Isotonic subgroup selection

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Collaborators

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University of Edinburgh

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Task. *Subgroup selection* in regression: Identify a subset of the covariate domain on which the regression function satisfies a particular property (e.g. exceeds a threshold).

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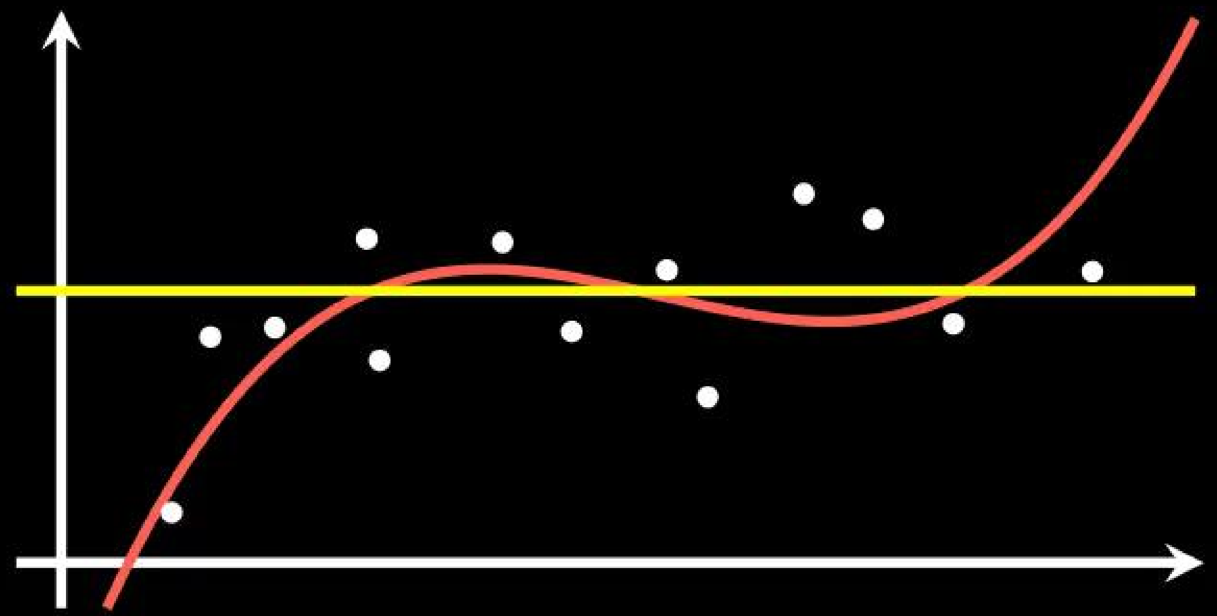

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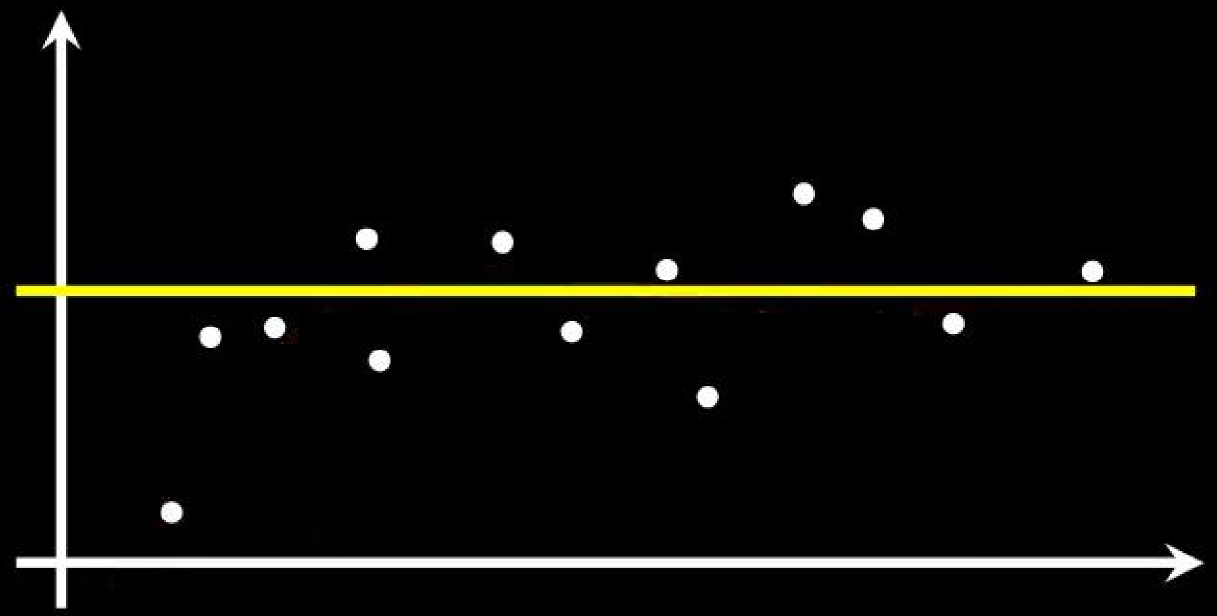

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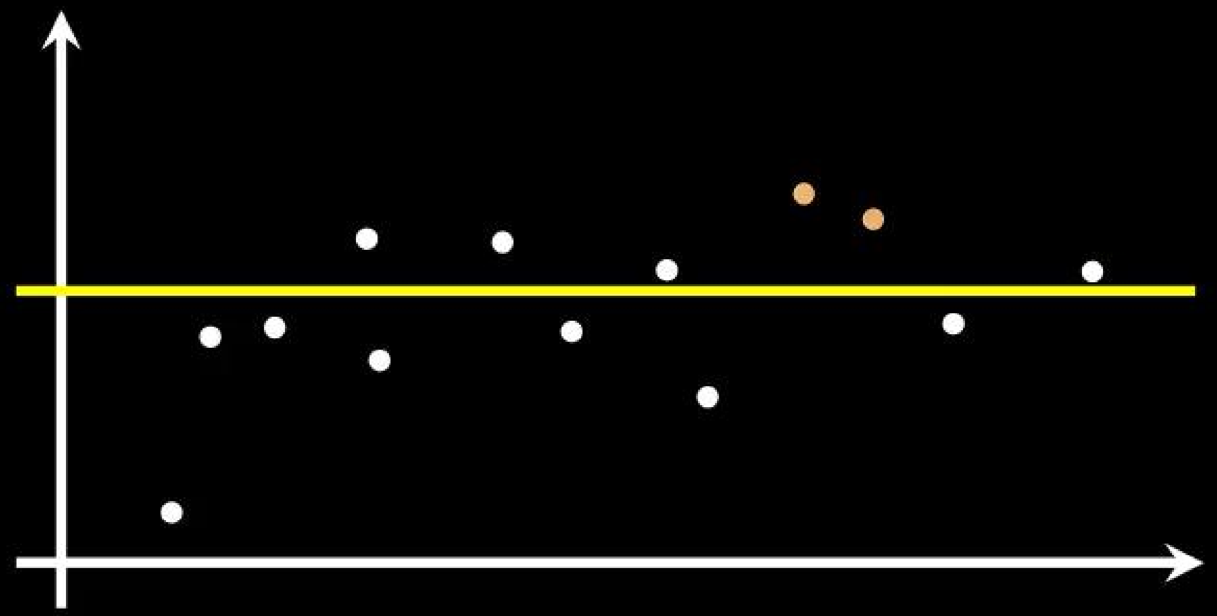

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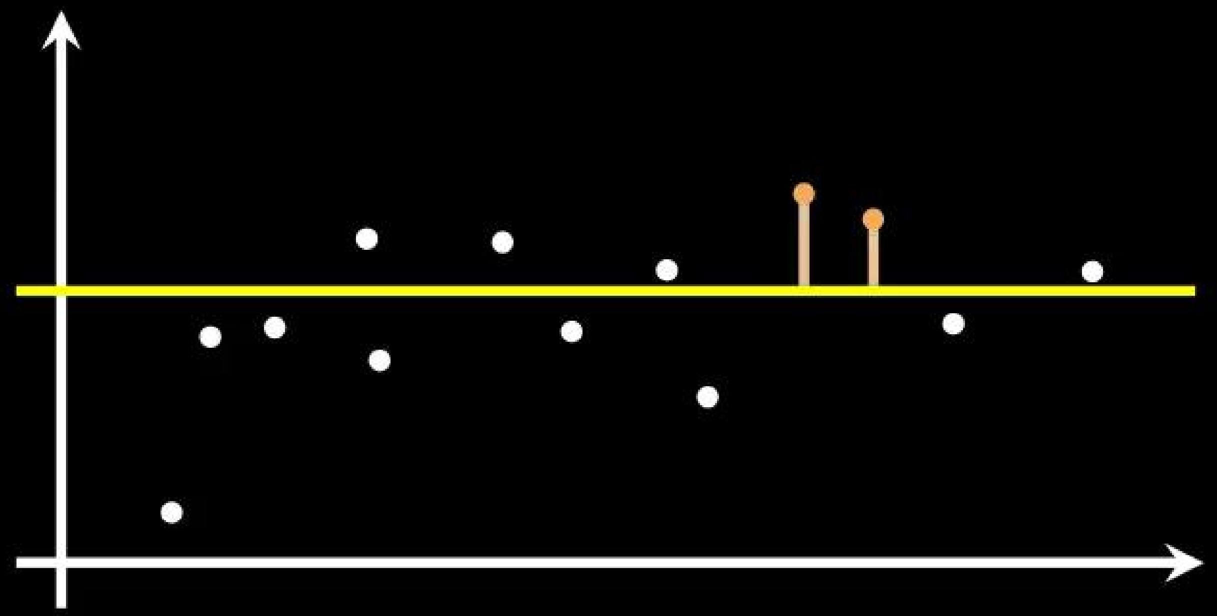

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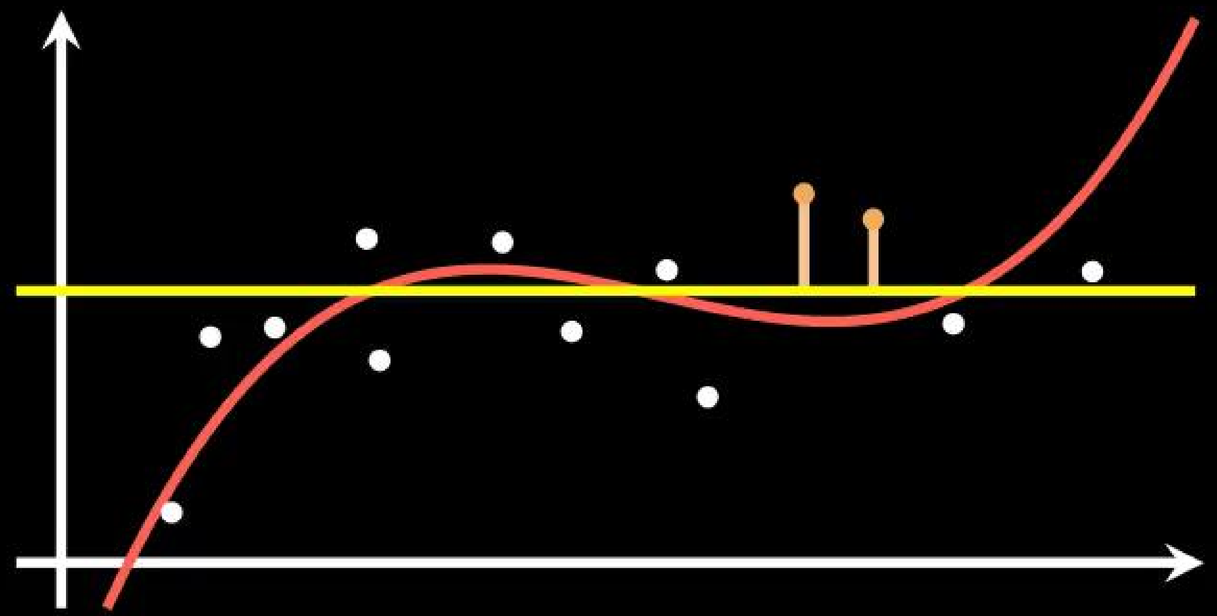

Example. Efficacy of a new vaccine.

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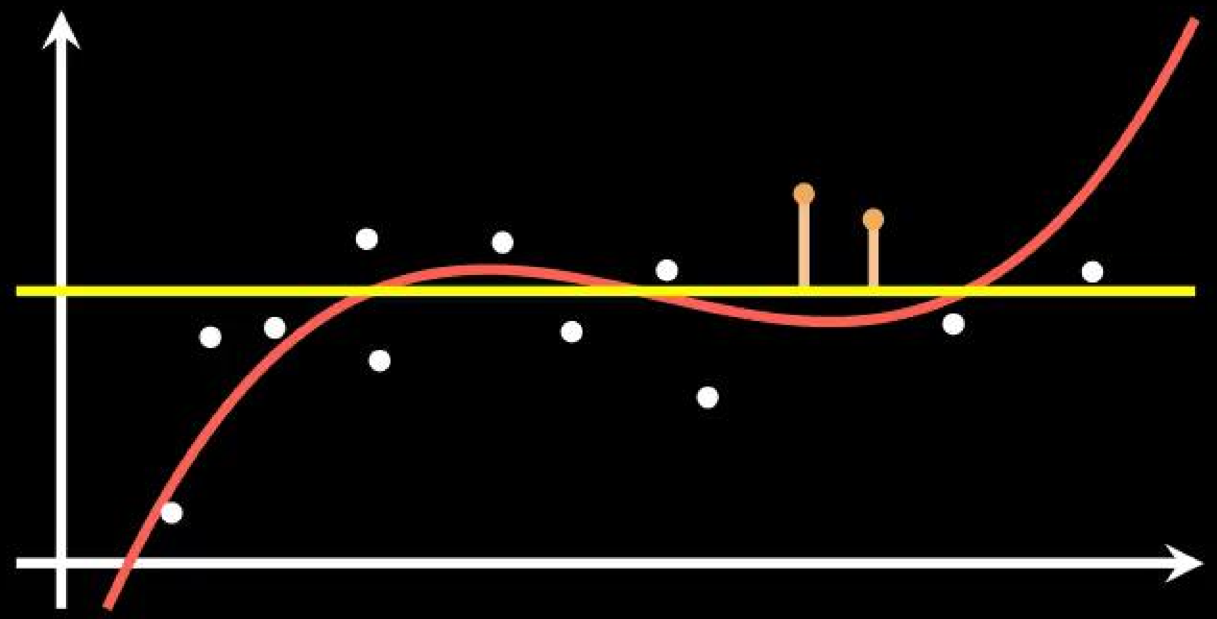

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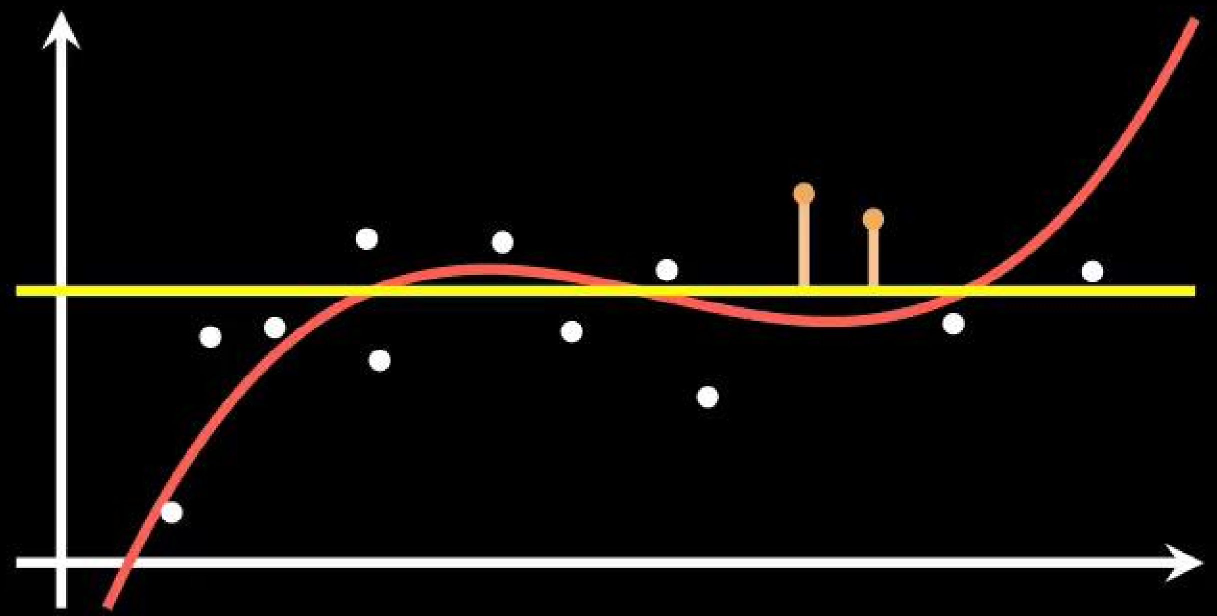

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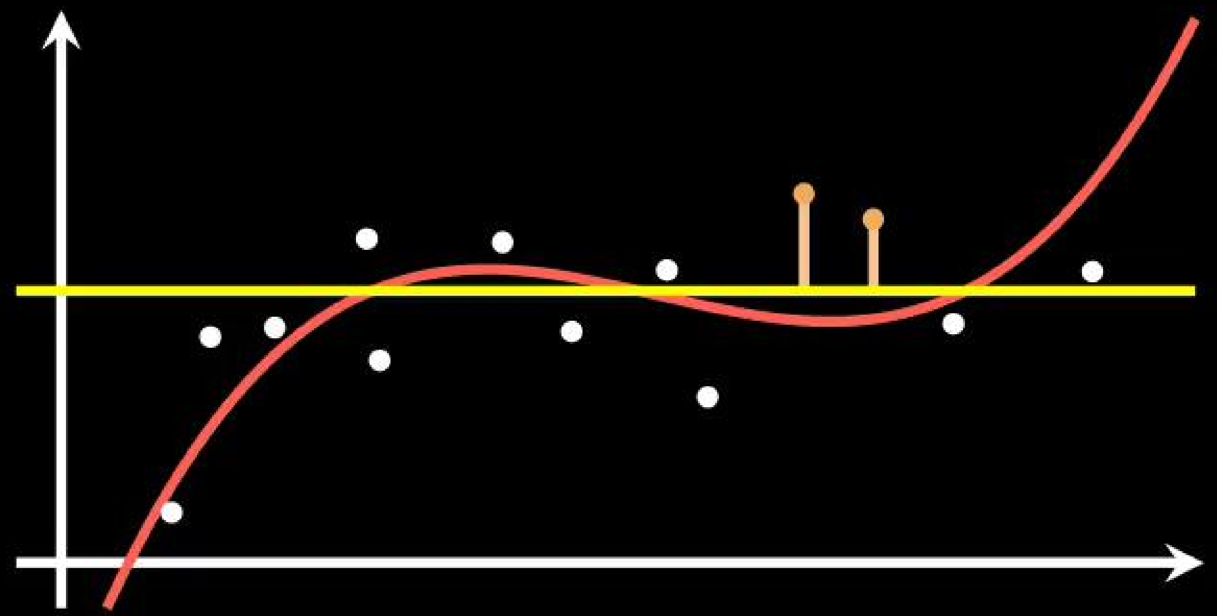

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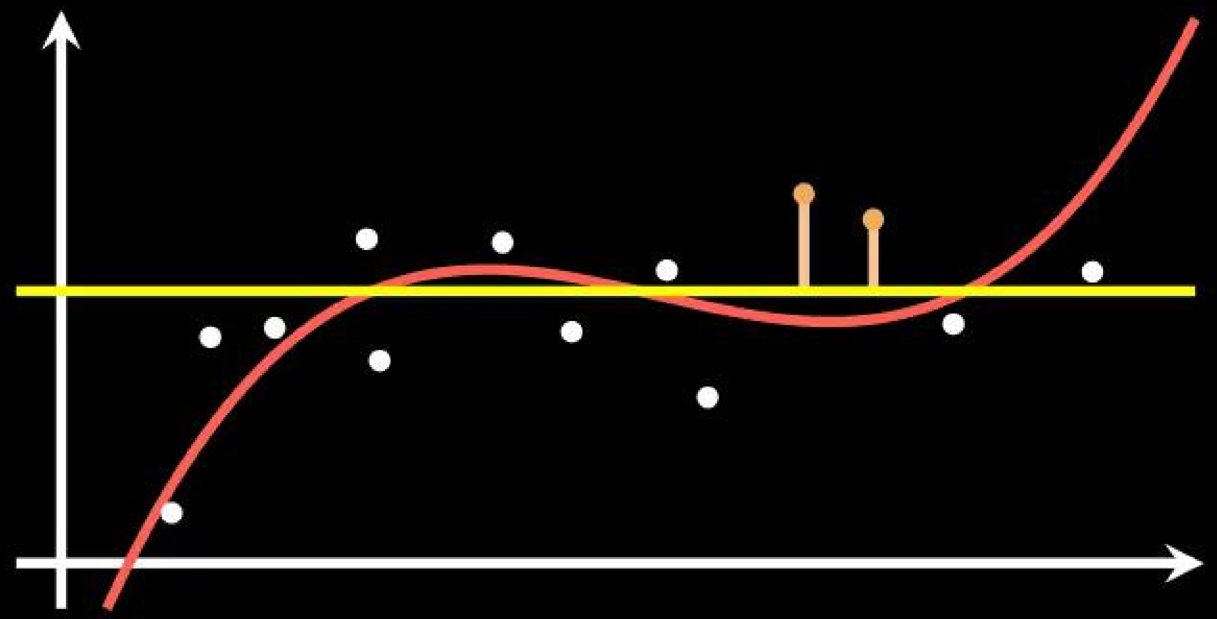

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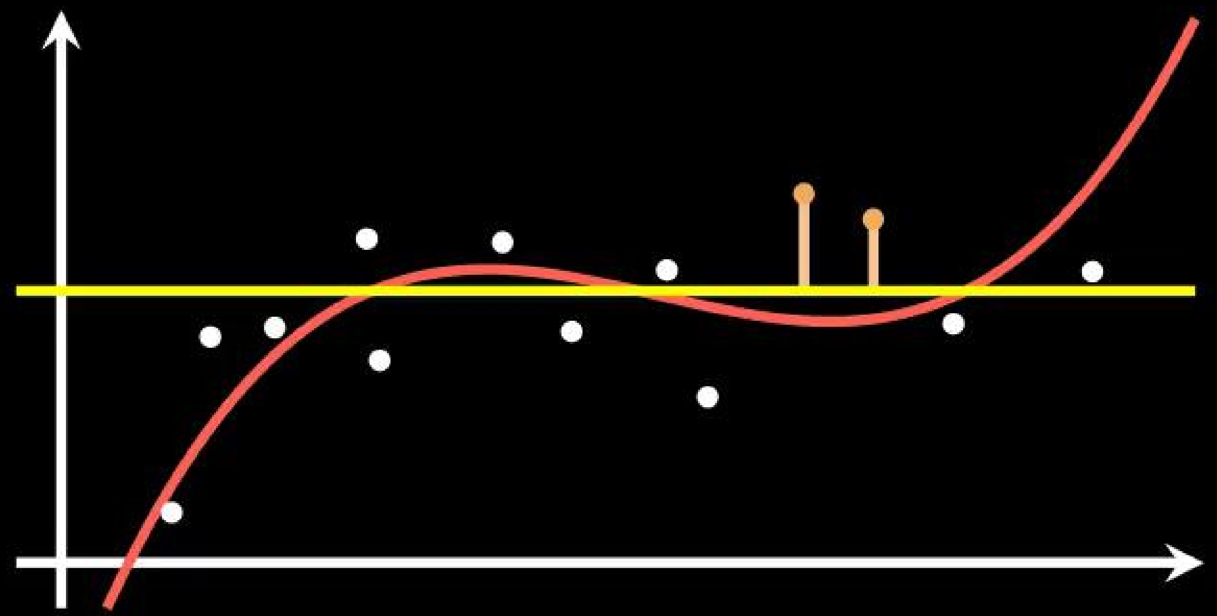

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$\longrightarrow$ Asymmetry of errors

