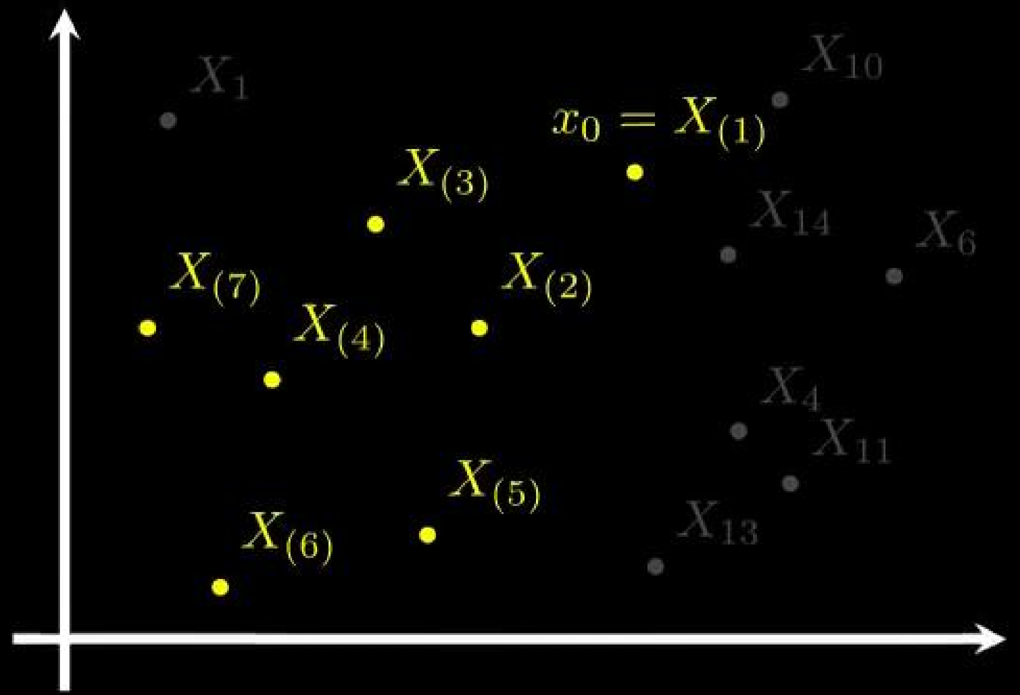
Let $X_{(j)}$ be the jth nearest neighbour of x_0 among X_i, $i \in \mathcal{I}(x_0)$, in sup-norm and let $Y_{(j)}$ be the corresponding response.

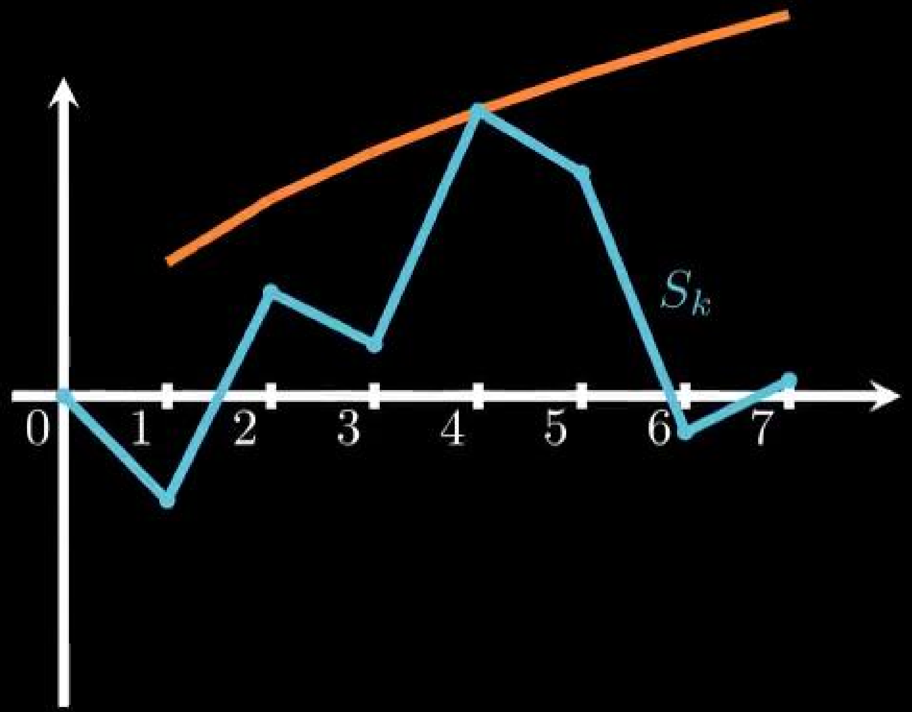
Let

$$S_k := \sum_{j=1}^{k} \frac{Y_{(j)} - \tau}{\sigma}.$$

Then S_k is a supermartingale under $P \in H_0(x_0)$. Combination with time-uniform bounds by Howard et al. (2021) gives p-values from this martingale test (Duan et al., 2020).

Construct p-values $\hat{p}_i$ for $H_0(X_i)$, $i \in [m]$





Definition. For $\sigma > 0$, $x \in \mathbb{R}^d$, let

$$\hat{p}_{\sigma,\tau}(x) := 1 \wedge \min_{k \in [n(x)]} 5.2 \exp\left\{-\frac{(S_k \vee 0)^2}{2.0808k} + \frac{\log\log(2k)}{0.72}\right\},$$

whenever $n(x) > 0$, and $\hat{p}_{\sigma,\tau}(x) := 1$ otherwise.

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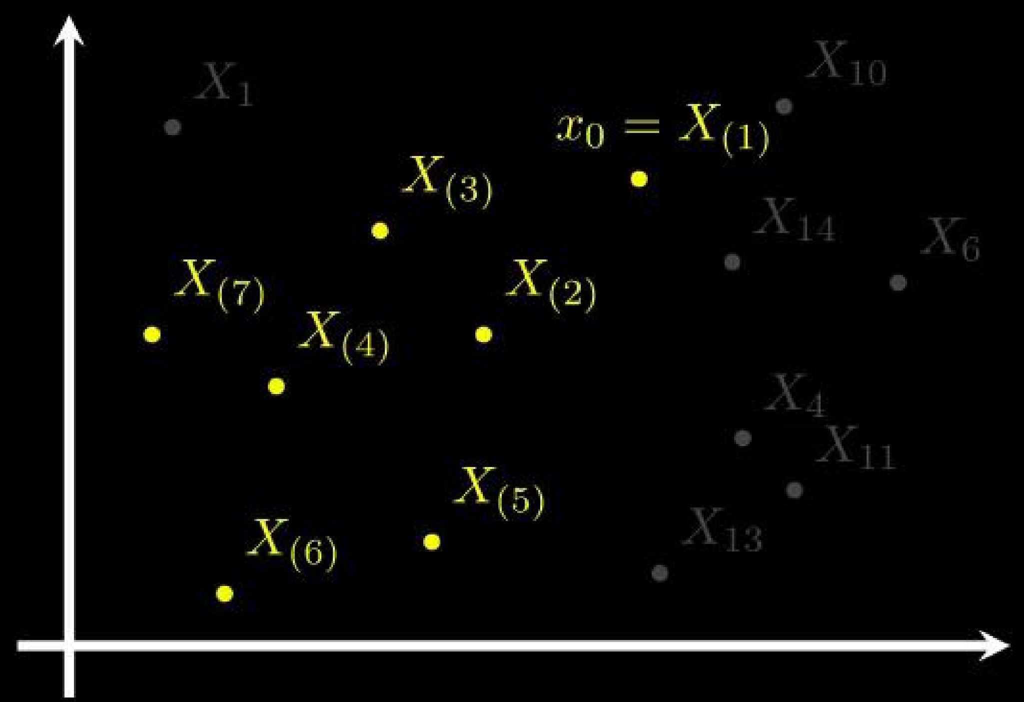