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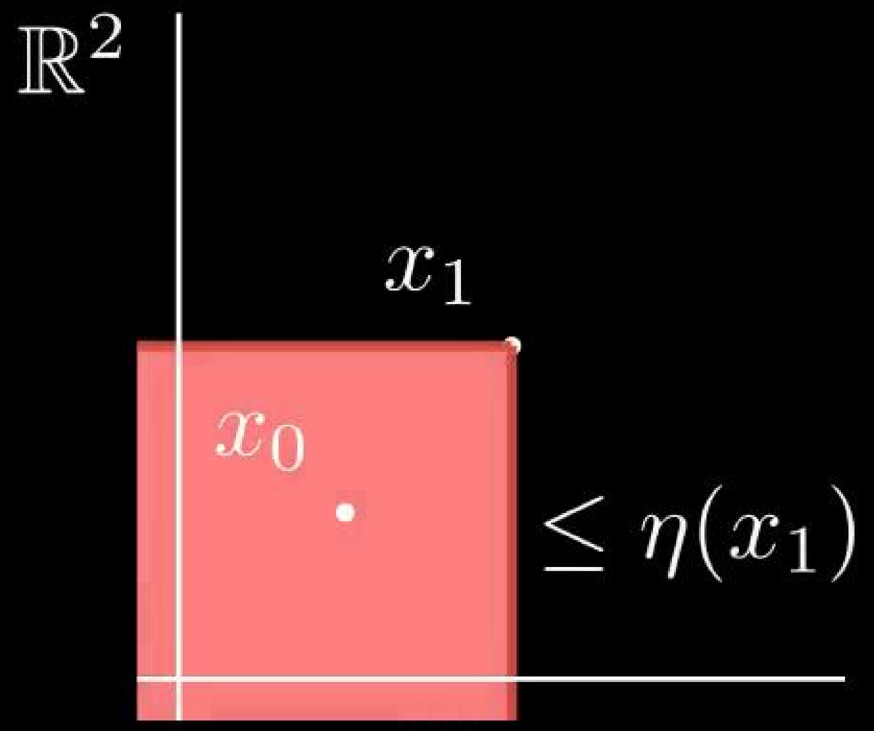

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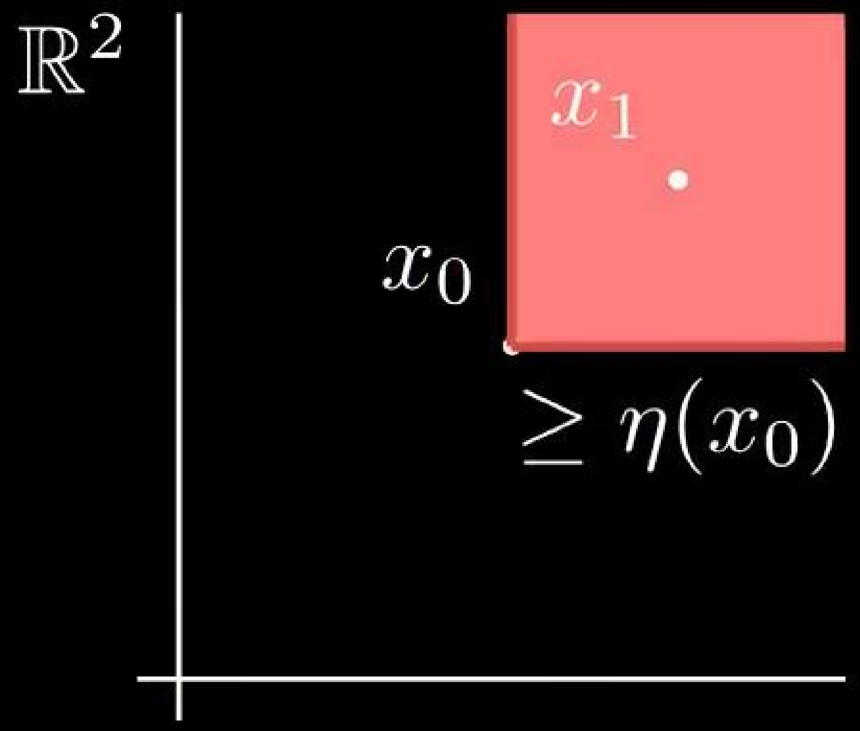

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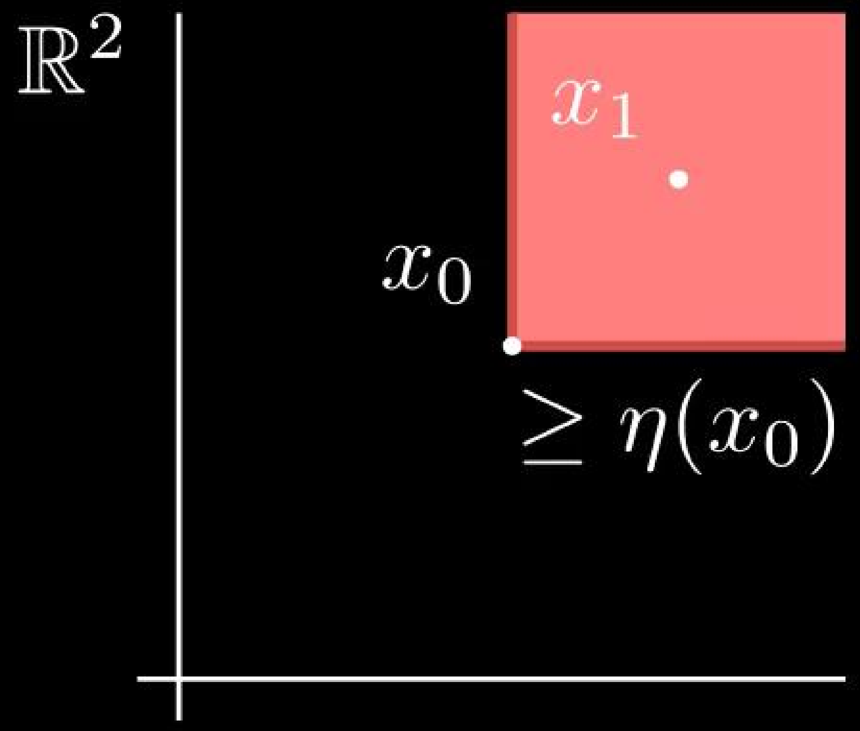

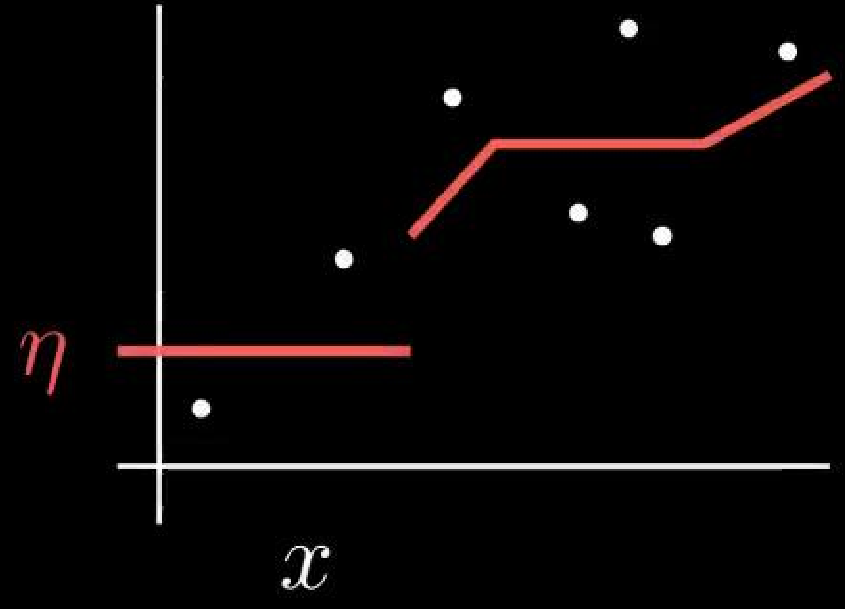

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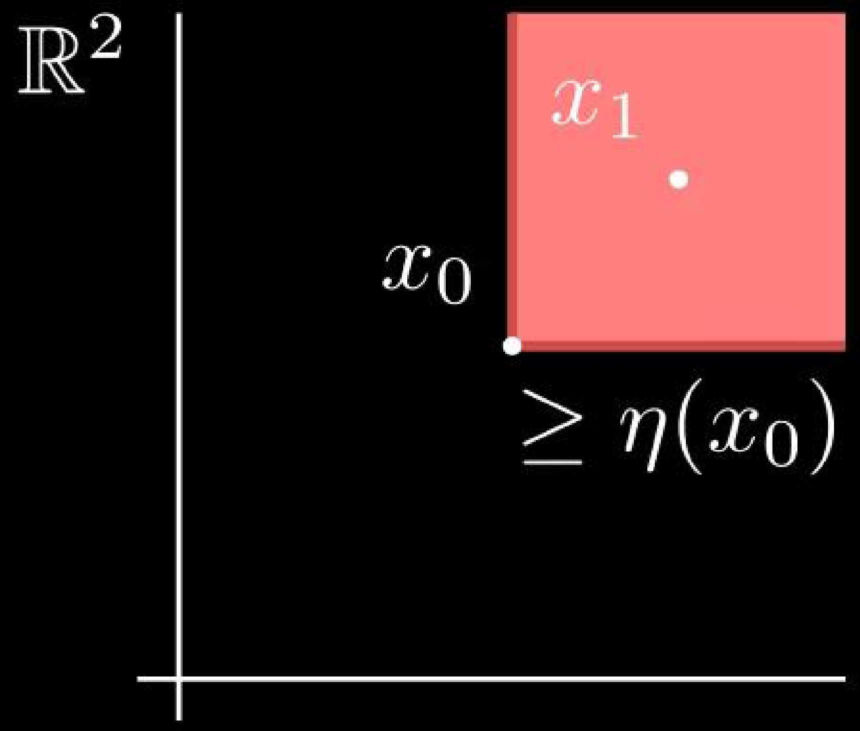
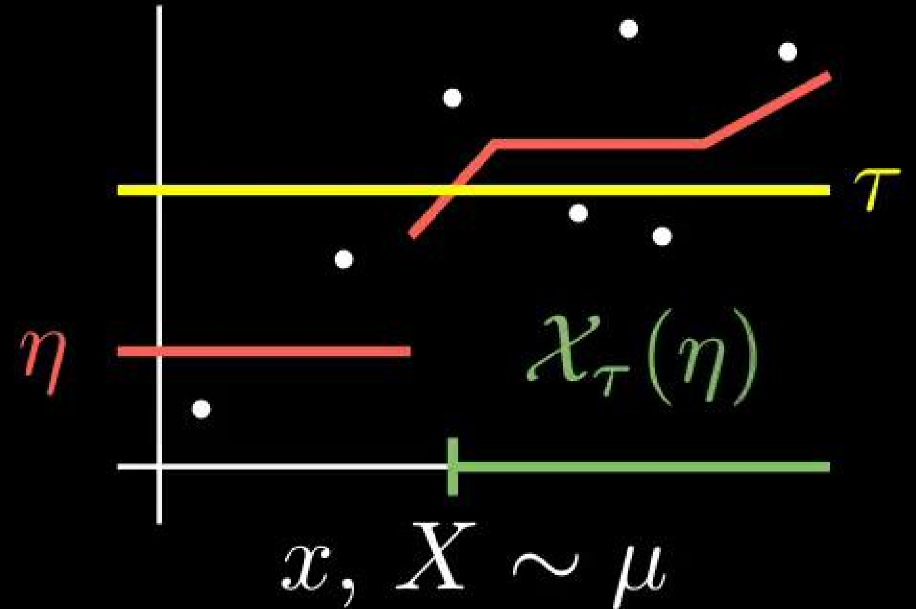


Notation:

- 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.



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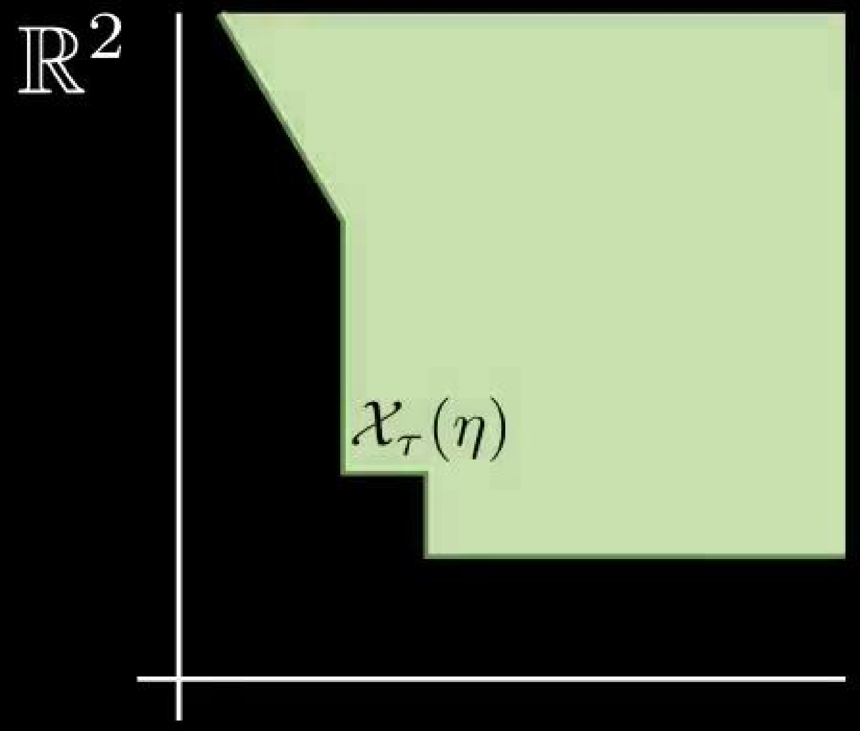
Writing $\mathcal{D} := \big((X_1, Y_1), \ldots, (X_n, Y_n)\big) \sim P^n$, we want $\hat{A} : \mathcal{D} \mapsto \hat{A}(\mathcal{D}) \subseteq \mathbb{R}^d$ such that:



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

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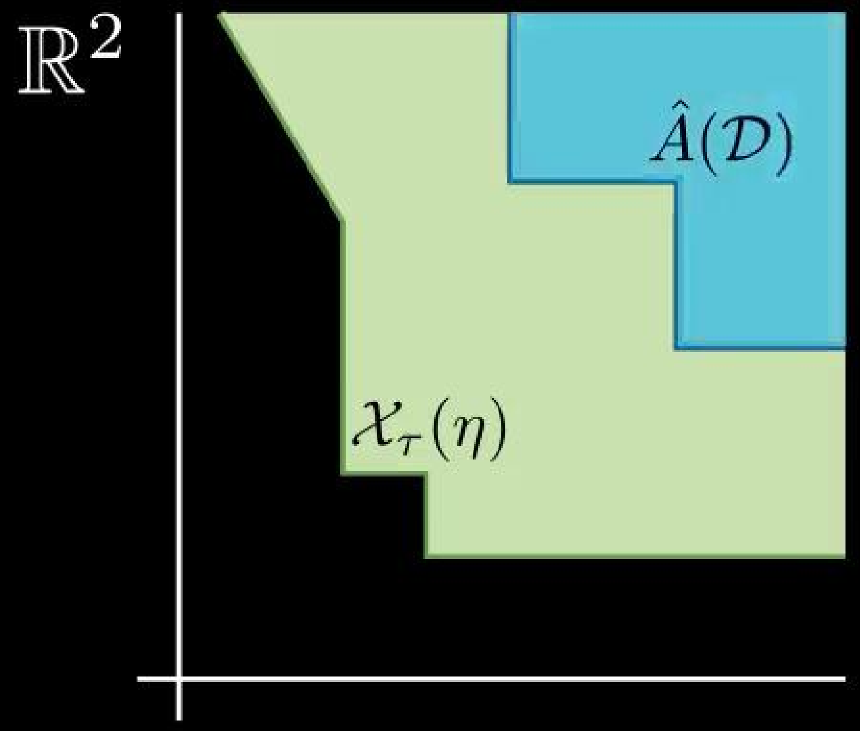

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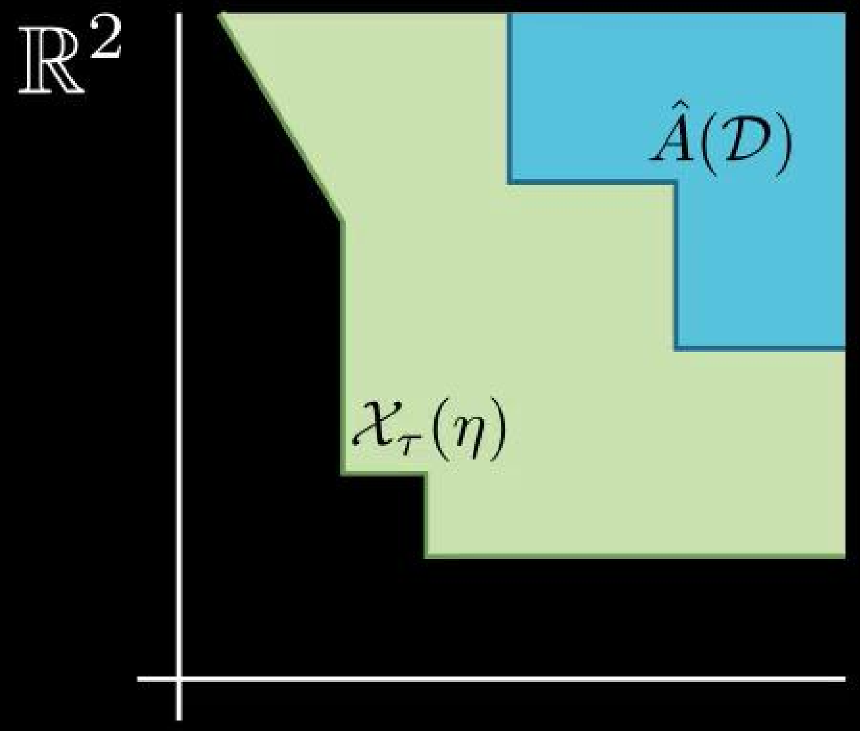
Power: Want small expected regret

$$R_\tau(\hat{A}) := \mathbb{E}\big\{\mu\big(\mathcal{X}_\tau(\eta) \setminus \hat{A}(\mathcal{D})\big)\big\}.$$



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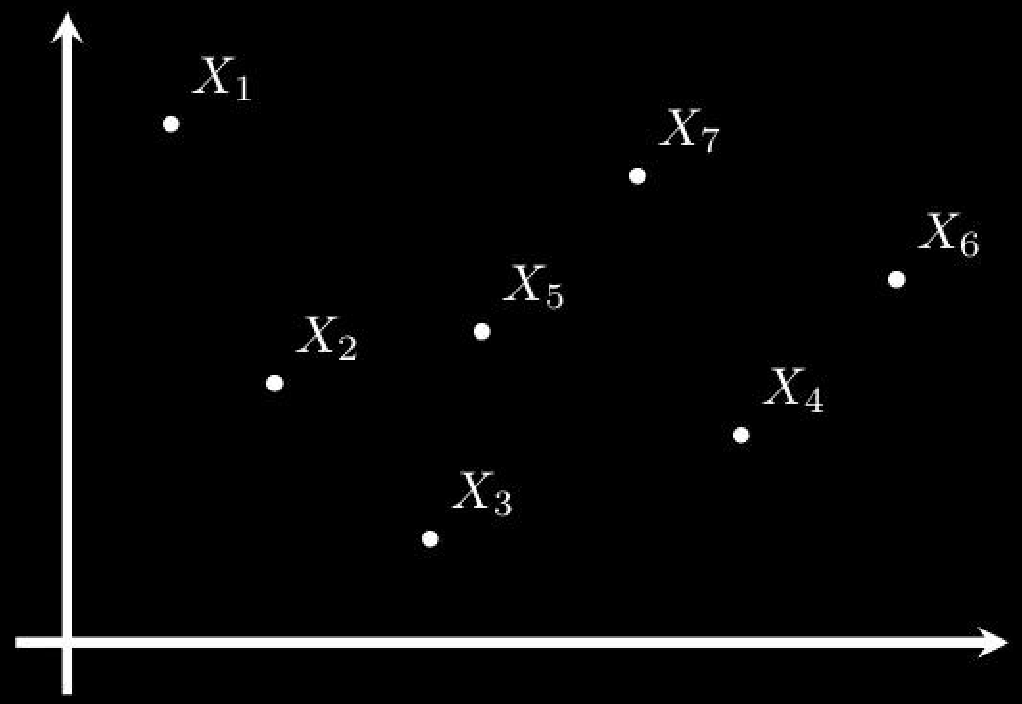

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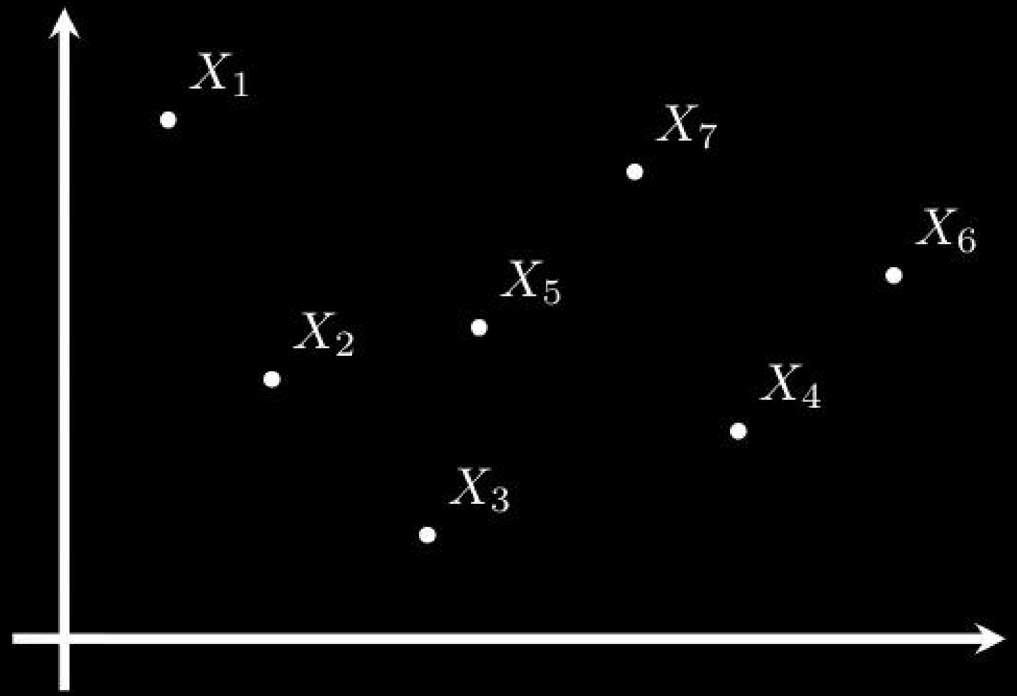

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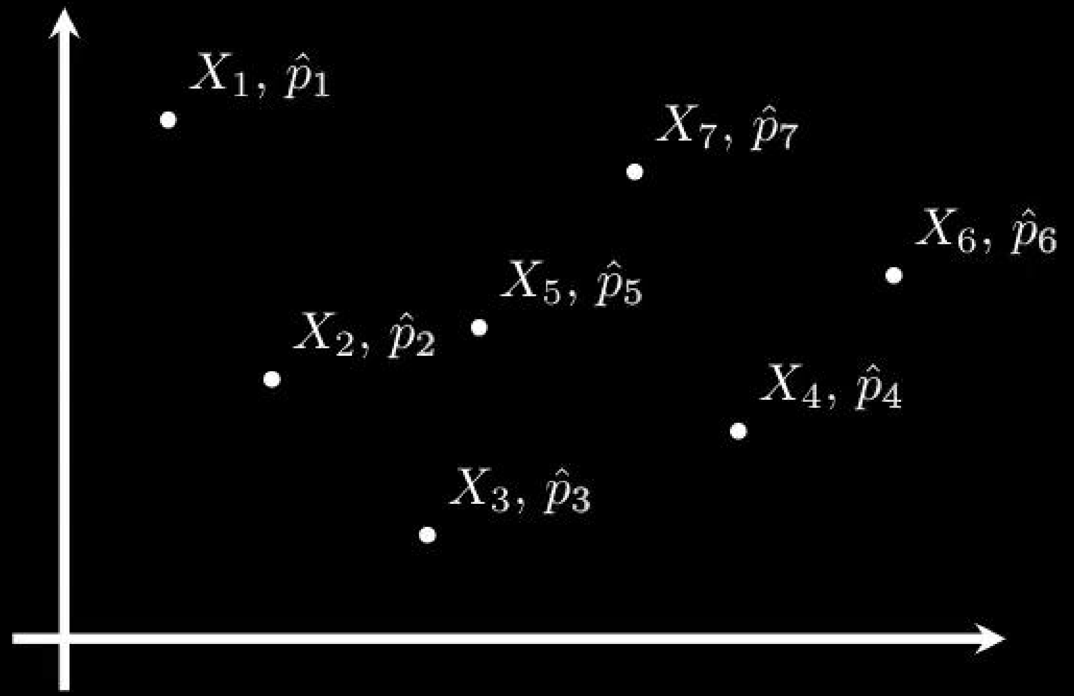

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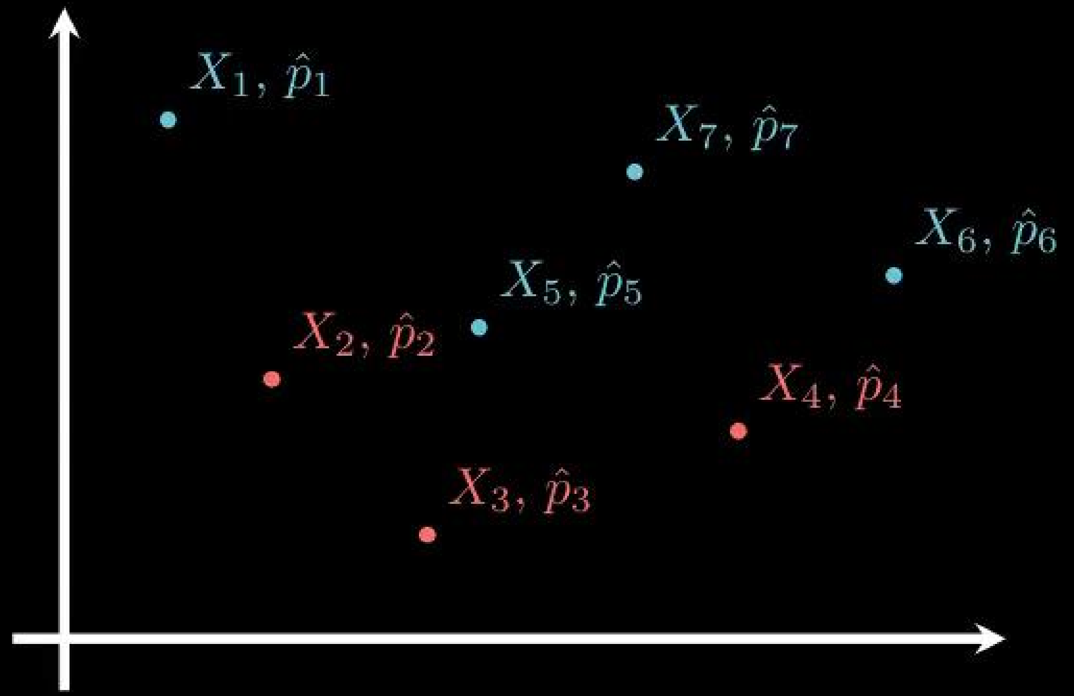

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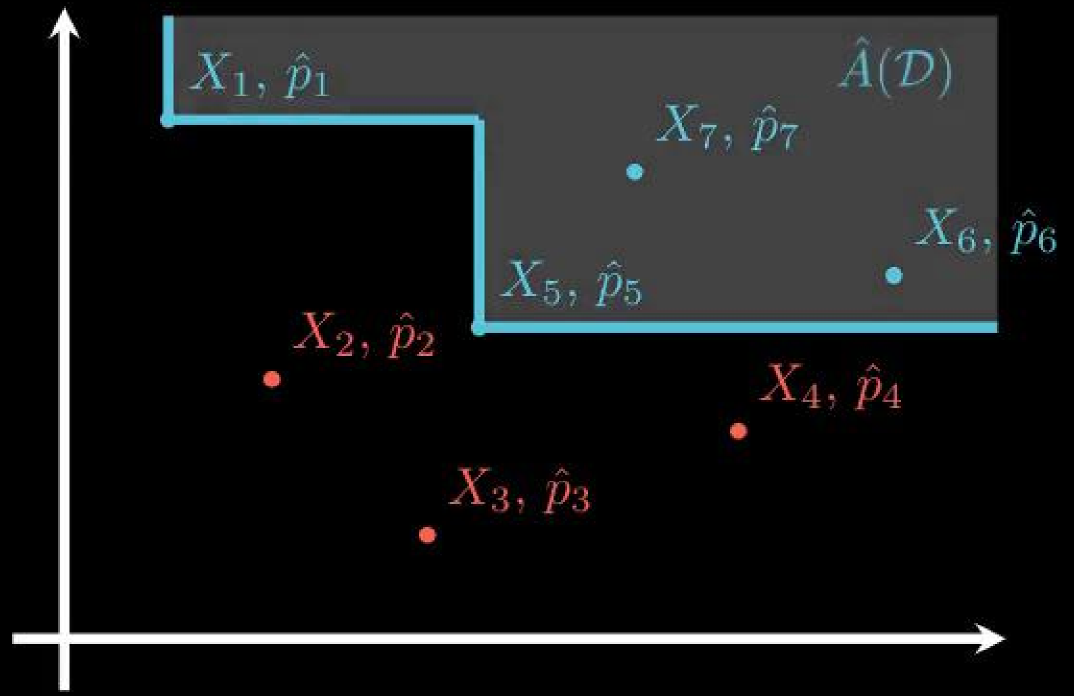

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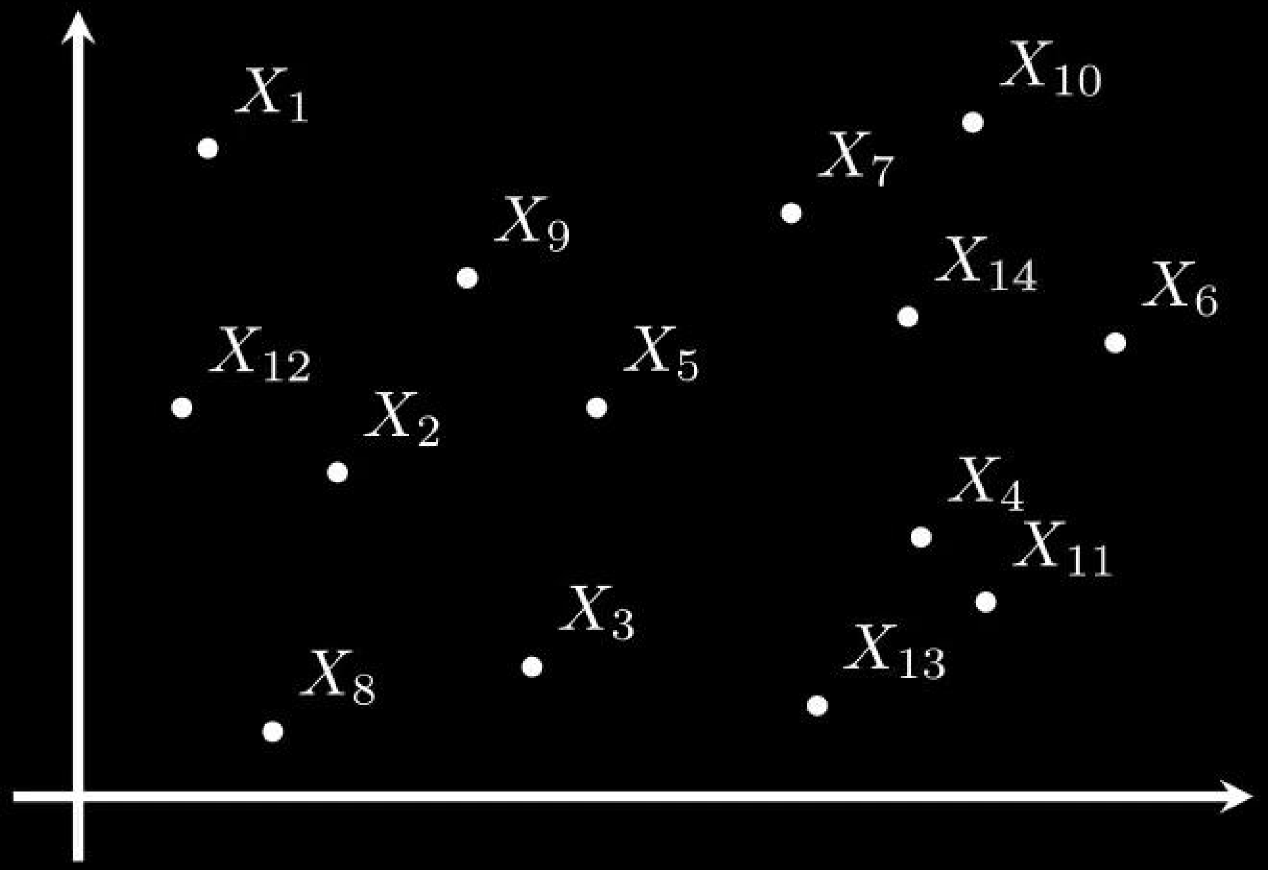

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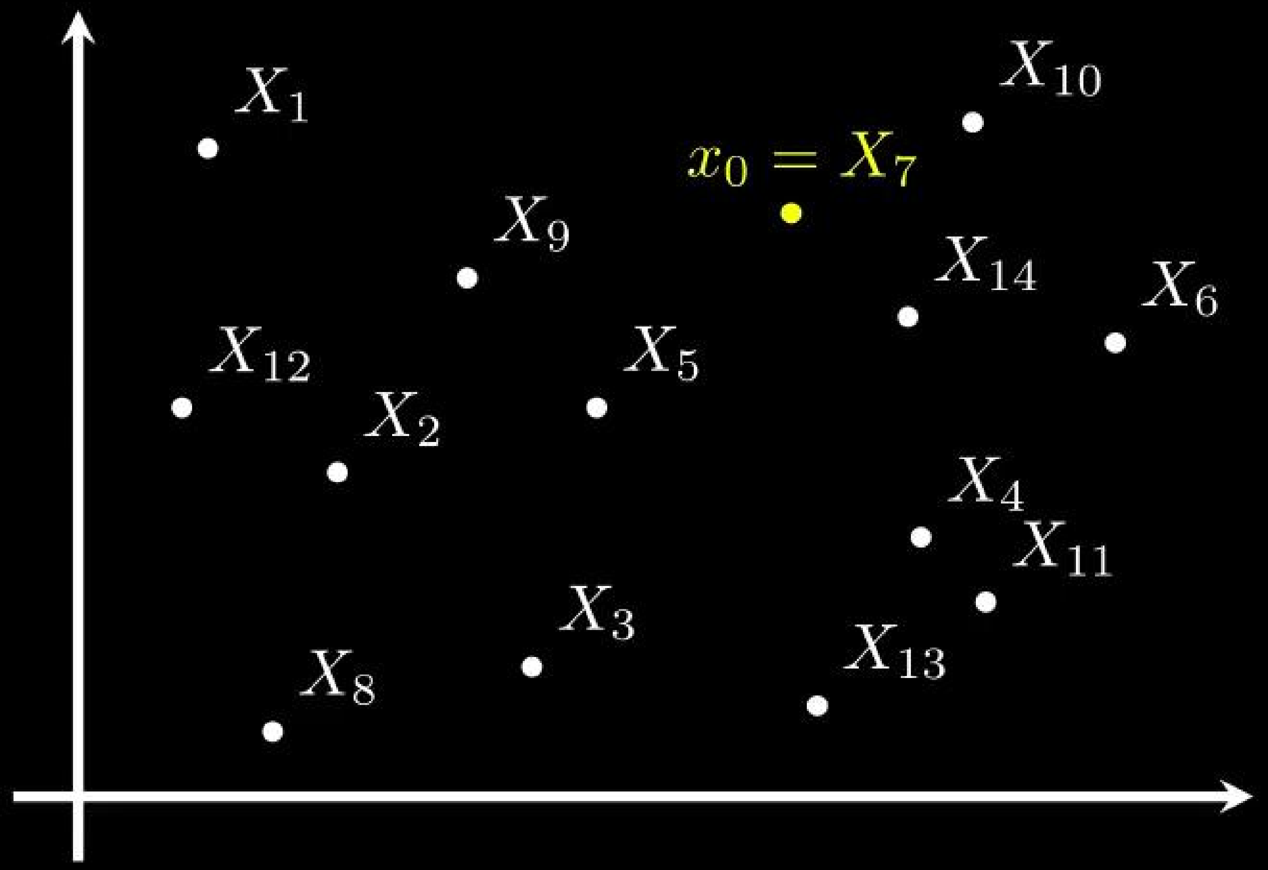

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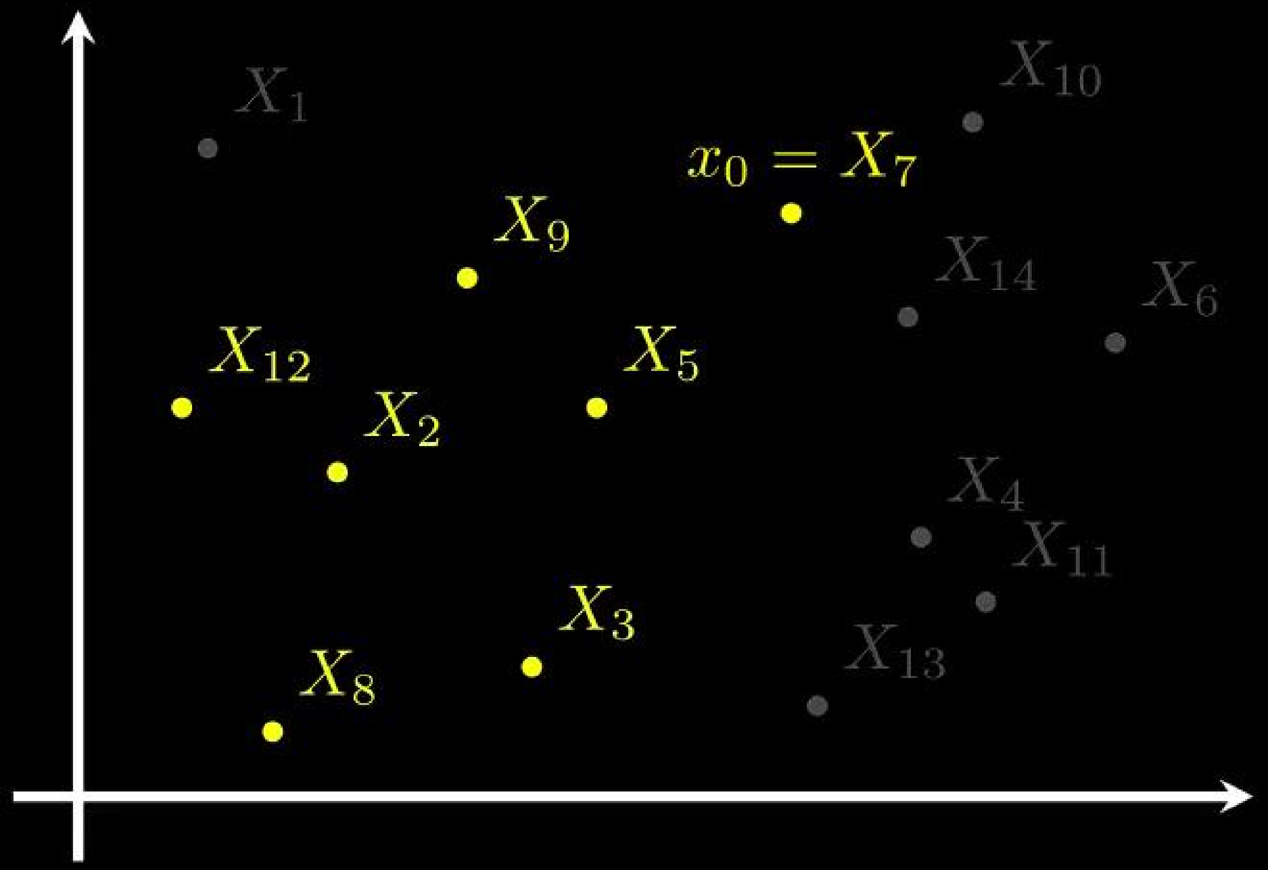

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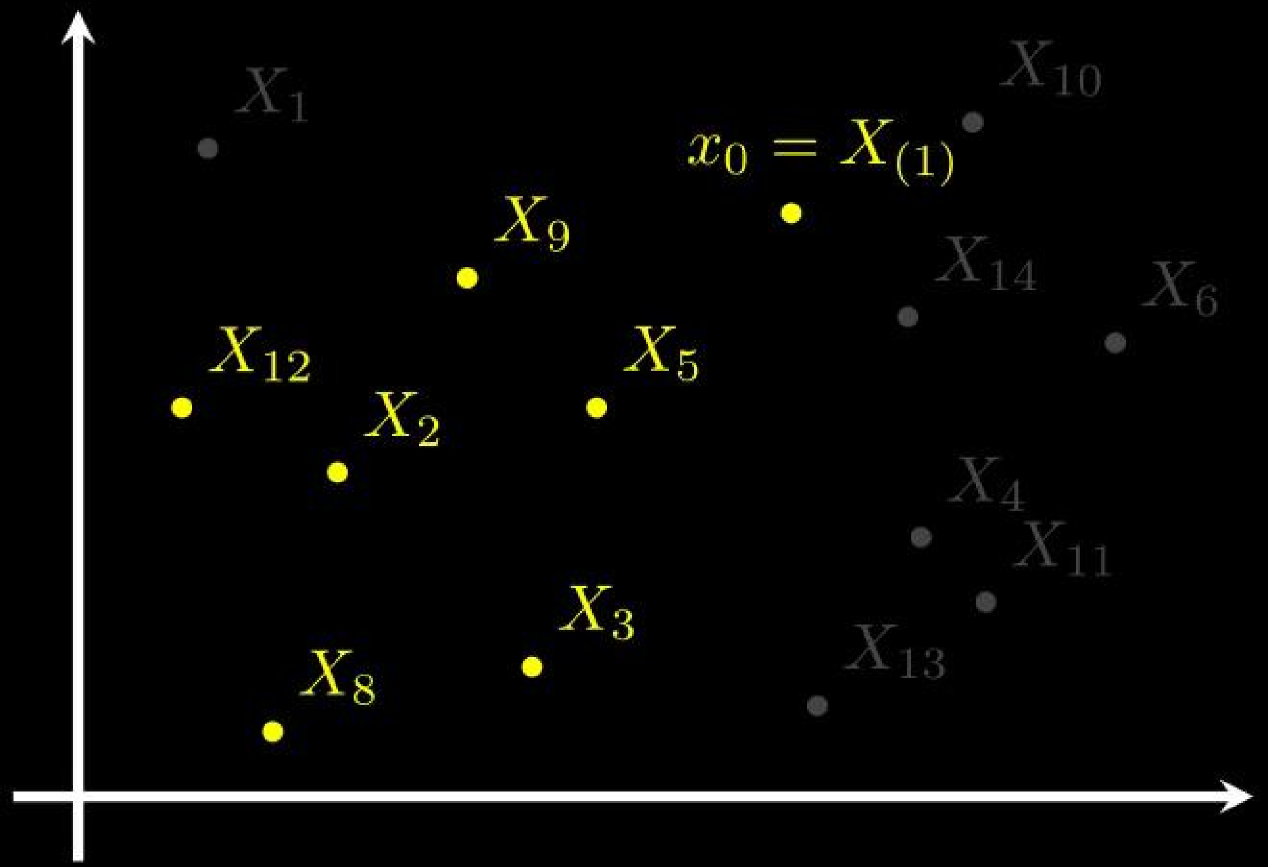

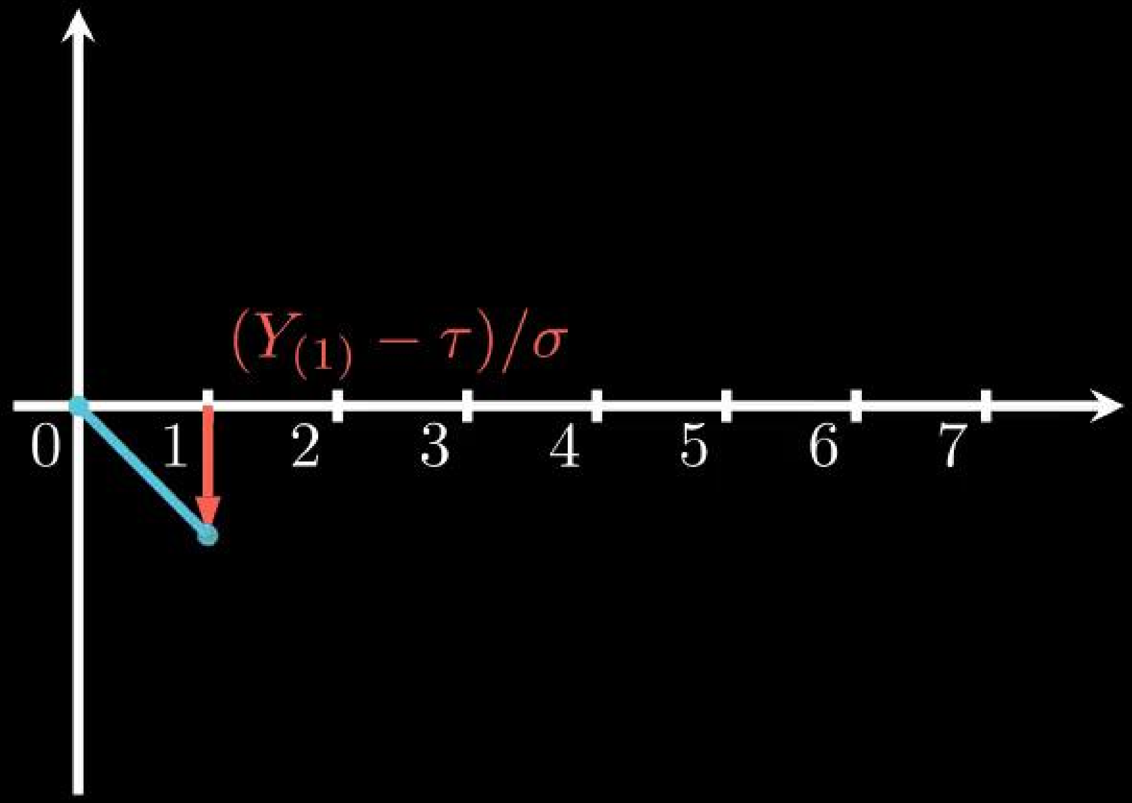

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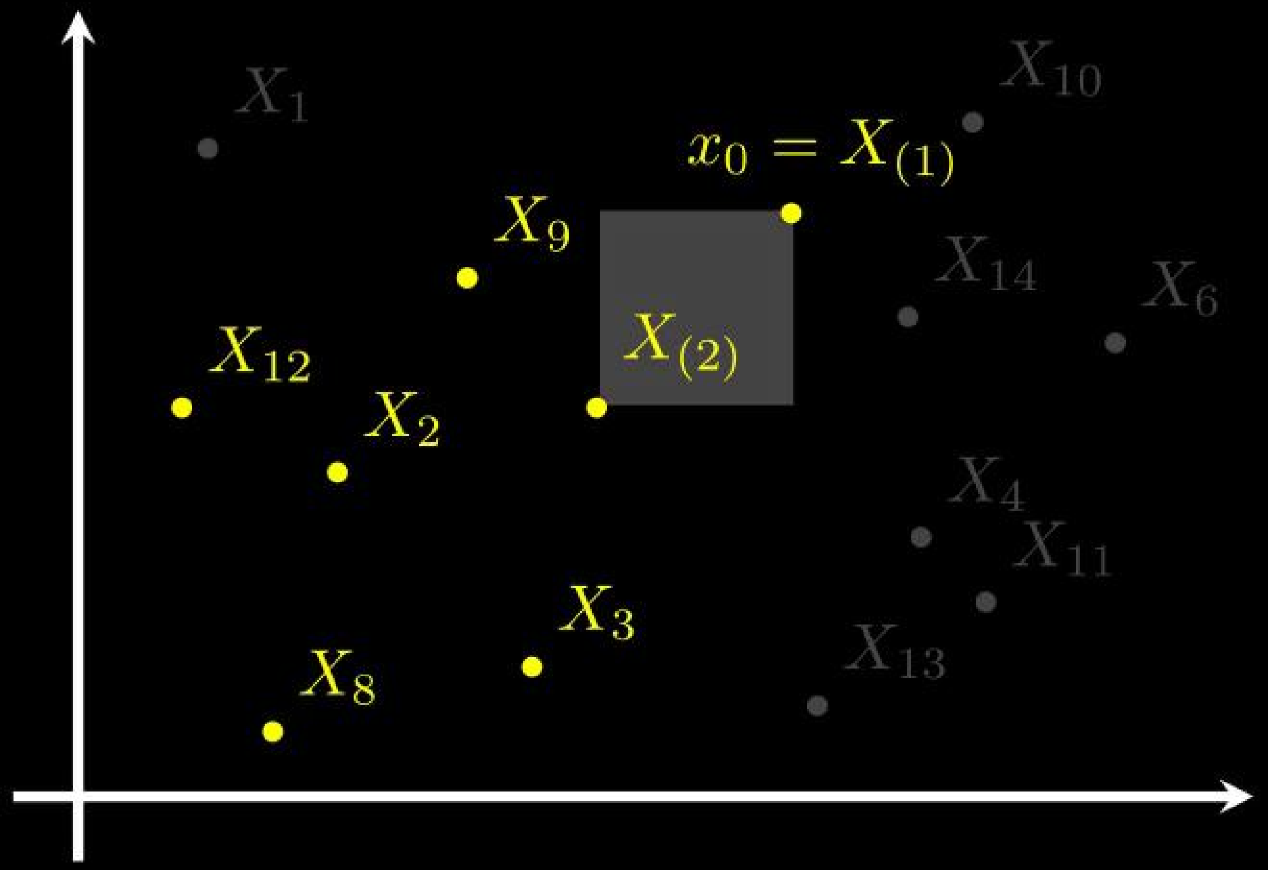