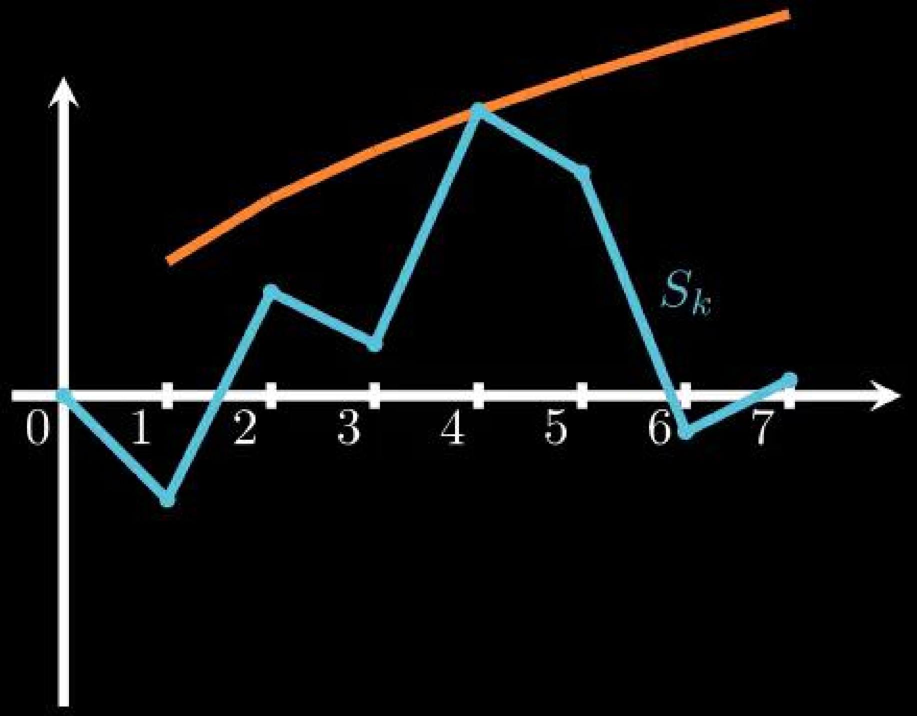

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Lemma. When $\eta(x) < \tau$, we have $\mathbb{P}\{\hat{p}_{\sigma,\tau}(x) \leq t \mid (X_i)_{i \in [n]}\} \leq t$ for all $t \in (0,1)$.

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Consider adaptation to σ^2 when $Y - \eta(X)|X \sim \mathcal{N}(0, \sigma^2)$.

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$$\bar{p}^k_\tau(x) := \frac{1}{\hat{\sigma}^k_{0,k} e^{k/2}} \cdot \prod_{j=1}^{k} \hat{\sigma}_{1,j-1} \exp\left\{ \frac{\big(Y_{(j)} - \bar{Y}_{1,j-1}\big)^2}{2\hat{\sigma}^2_{1,j-1}} \right\},$$

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Lemma. When $\eta(x) < \tau$, we have $\mathbb{P}\big\{\bar{p}_\tau(x) \leq t | \mathcal{D}_X\big\} \leq t$ for all $t \in (0, 1)$.

Extension II: Classification

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Simulations

We conduct a simulation study to compare with other choices of multiple testing procedure. We take $\mu = \mathrm{Unif}\big([0,1]^d\big)$, $Y - \eta(X)|X \sim \mathcal{N}(0,\sigma^2)$ and our regression functions η are obtained by rescaling f to $[0,1]$ on $[0,1]^d$:

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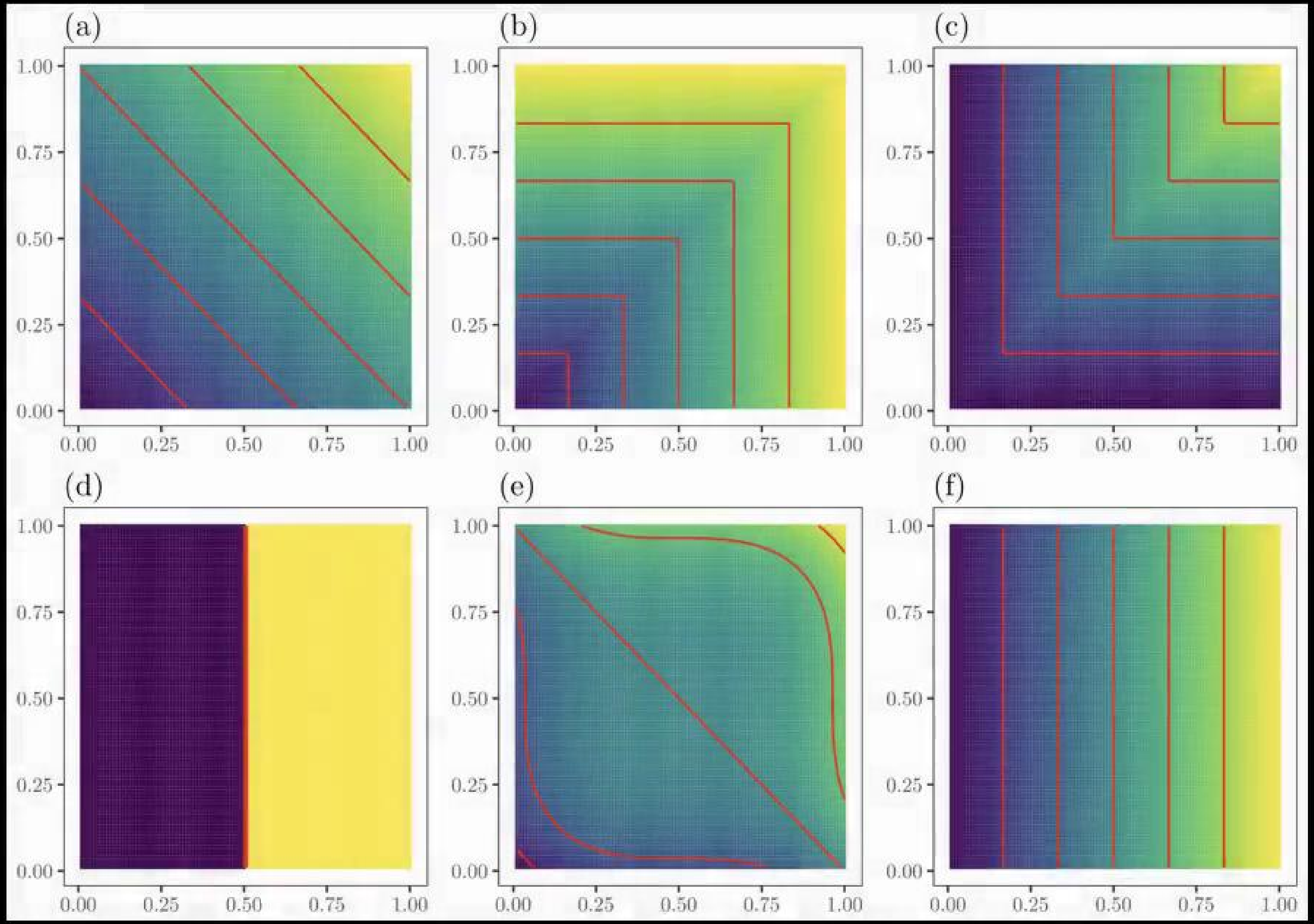
Label	Function f	τ	$\gamma(P)$
(a)	$\sum_{j=1}^d x^{(j)}$	$1/2$	1
(b)	$\max_{1\le j\le d} x^{(j)}$	$1/2^{1/d}$	1
(c)	$\min_{1\le j\le d} x^{(j)}$	$1-1/2^{1/d}$	1
(d)	$\mathbb{1}_{(0.5,1]}\big(x^{(1)}\big)$	$1/2$	0
(e)	$\sum_{j=1}^d \big(x^{(j)}-0.5\big)^3$	$1/2$	3
(f)	$x^{(1)}$	$1/2$	1