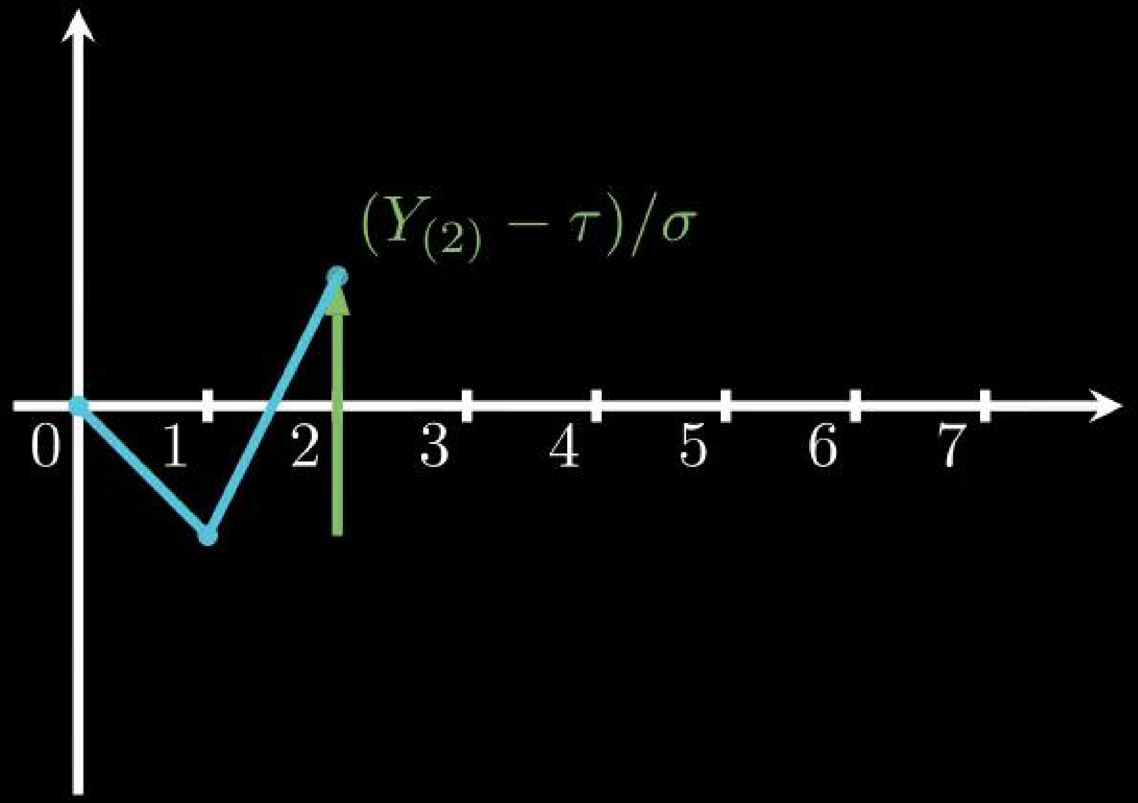

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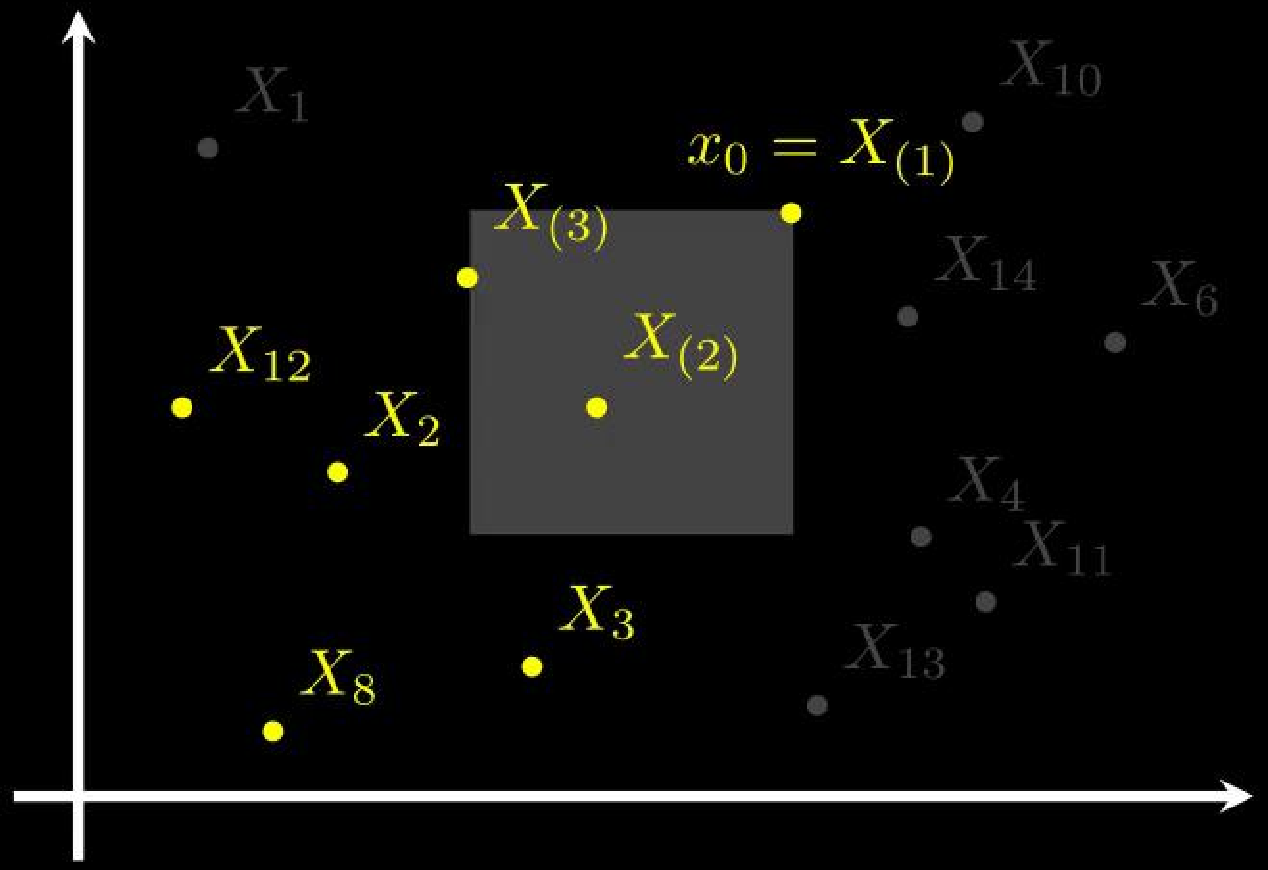

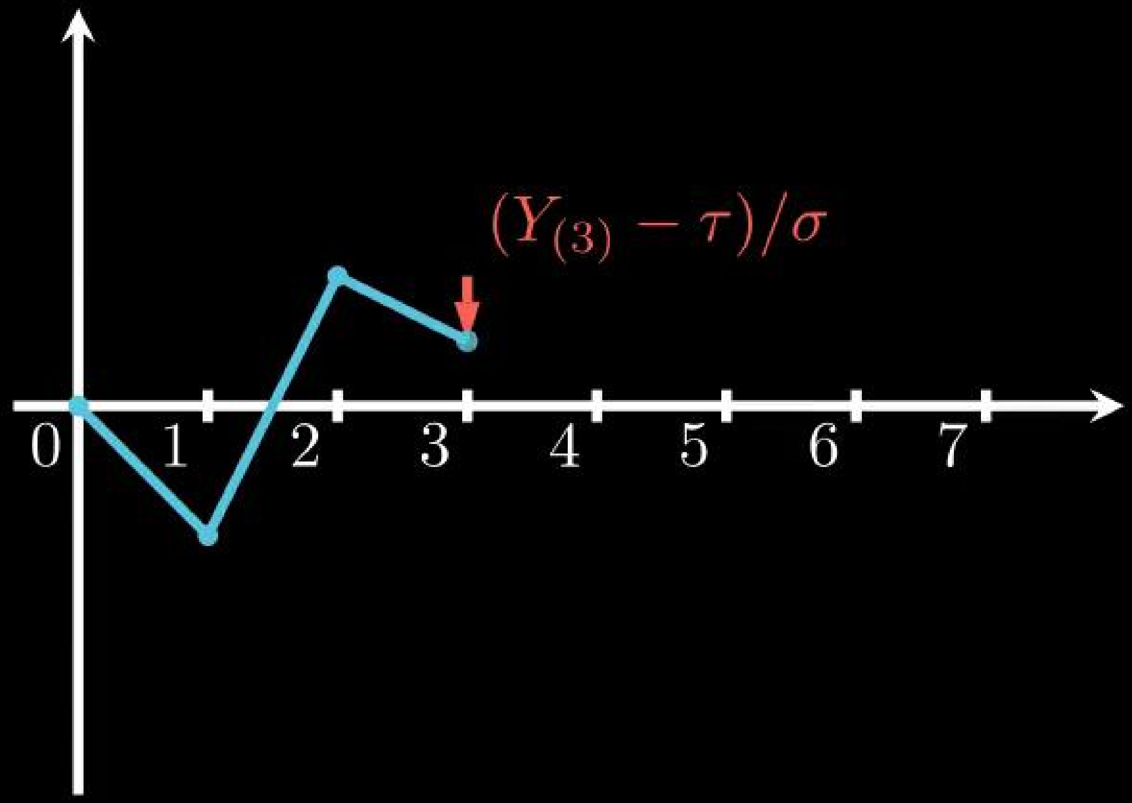

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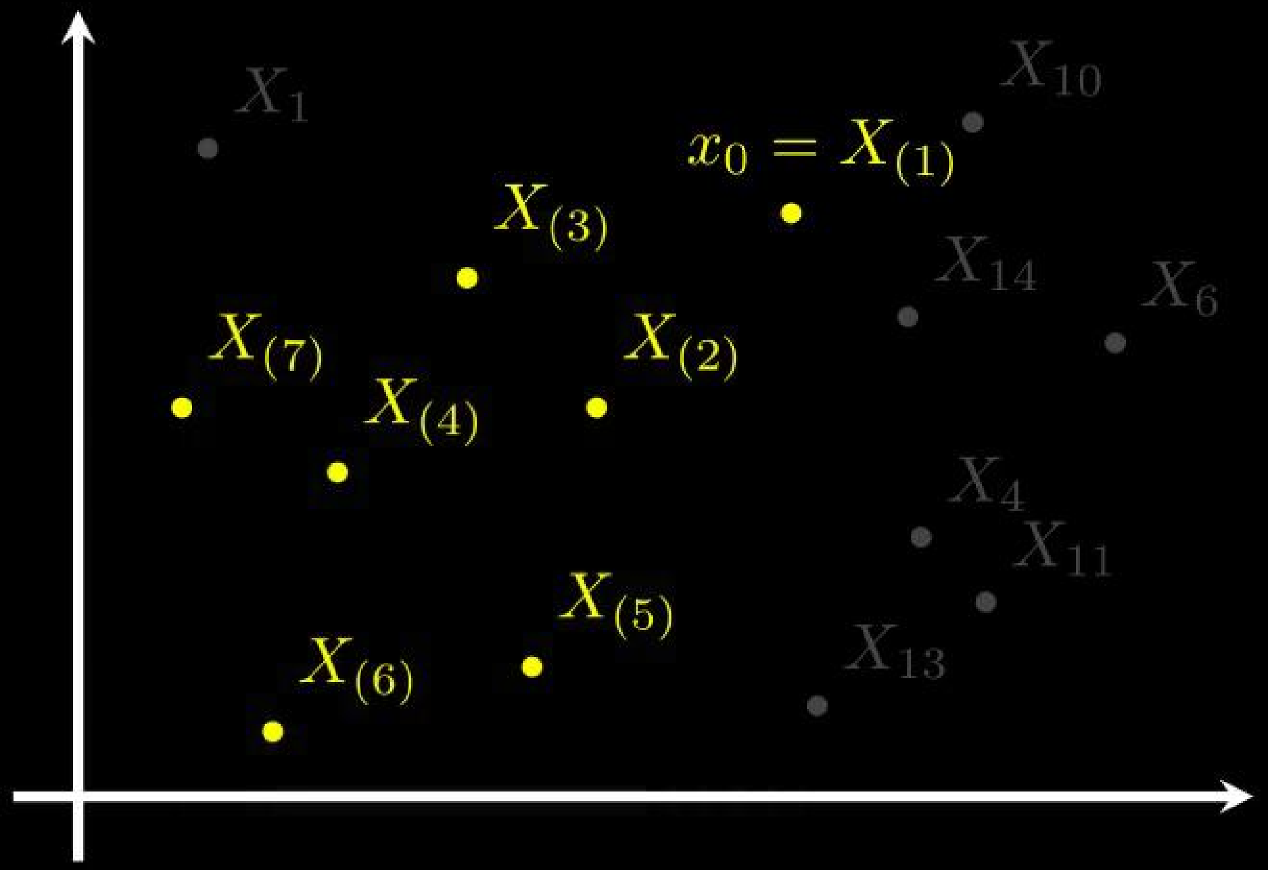

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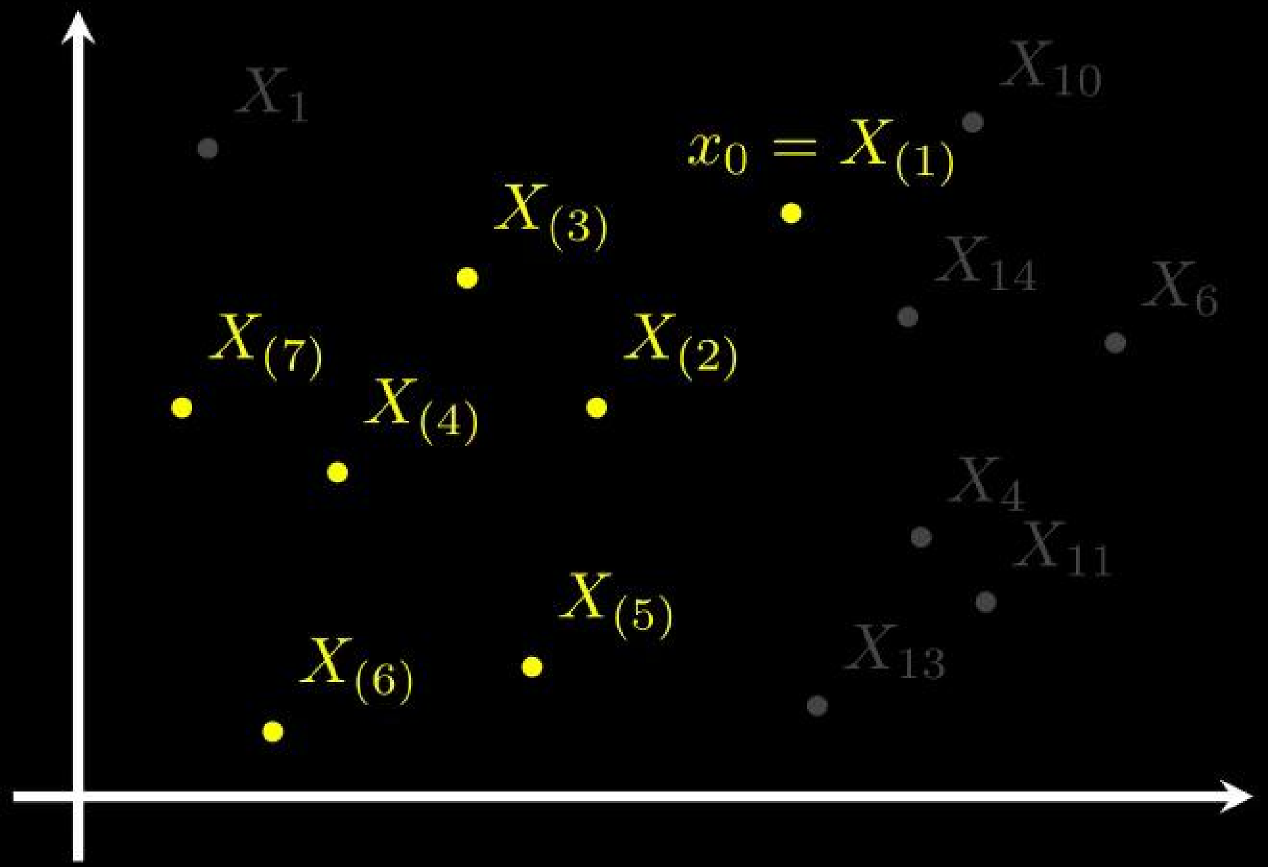

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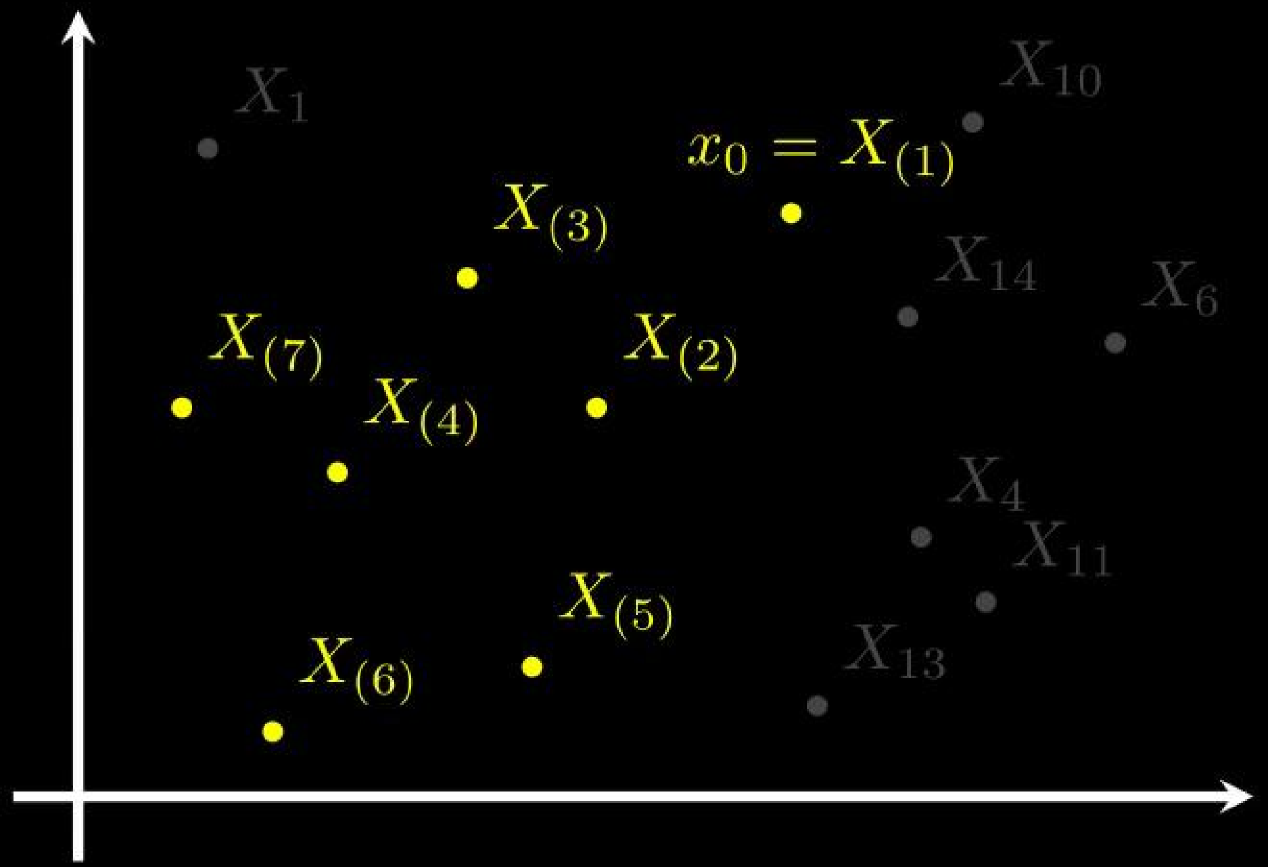

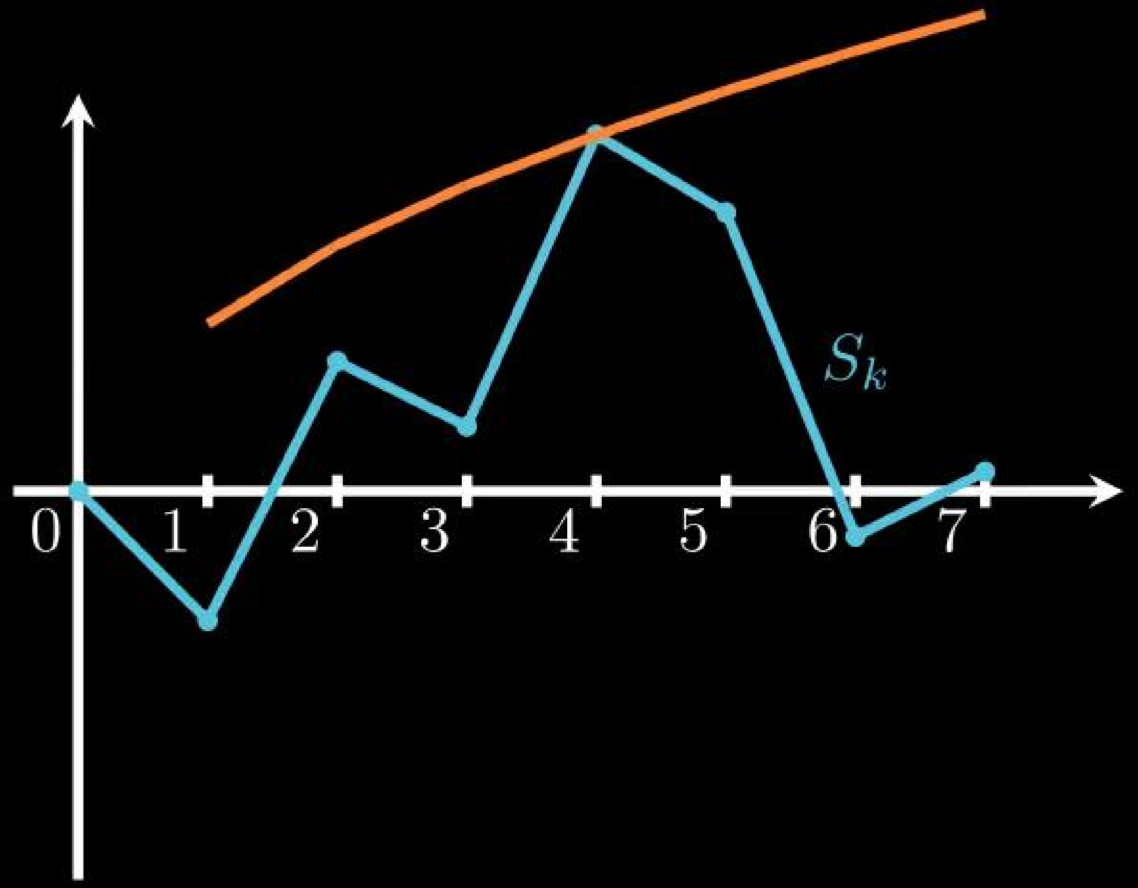

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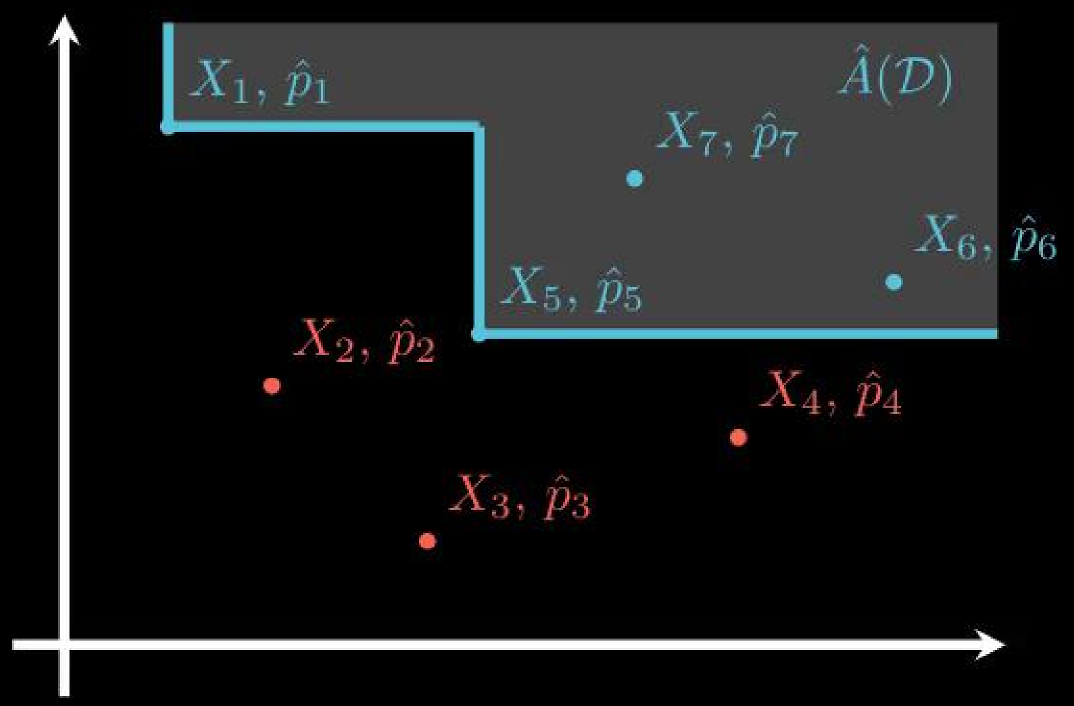