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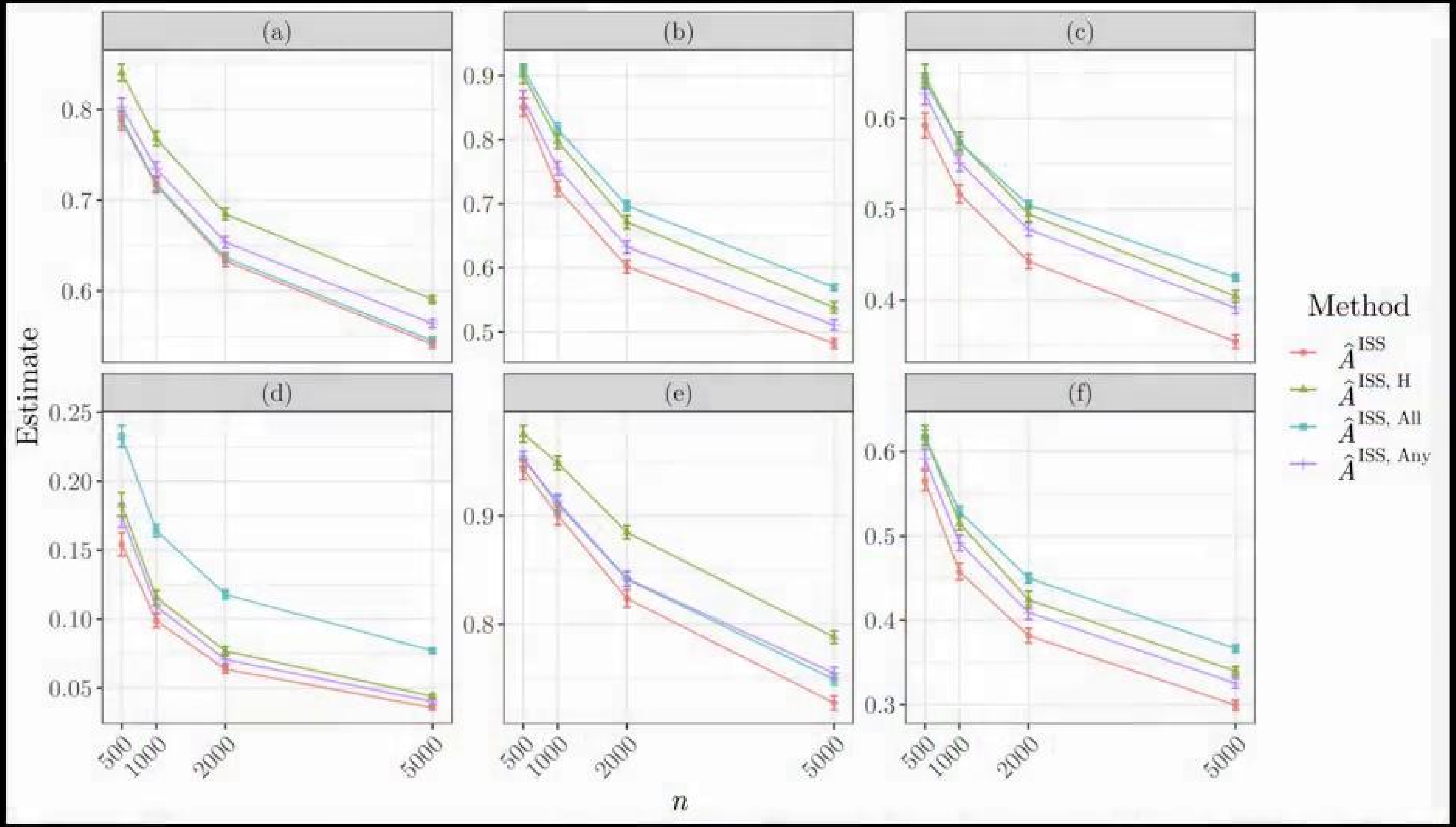

Here, $d = 2$, $\sigma = 1/4$.

See also Meijer and Goeman (2015).