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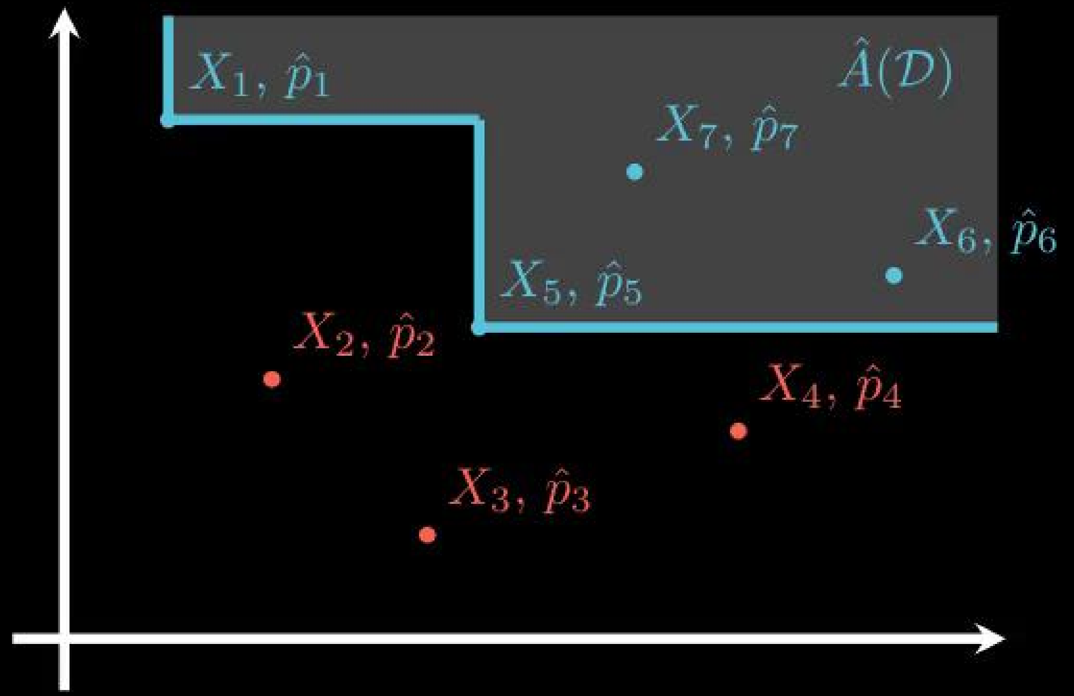

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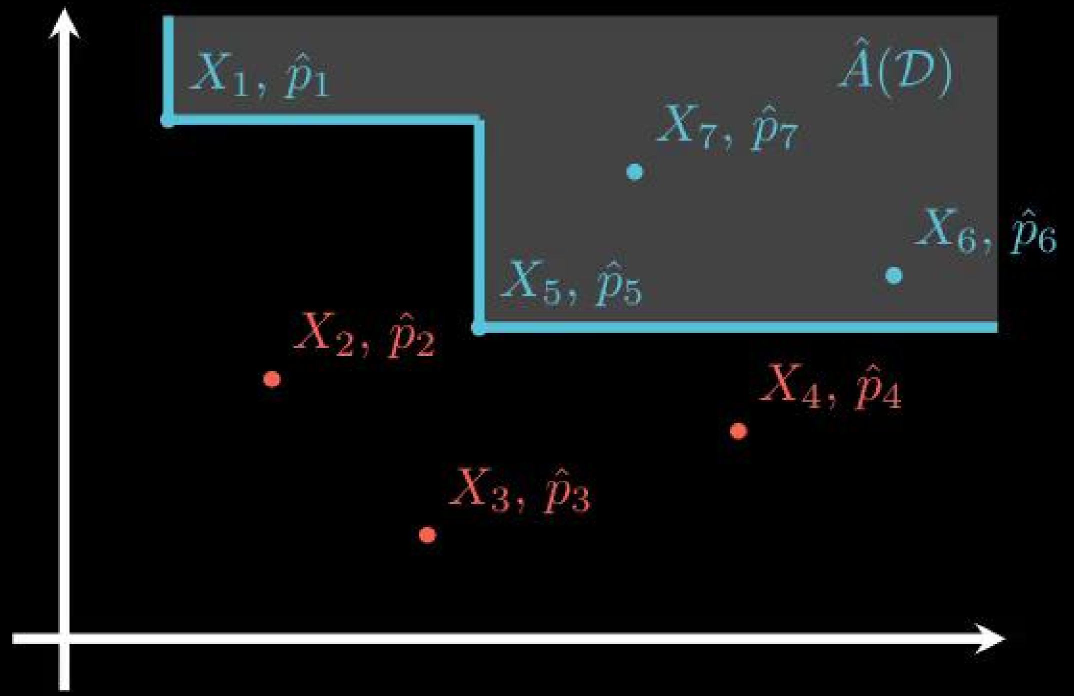

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2. Apply a *multiple testing procedure* with FWER-control at level α to reject $\mathcal{R}_\alpha \subseteq [n]$;
3. Output $\hat{A} := \{x \in \mathbb{R}^d : X_\ell \preccurlyeq x \text{ for some } \ell \in \mathcal{R}_\alpha\}$.

Type I error control

Write $\hat{A}^{\mathrm{ISS}} \equiv \hat{A}^{\mathrm{ISS}}_{\sigma,\tau,\alpha}(\mathcal{D})$ for the resulting selected subgroup.

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

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

Power and Optimality

Let $\sigma, \gamma, \lambda > 0$, $\theta > 1$. $\mathcal{P}_{\mathrm{MonReg}} \equiv \mathcal{P}_{\mathrm{MonReg},d}(\sigma, \tau, \gamma, \lambda, \theta)$ contains $P \in \mathcal{P}_{\mathrm{Mon},d}(\sigma)$ with:

1. η growing at least as quickly as $r \mapsto \lambda \cdot r^{\gamma}$ on the superlevel set near its boundary,
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Theorem. $\exists C(d,\theta) \geq 1$, such that for any $n \geq 1$ 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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Theorem. $\exists c(d, \gamma) \in (0,1)$, such that for any $n \geq 1$ and $\alpha \in (0,1)$,

$$\inf_{\hat{A} \in \hat{\mathcal{A}}_n(\tau, \alpha, \mathcal{P}_{\mathrm{MonReg}})} \sup_{P \in \mathcal{P}_{\mathrm{MonReg}}} R_{\tau}(\hat{A}) \geq c(d, \gamma) \left[1 \wedge \left\{ \left(\frac{\sigma^2}{n\lambda^2} \log_{+}\left(\frac{1}{5\alpha} \right) \right)^{1/(2\gamma+d)} + \frac{1}{n^{1/d}} \right\} \right].$$

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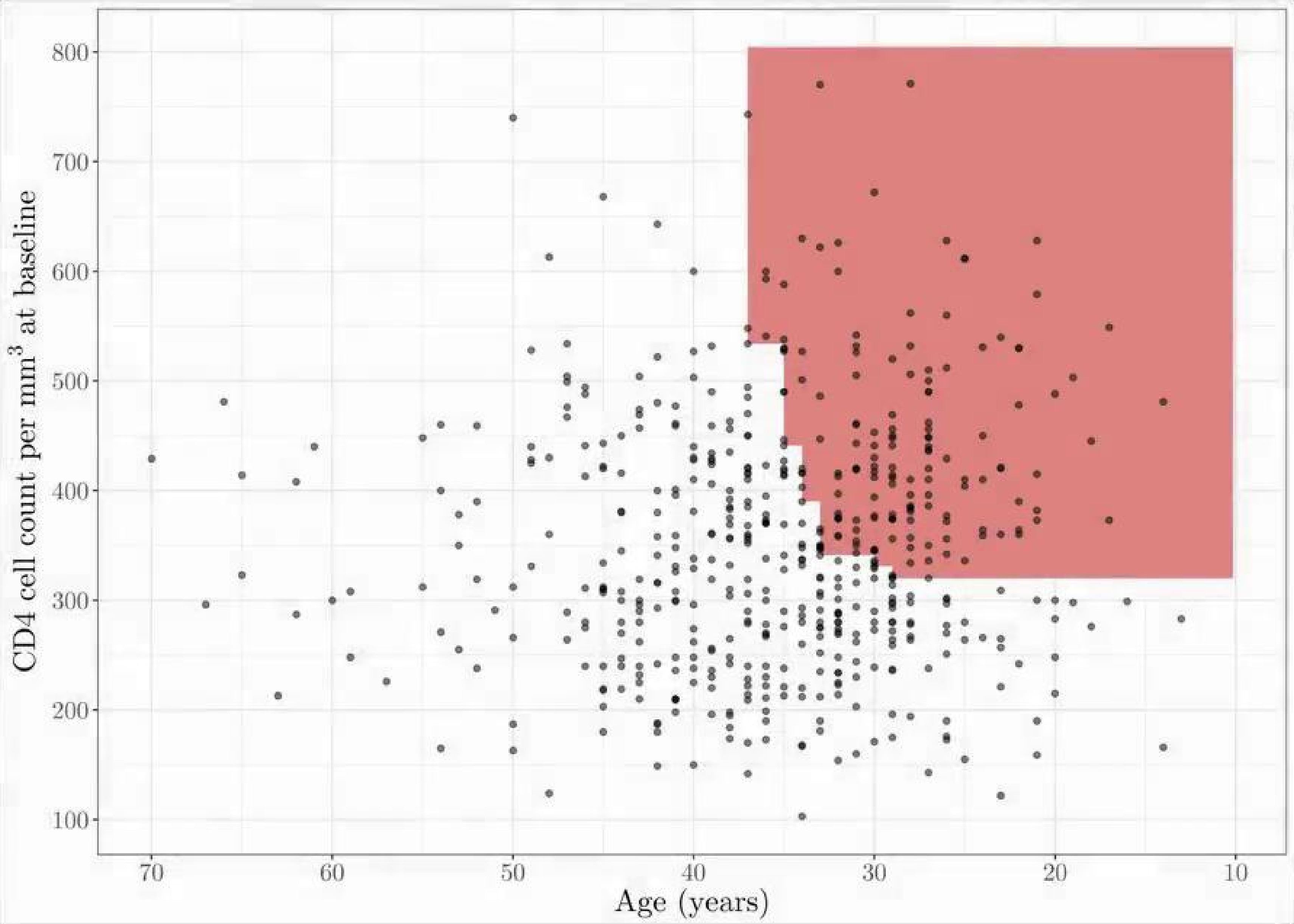
Application

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

- Adaptation to unknown variance of Gaussian errors.

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Take-home messages

Subgroup selection with strong Type I error guarantees is possible in the isotonic regression setting.

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

References and acknowledgement

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I am grateful for receiving the travel award that allowed me to present at ICSDS 2023.

Thank you!

Main reference:

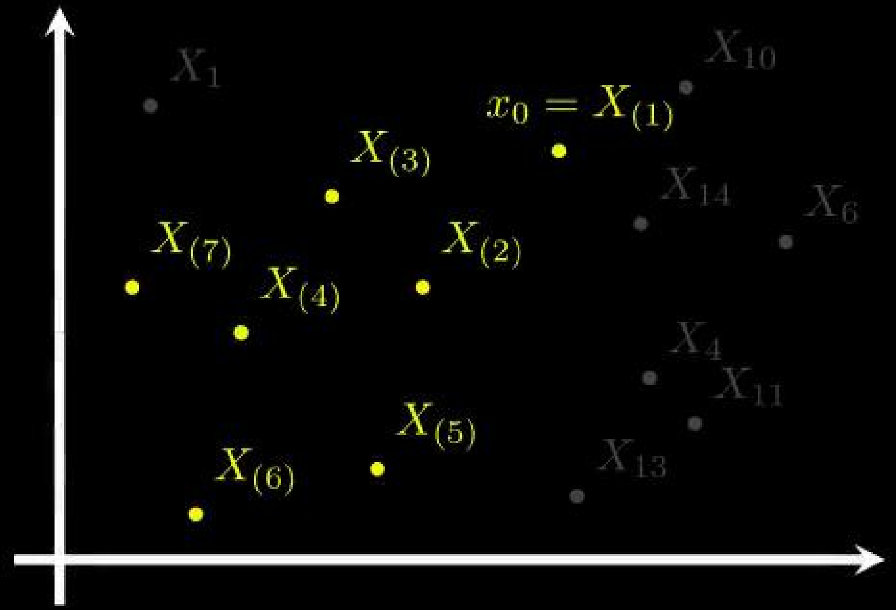
Müller, M. M., Reeve, H. W. J., Cannings, T. I. and Samworth, R. J. (2023) Isotonic subgroup selection. *arXiv preprint arXiv:2305.04852*.

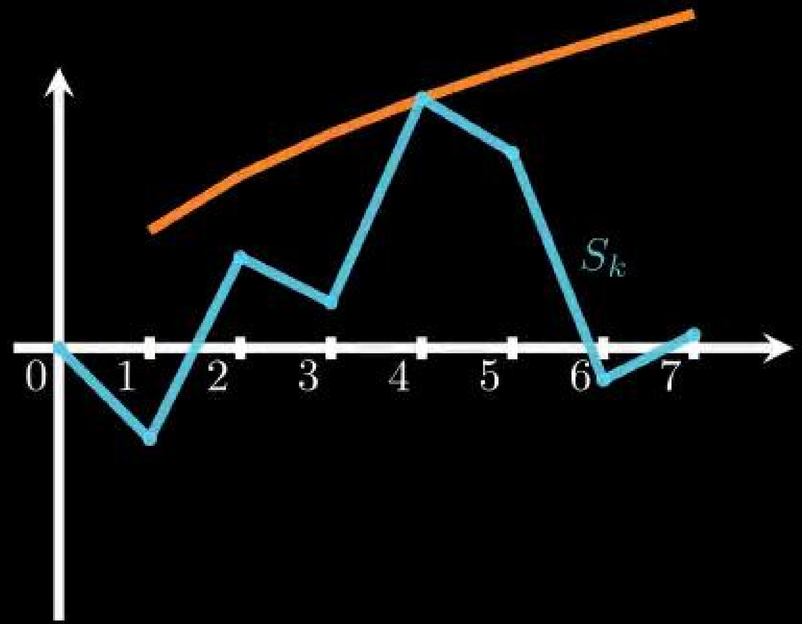
See manuelmmueller.github.io for data and `R`-code.

Appendix

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

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



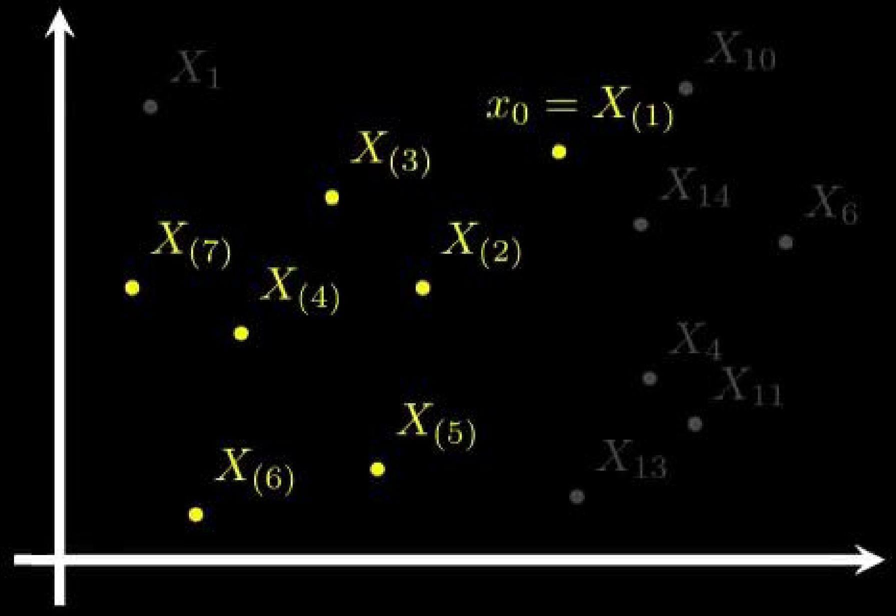


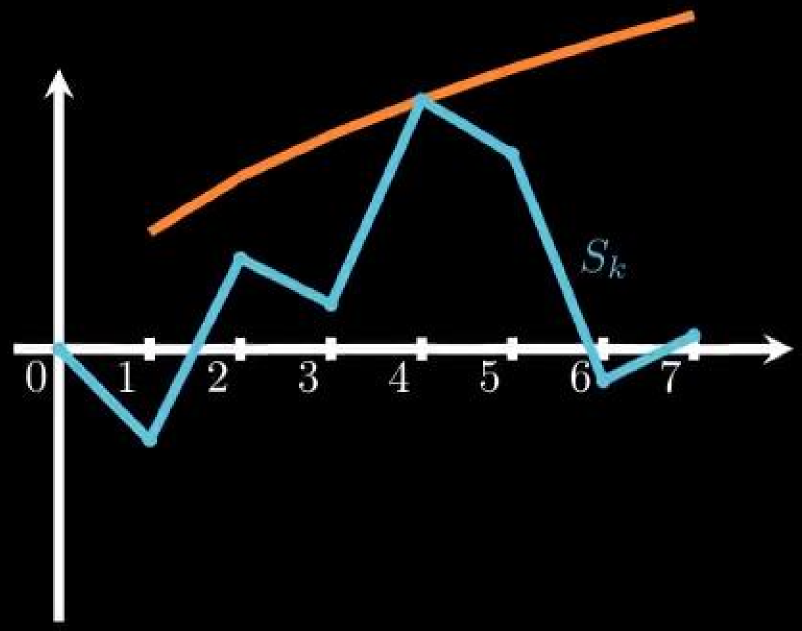
Denote $\mathcal{I}(x_0) := \{i \in [n] : X_i \preccurlyeq x_0\}$, $n(x_0) := |\mathcal{I}(x_0)|$.

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

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 $H_0(X_i)$, $i \in [n]$





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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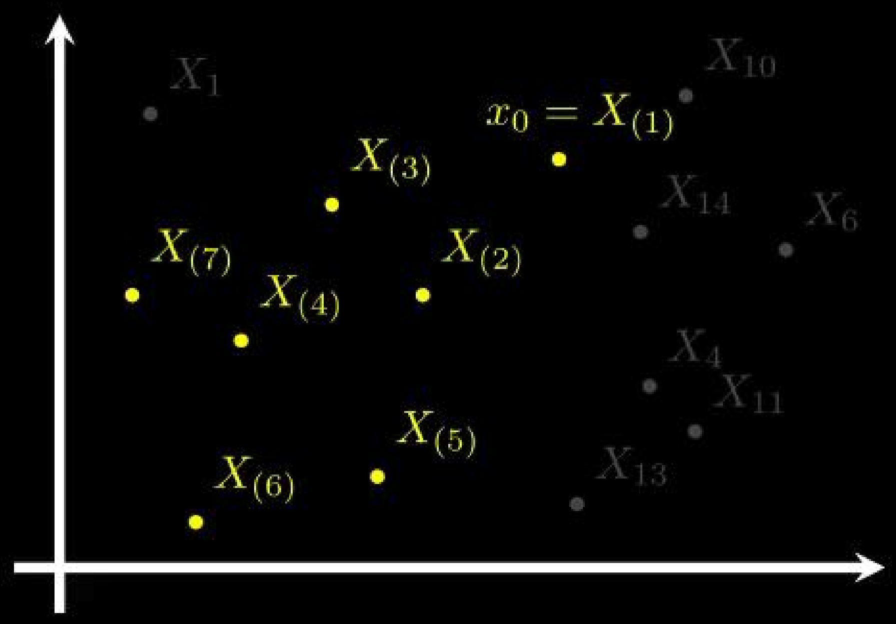

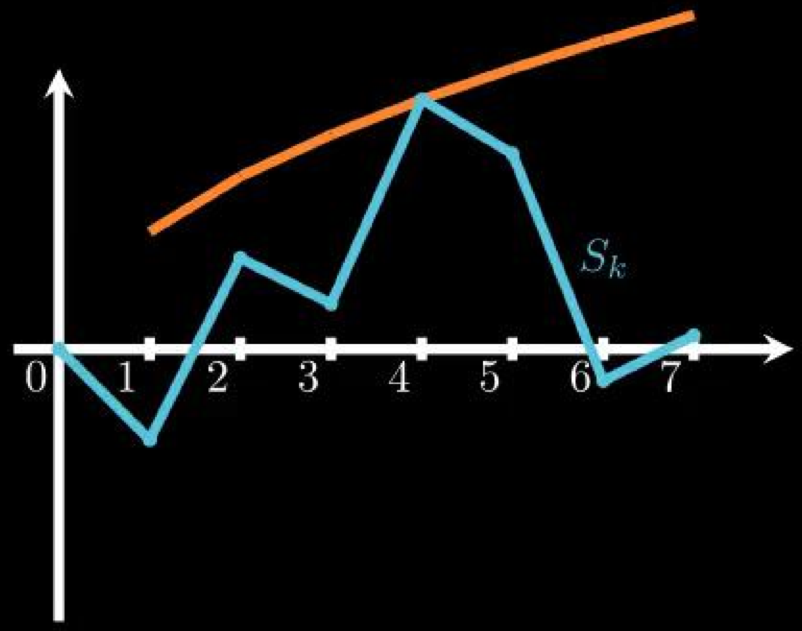

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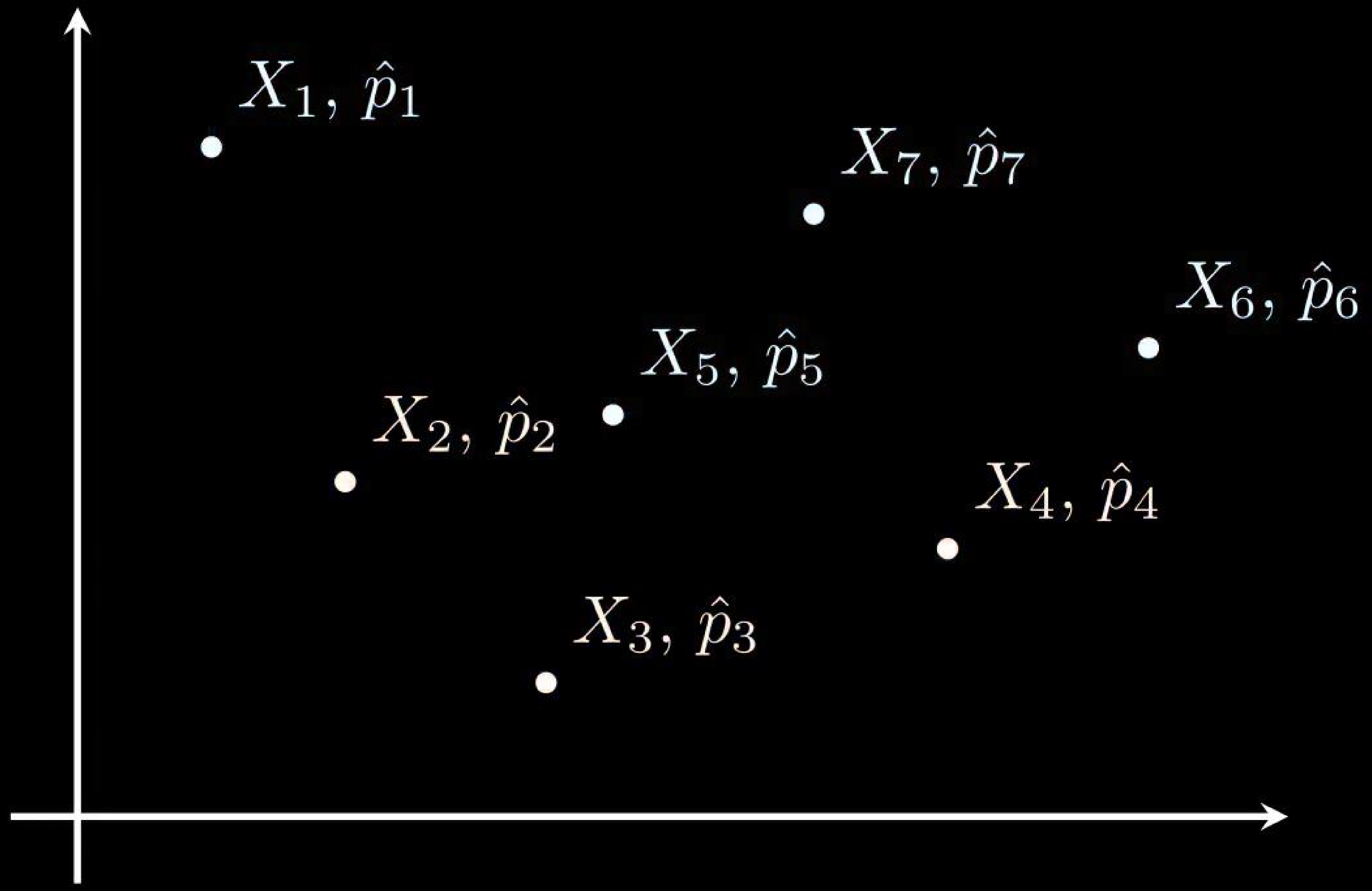
whenever $n(x) > 0$, and $\hat{p}_{\sigma,\tau}(x) := 1$ otherwise.

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 $t \in (0,1)$.

Multiple testing procedure

Key idea: logical relationships of hypotheses $H_0(X_i)$, $i \in [n]$, induce DAG with vertex set $[n]$. We combine the sequential rejection principle (Goeman and Solari, 2010) with careful α-budget allocation to construct a *DAG testing procedure.*



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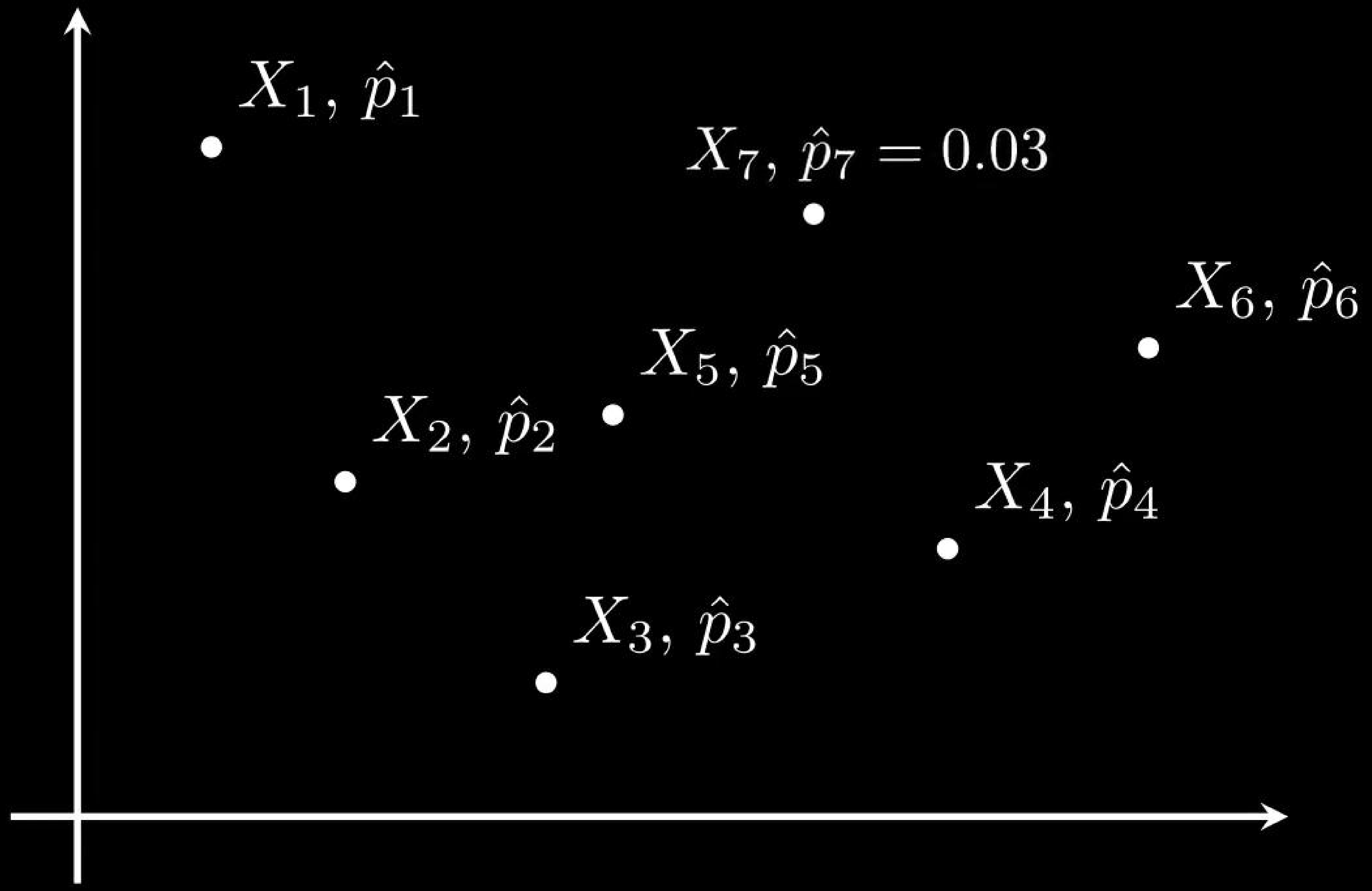

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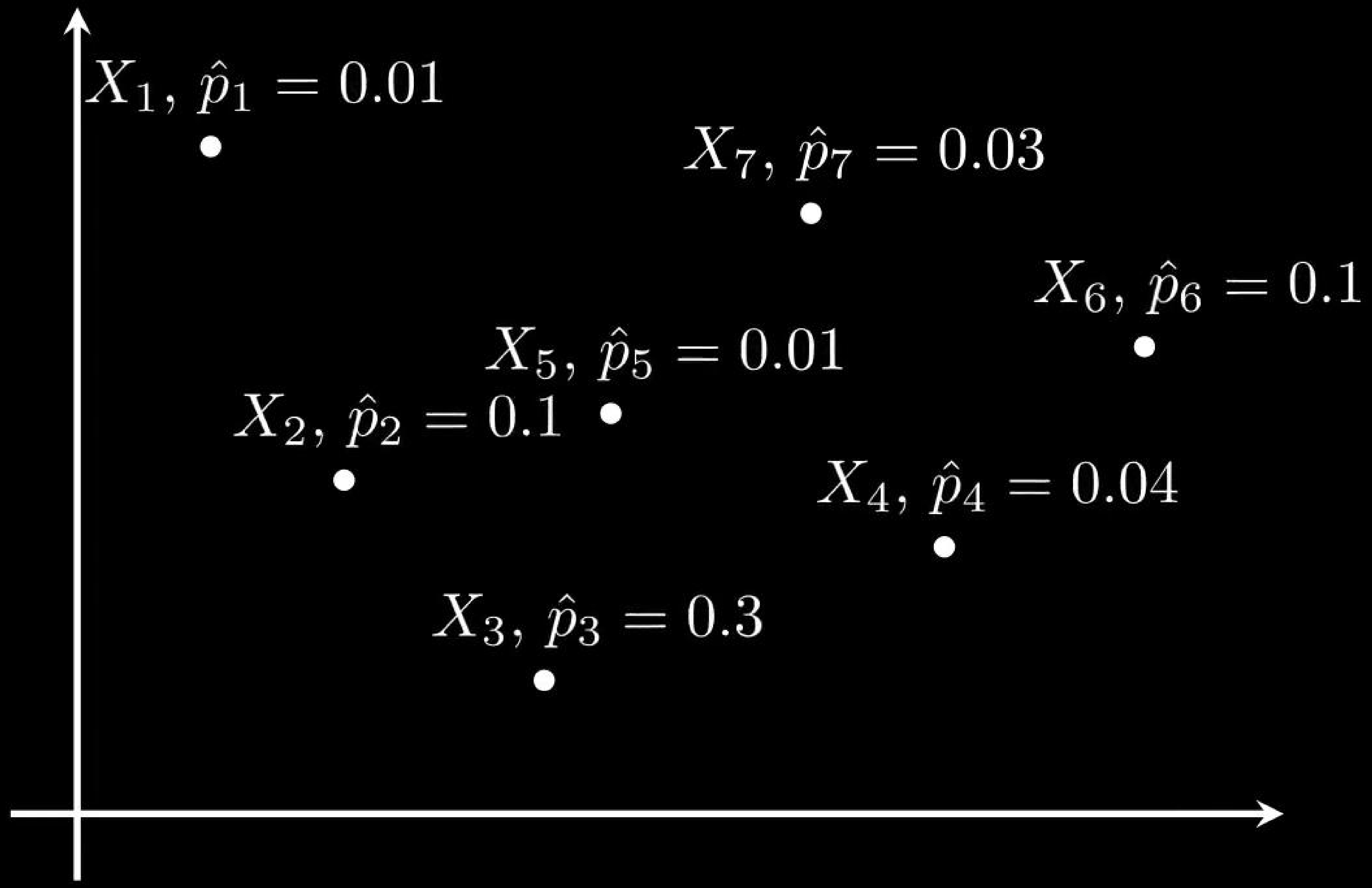

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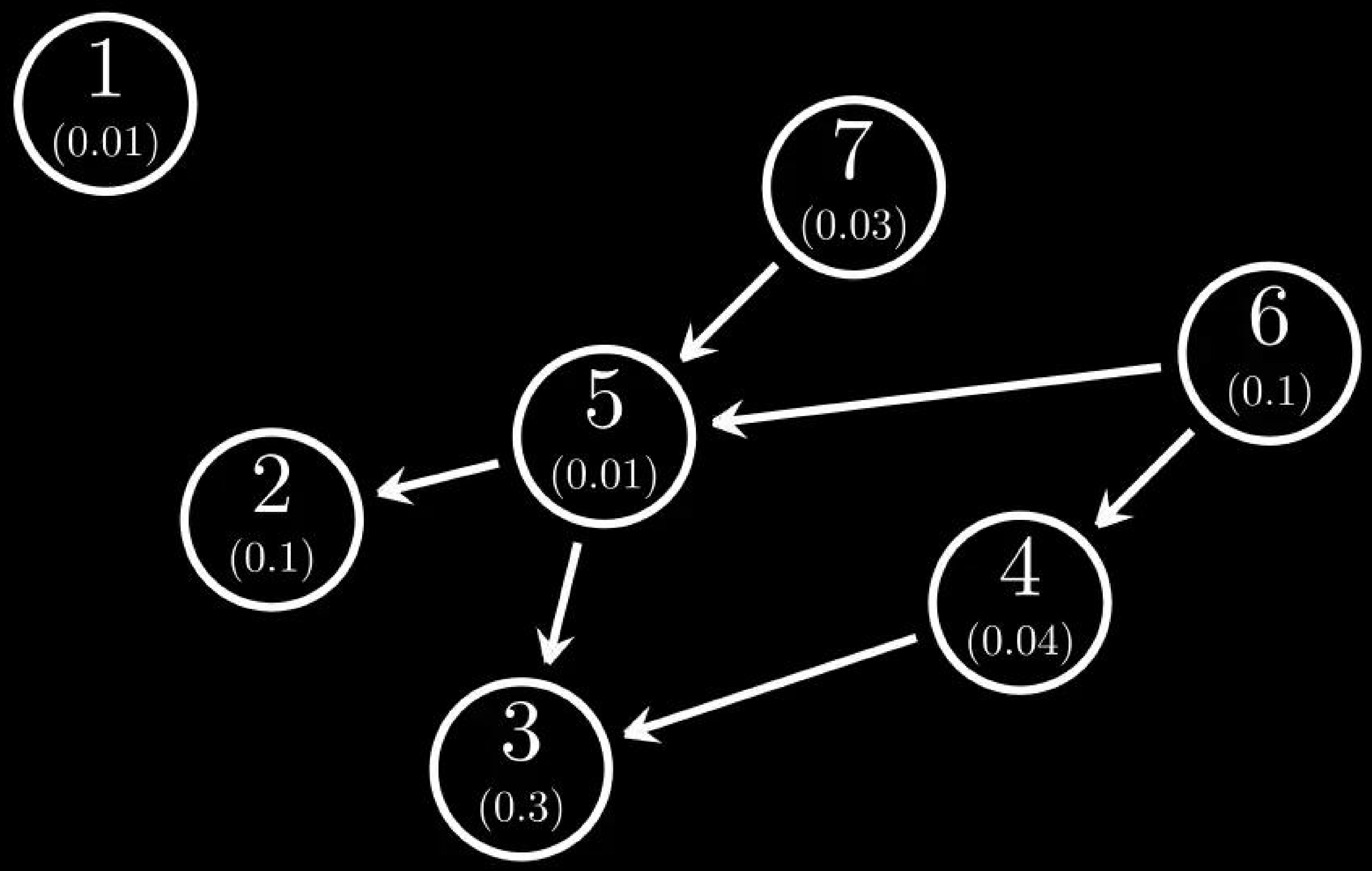

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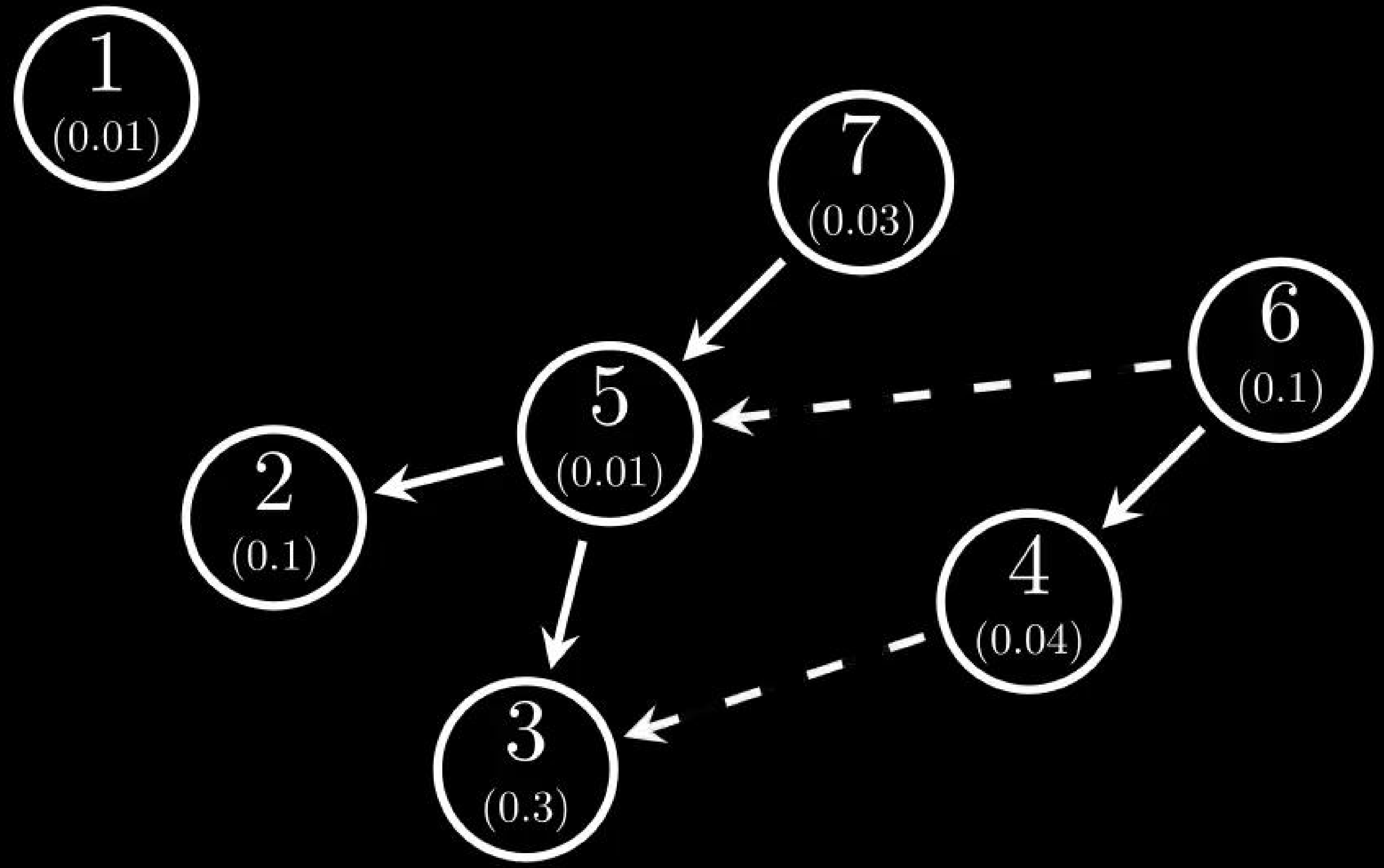

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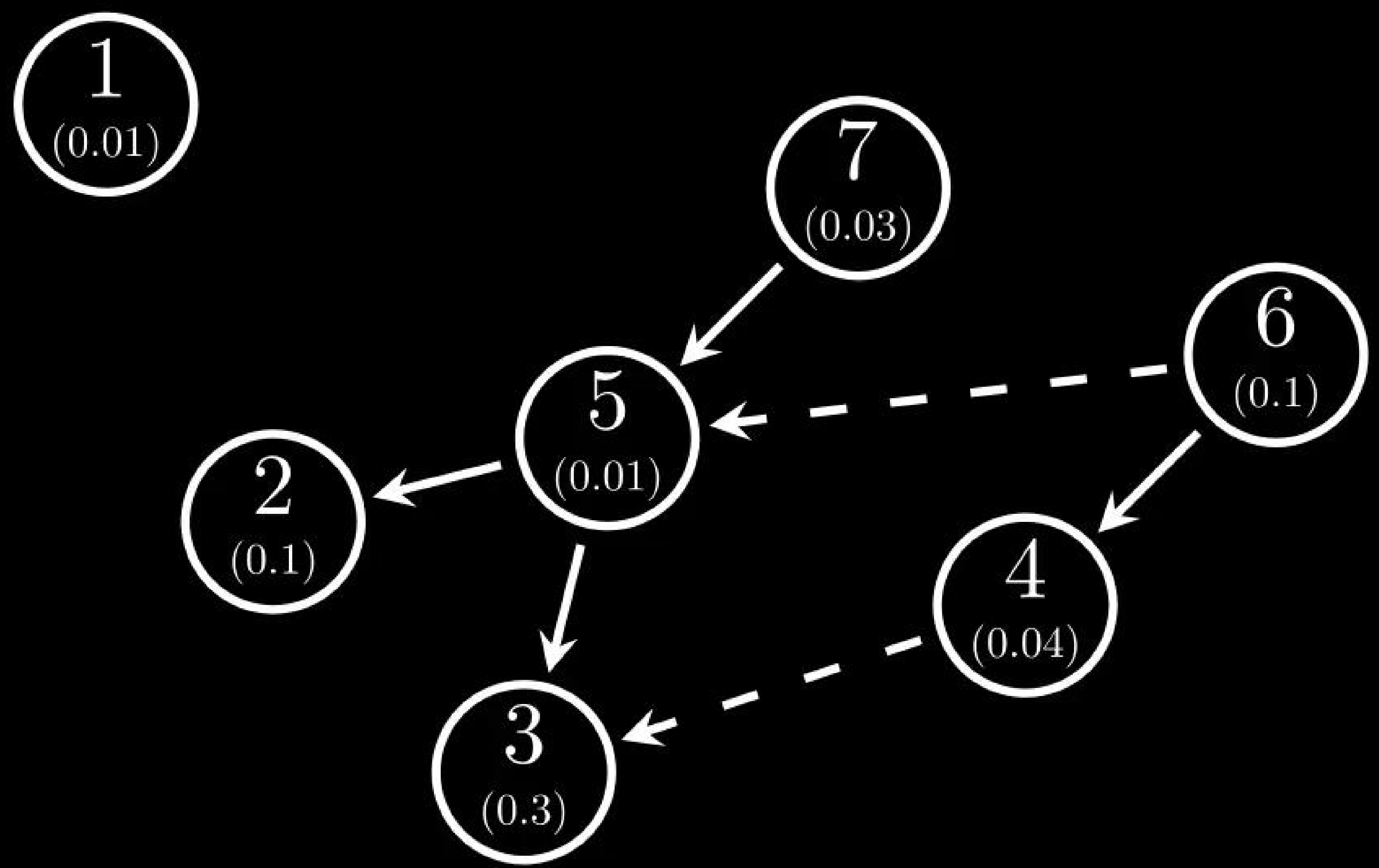

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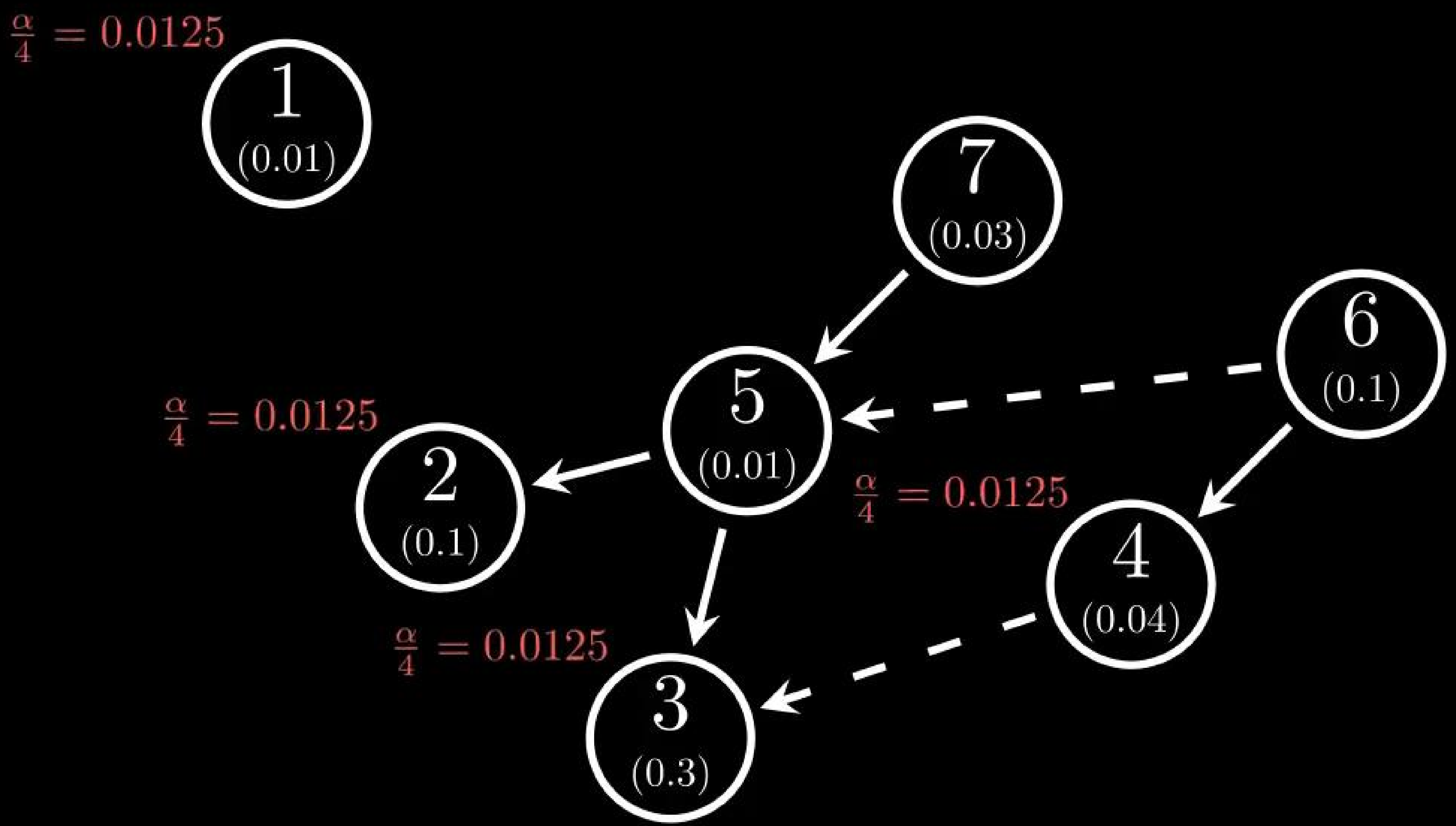

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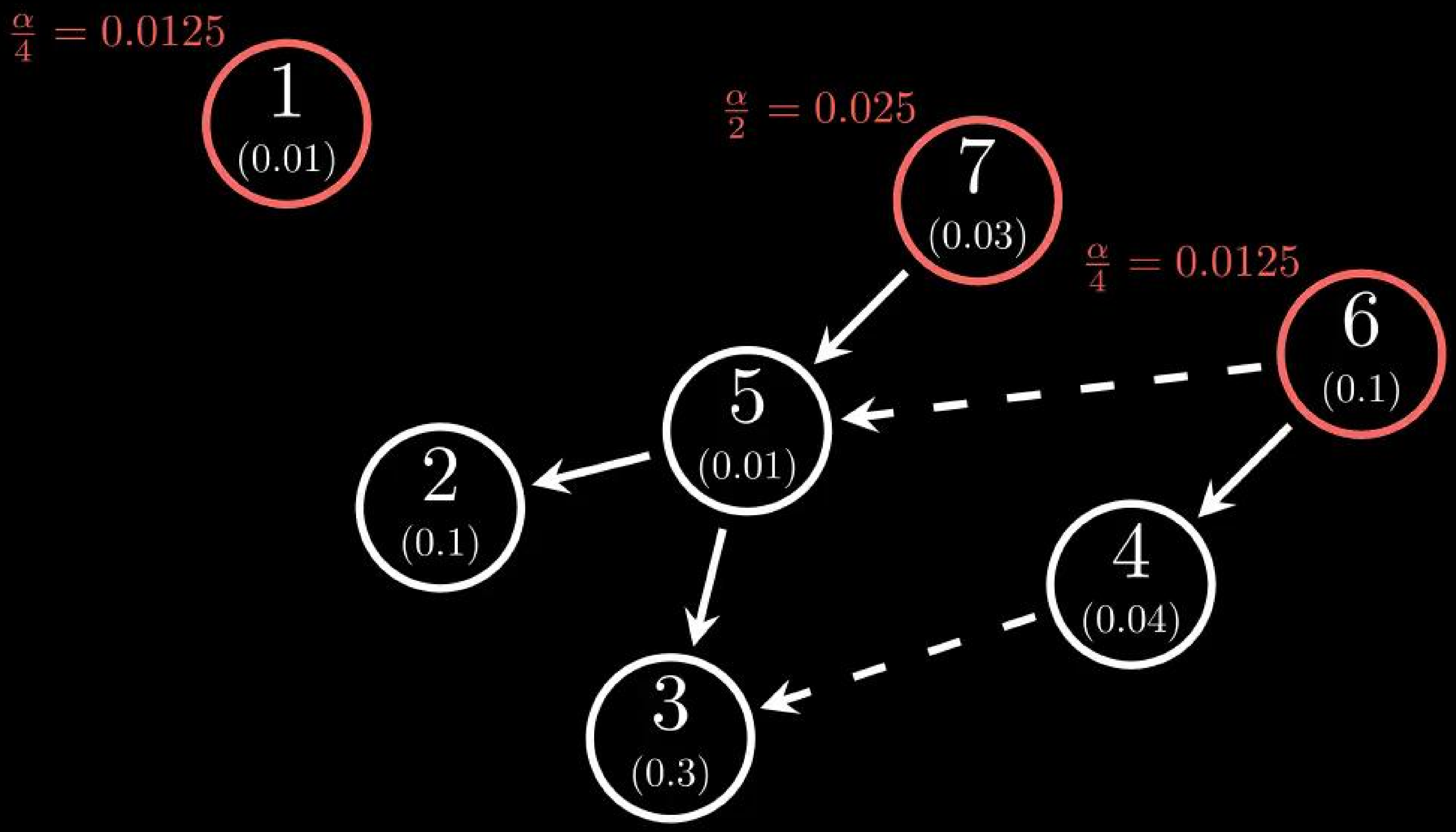

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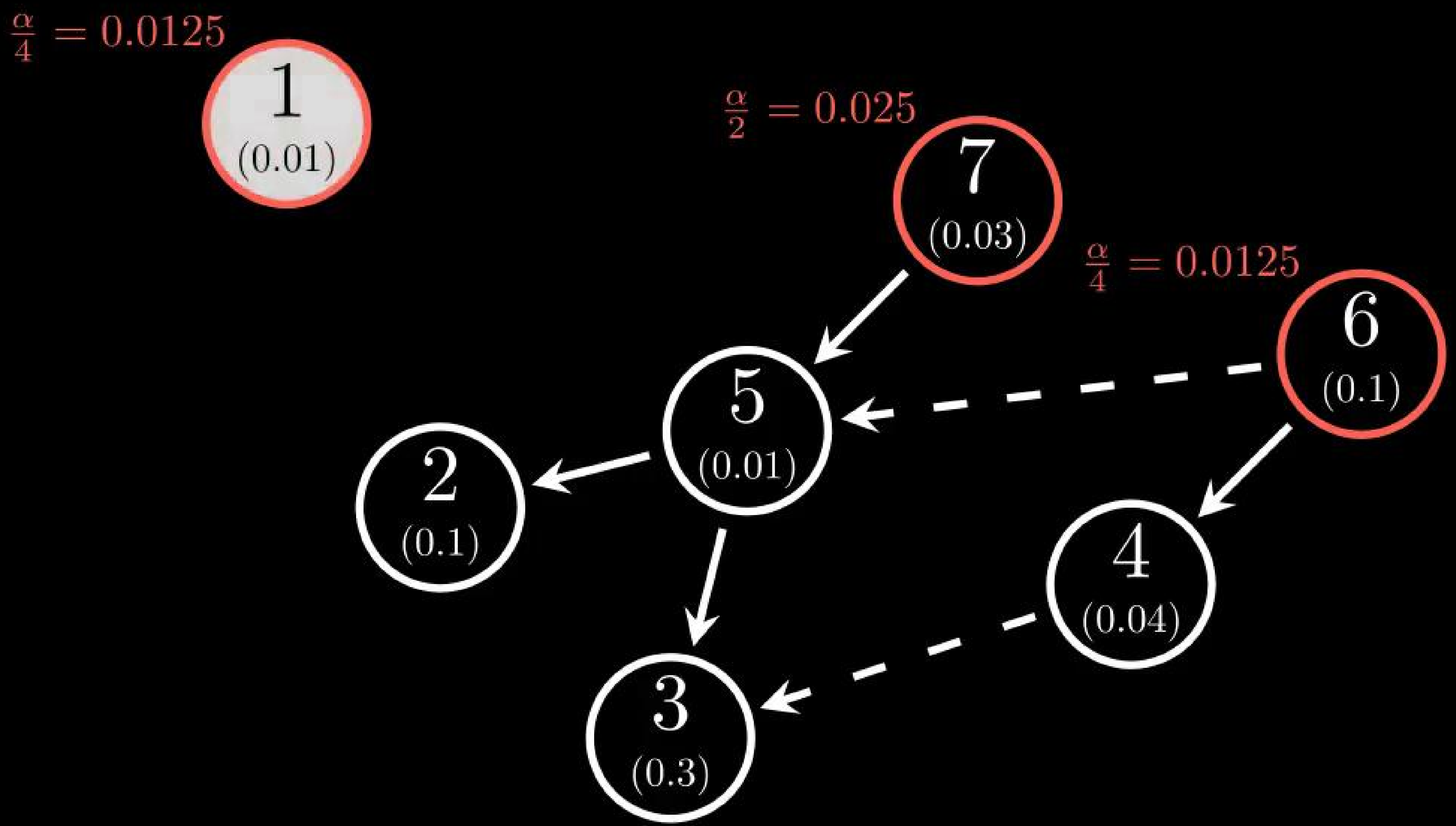

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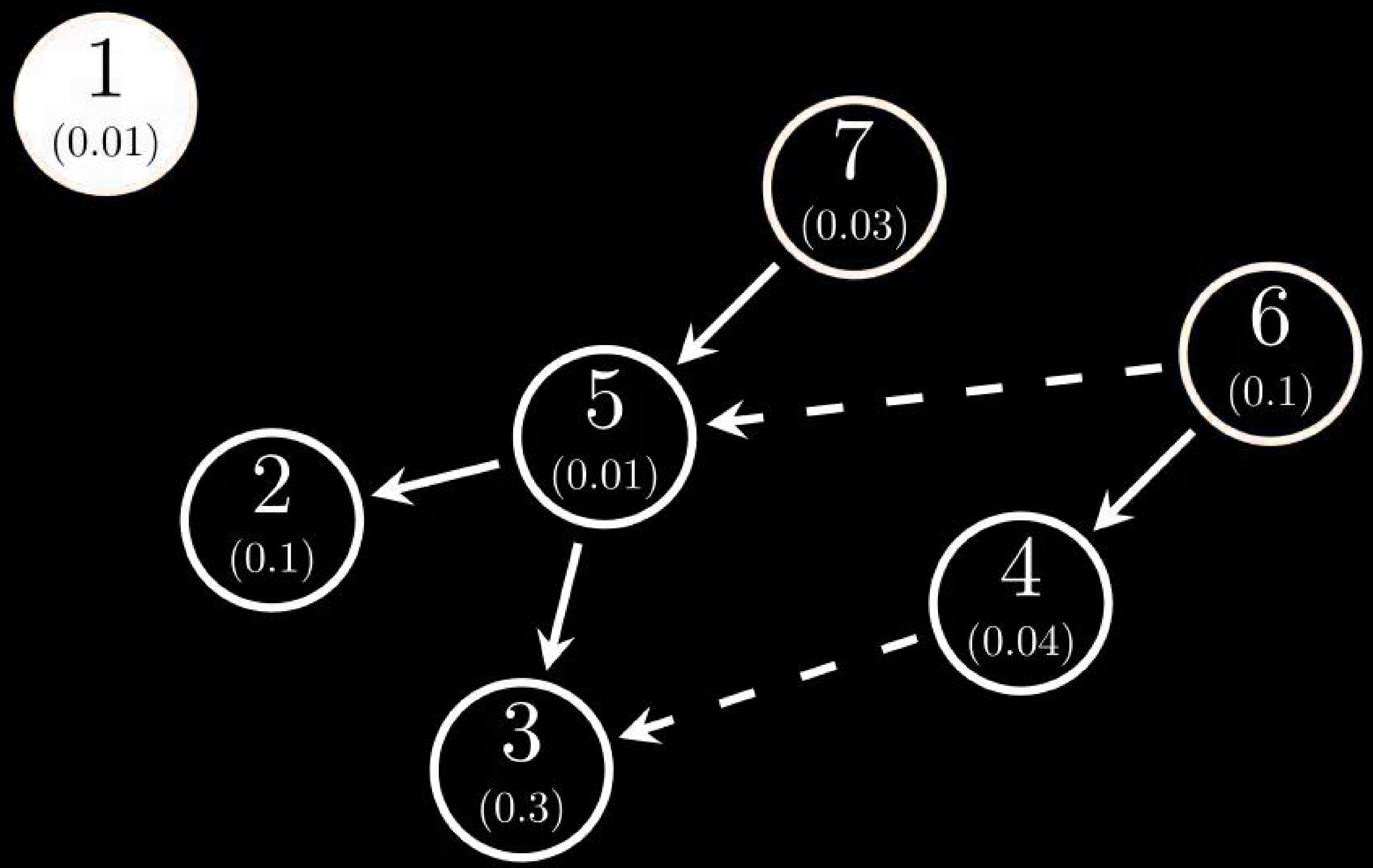

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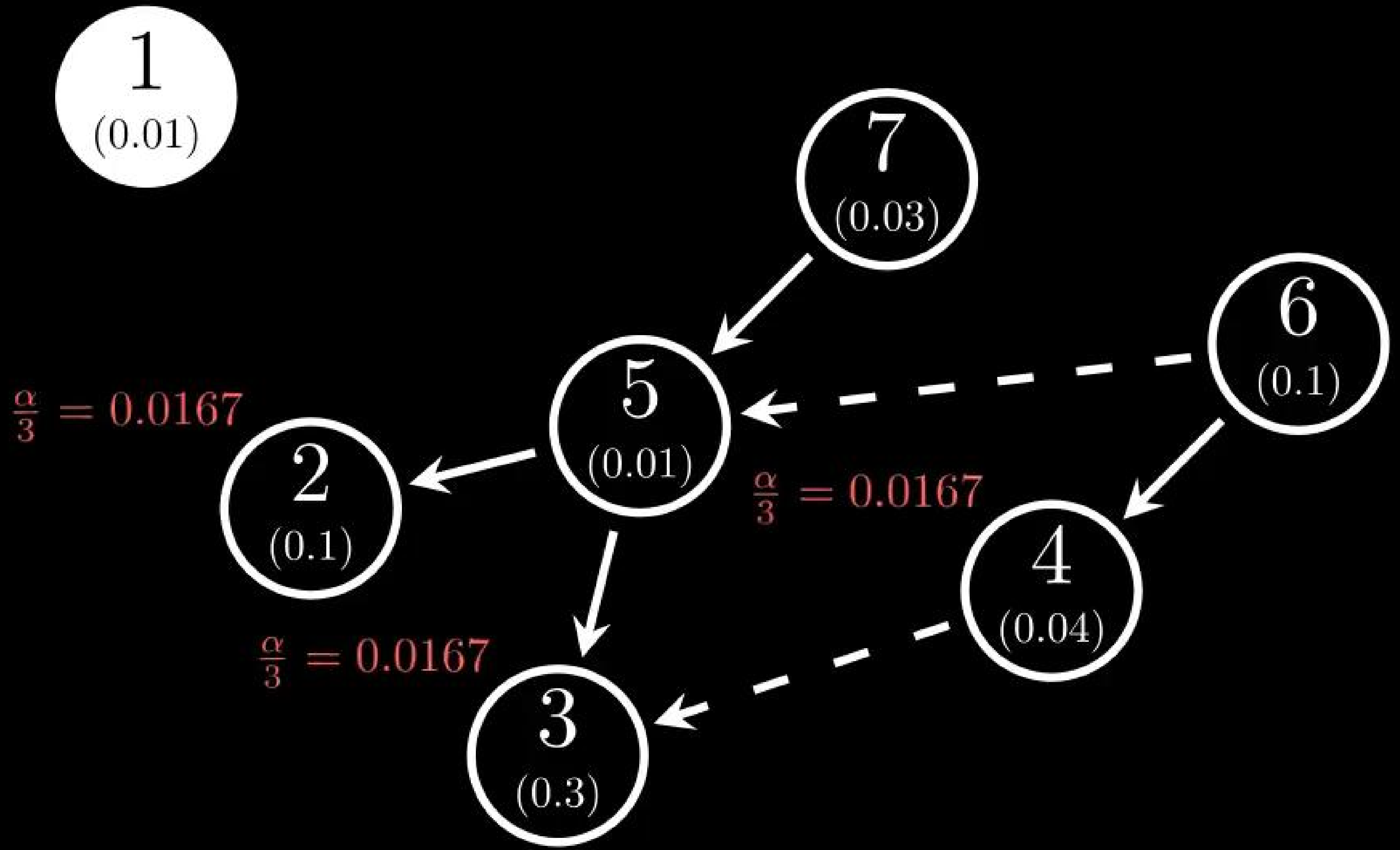

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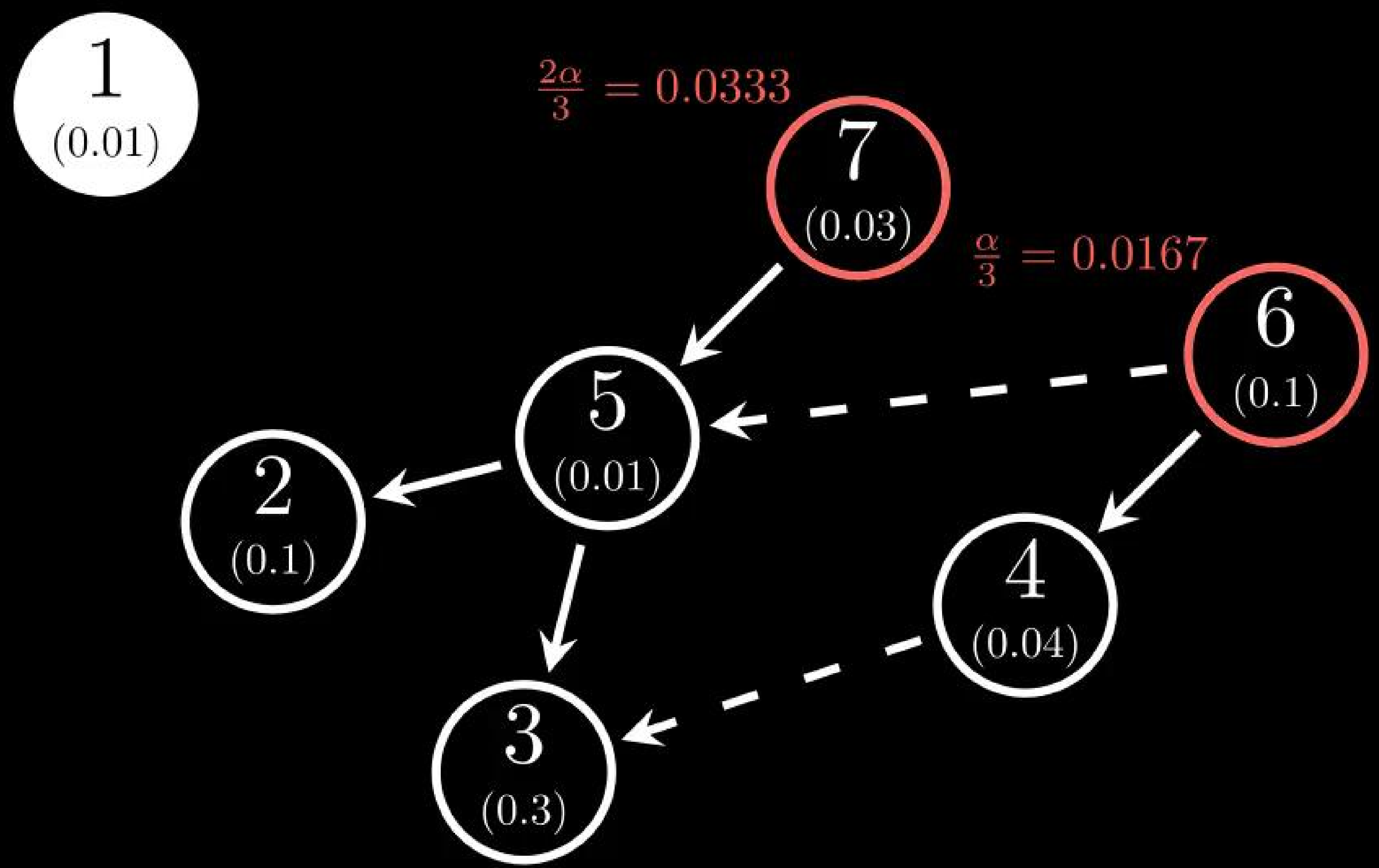

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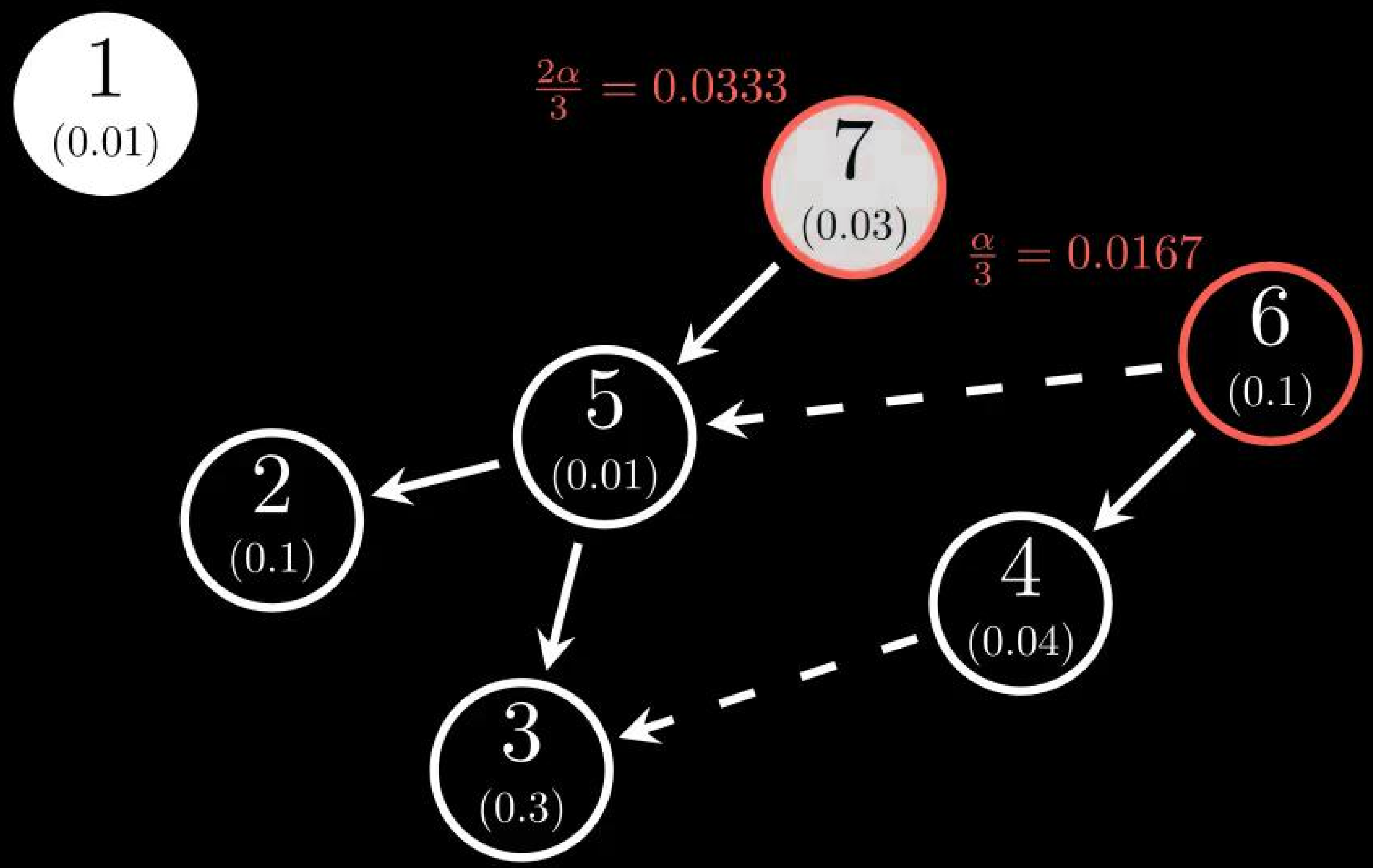

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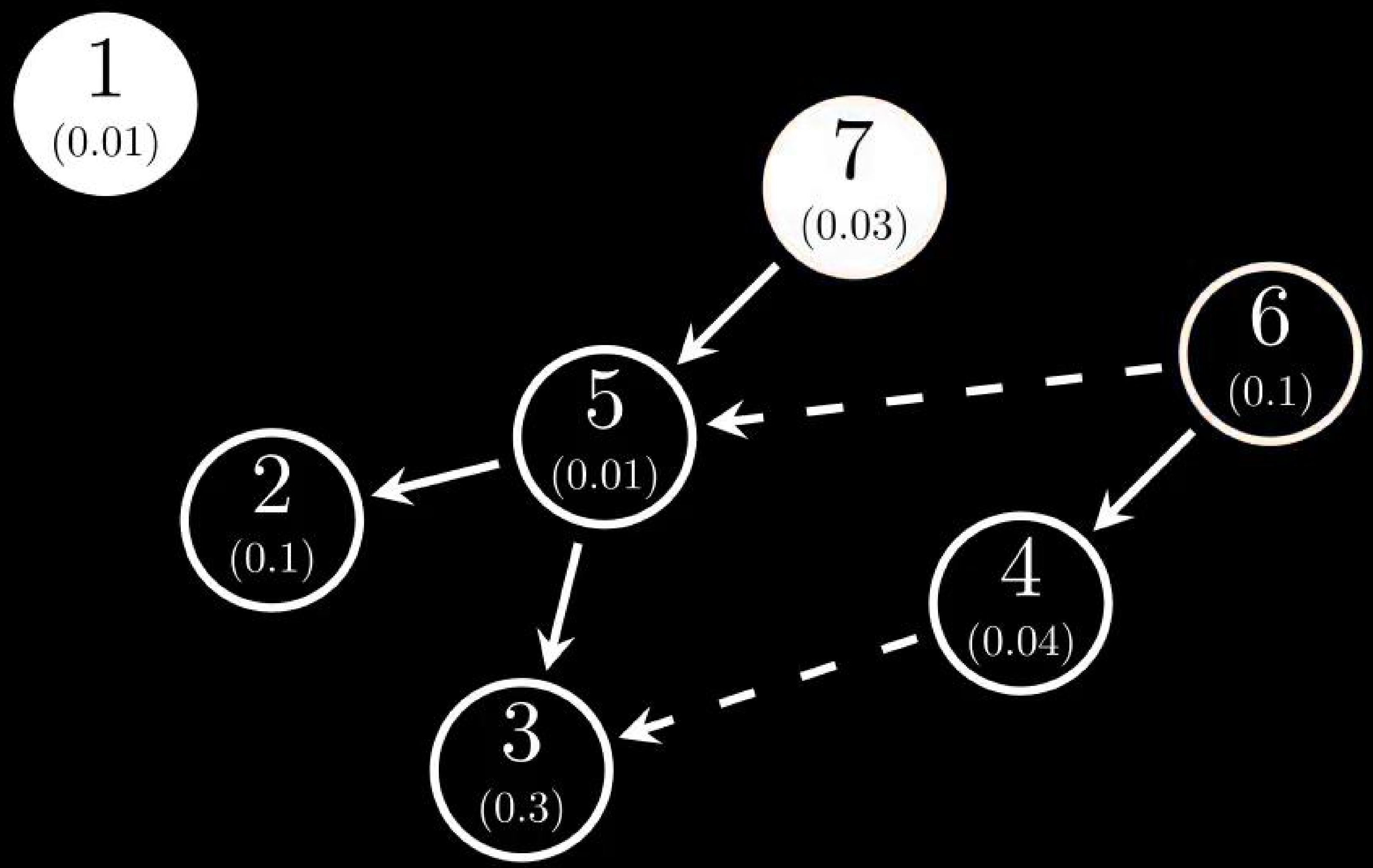

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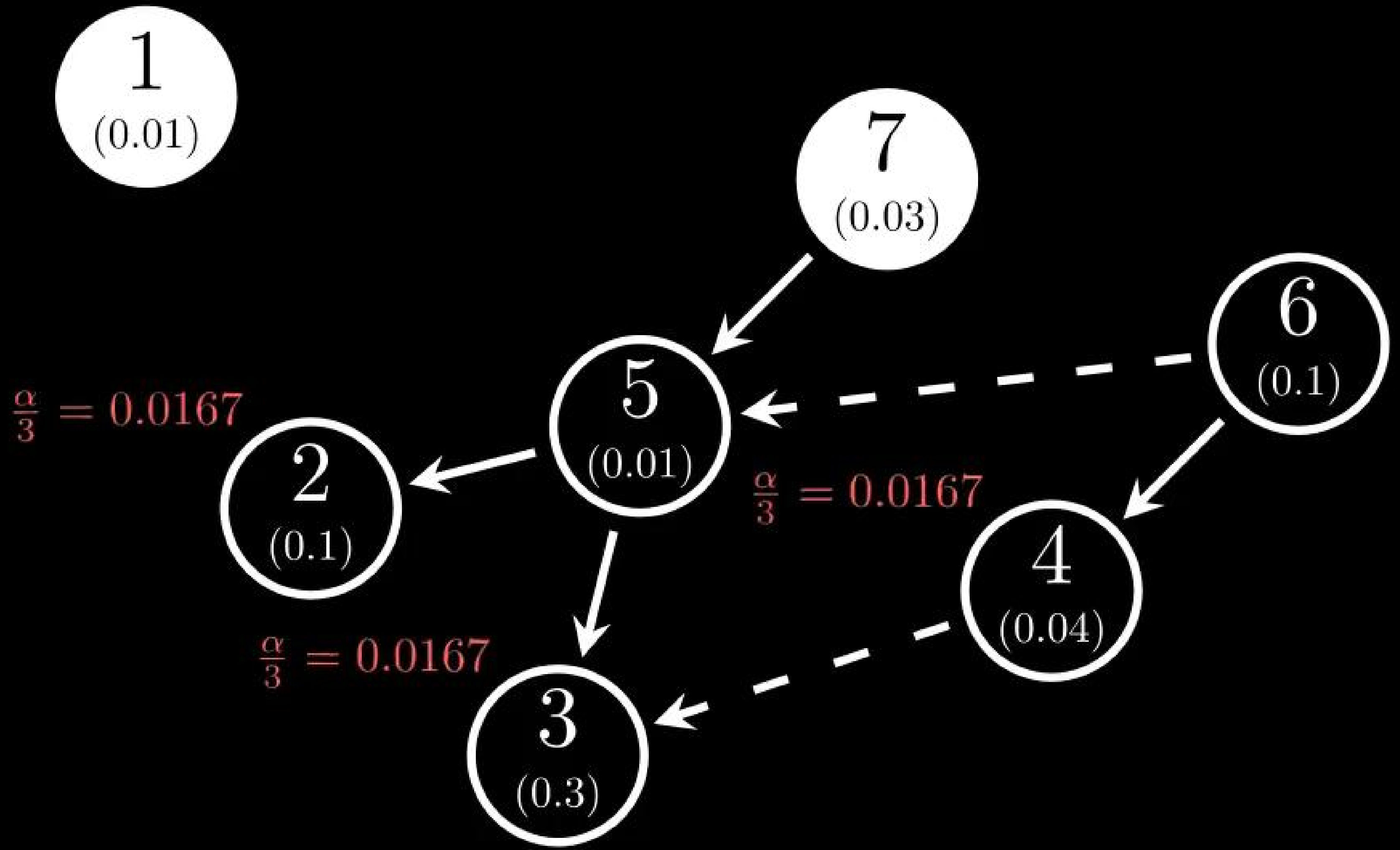

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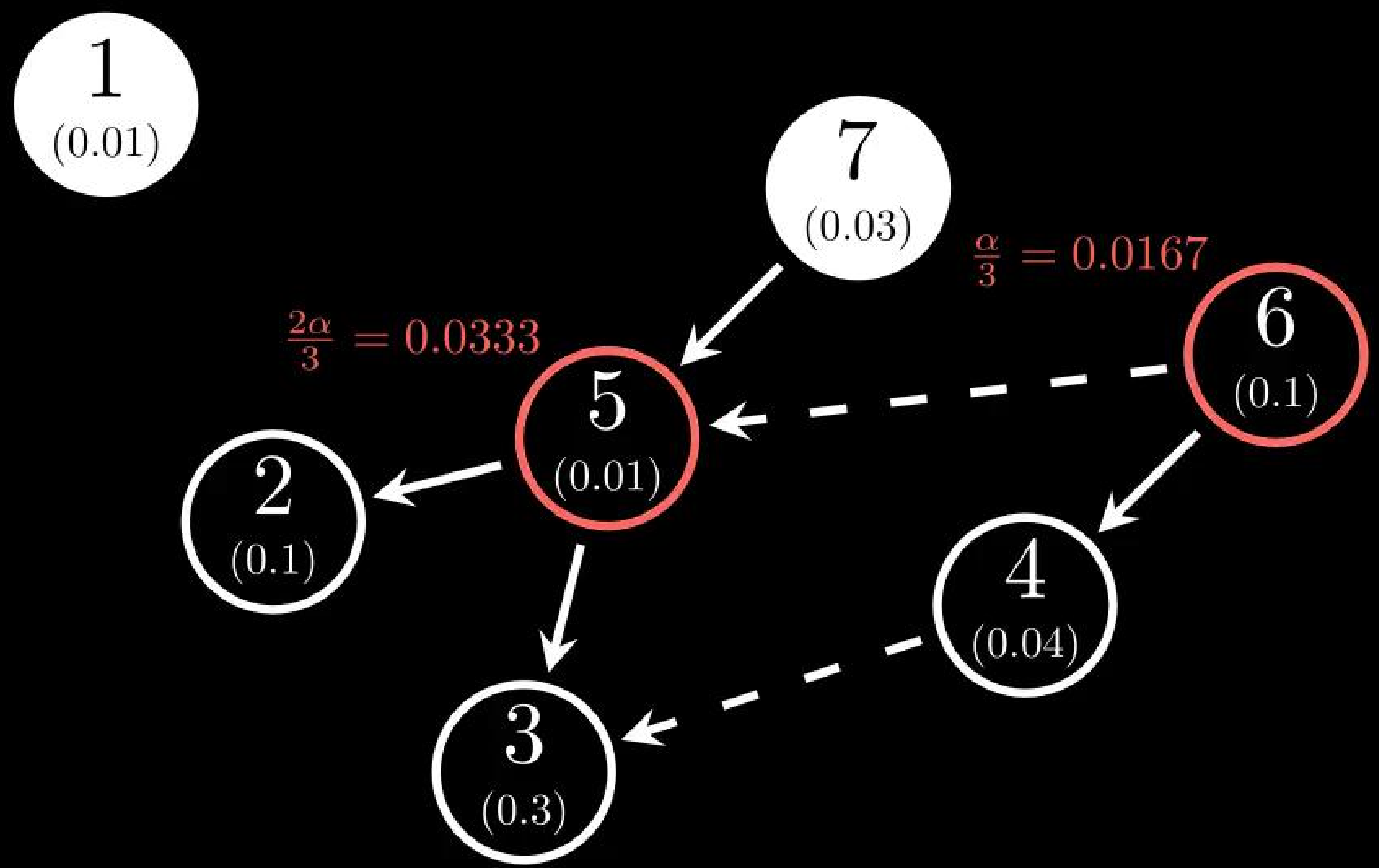

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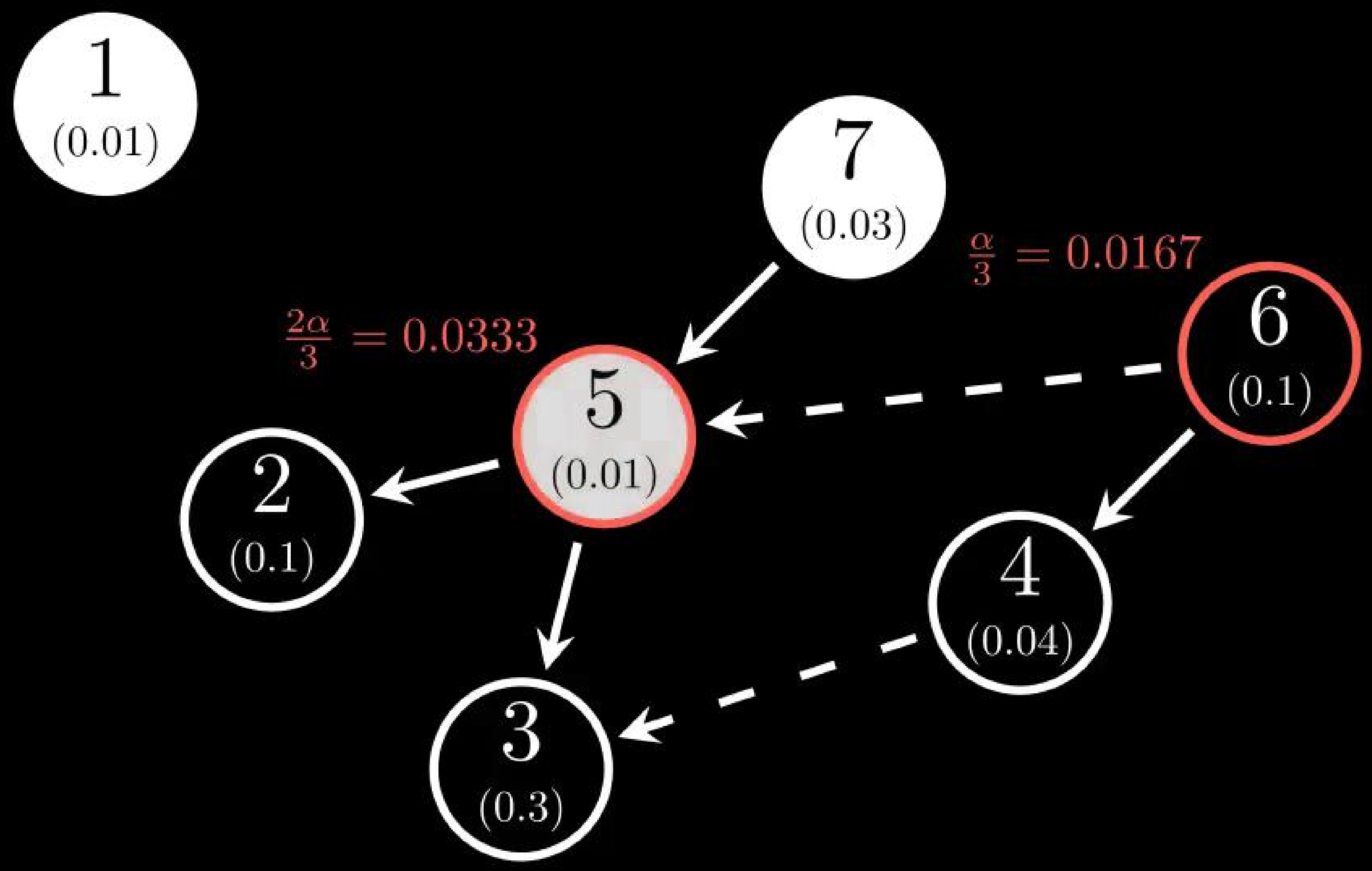

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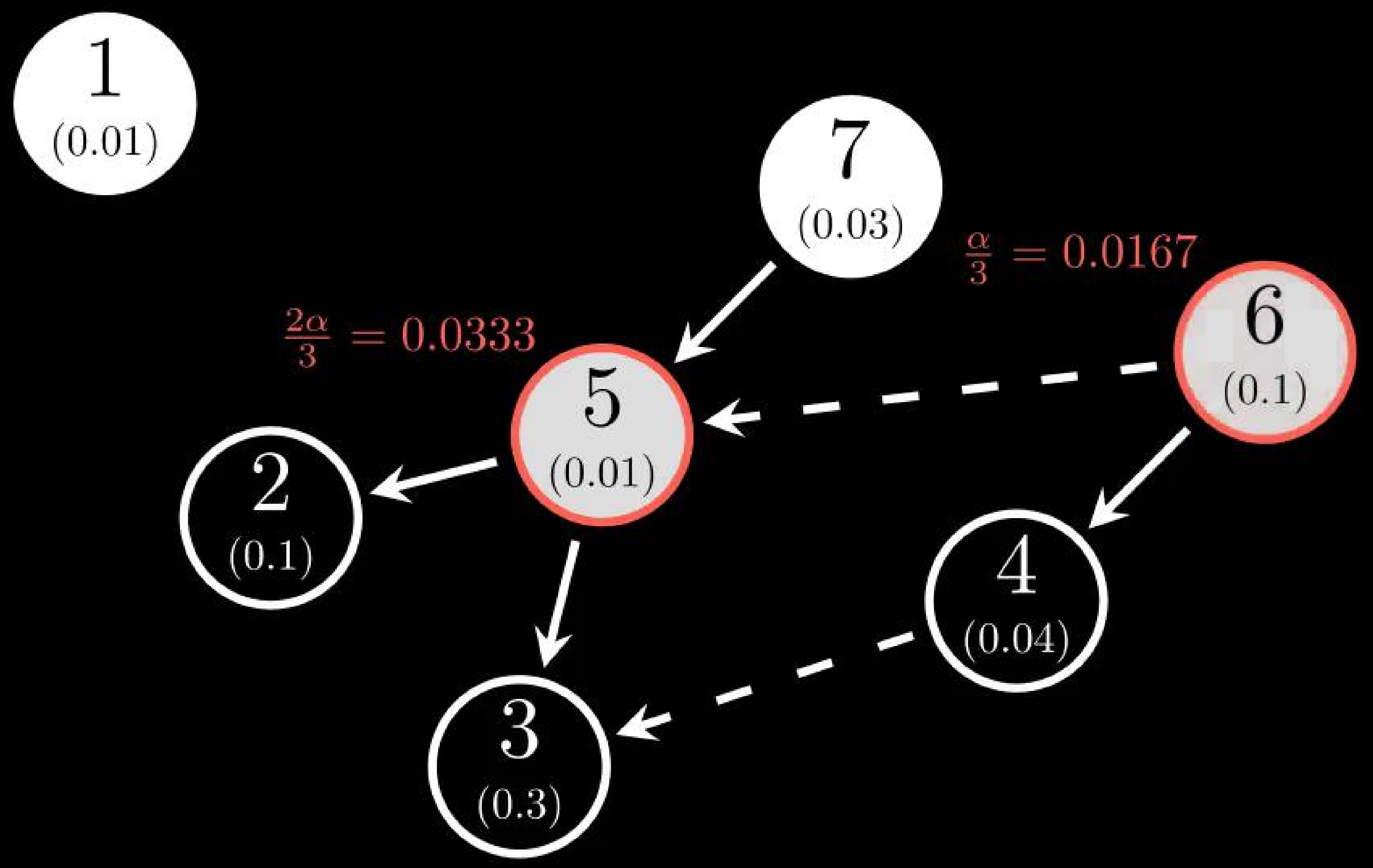

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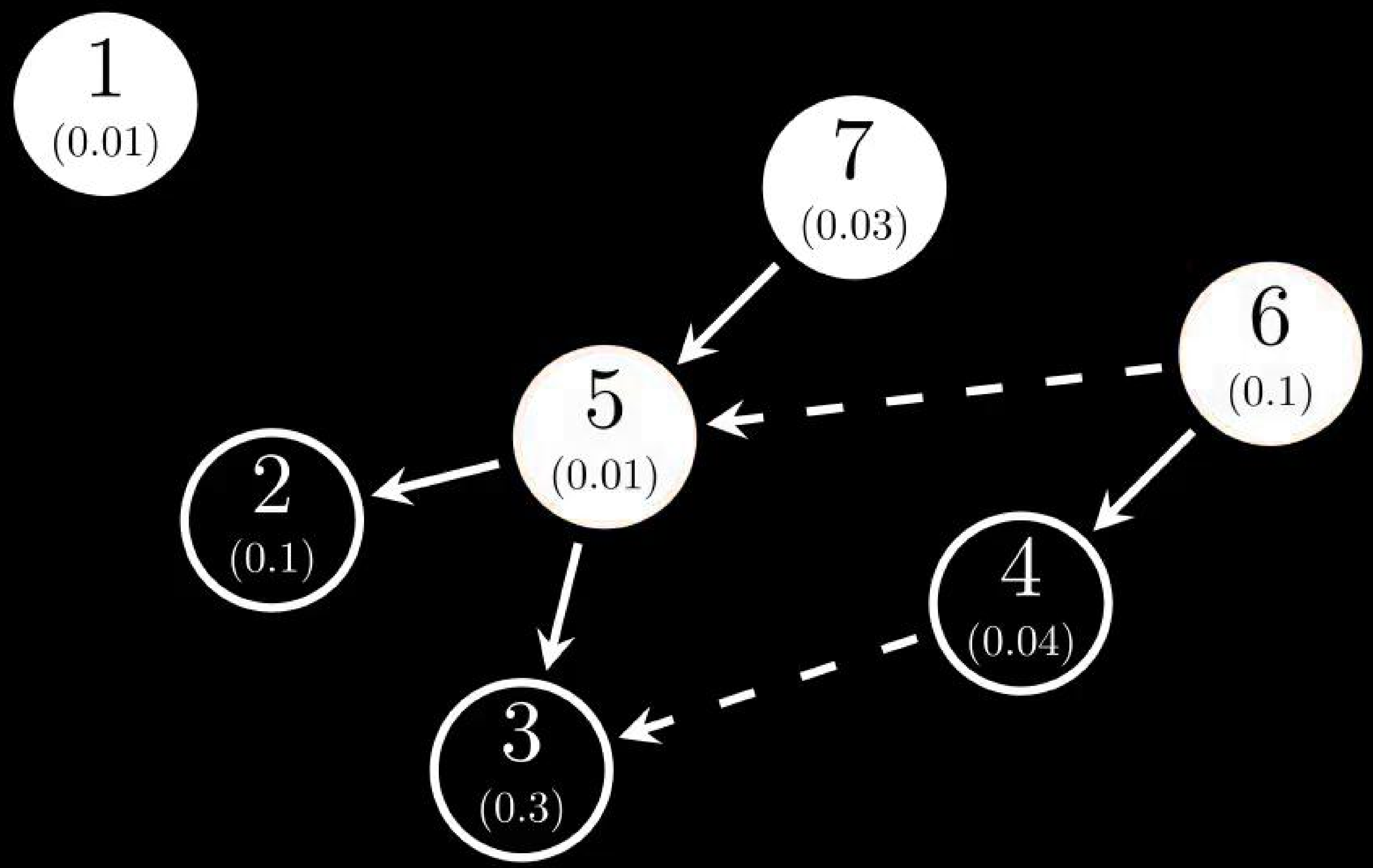

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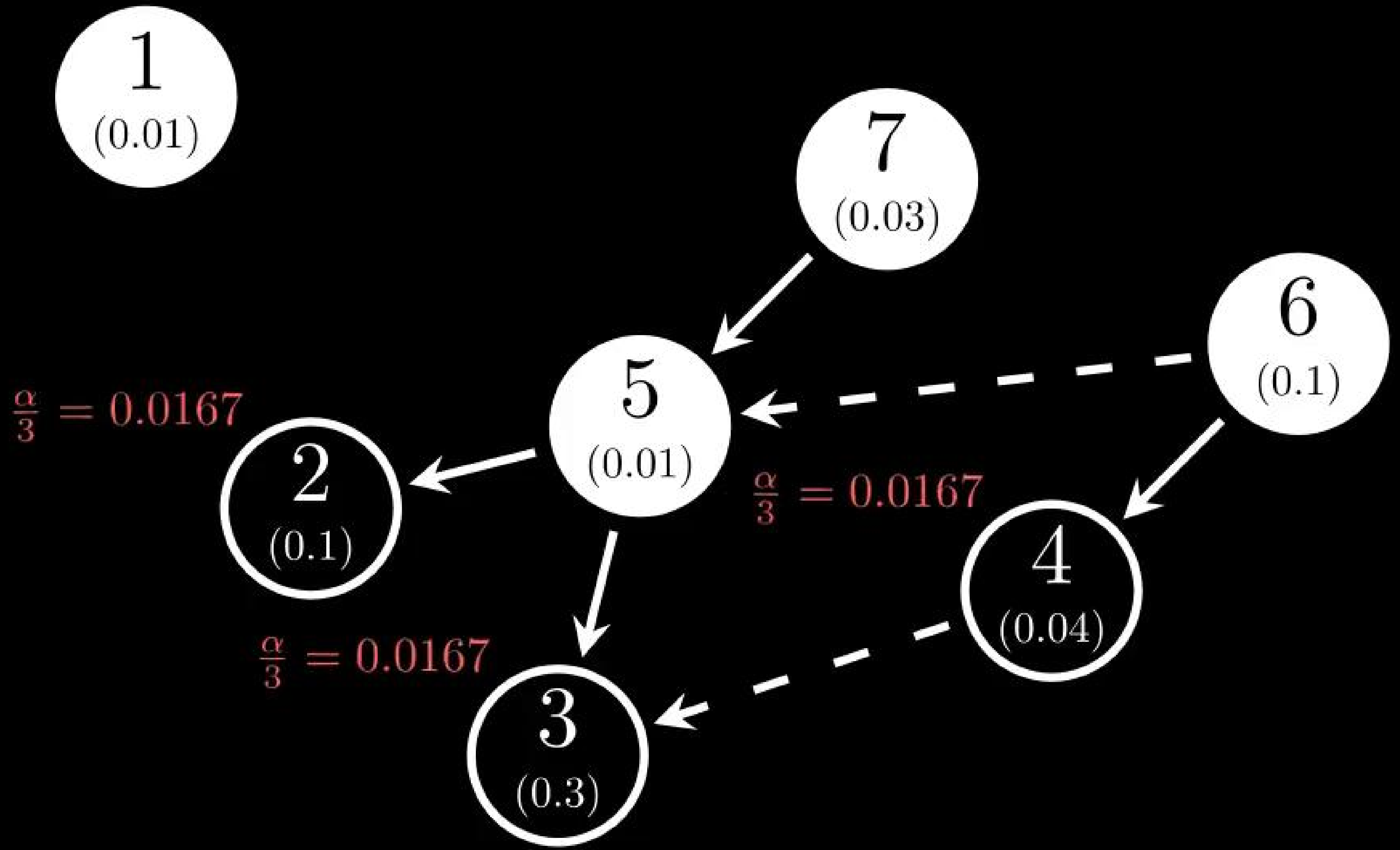

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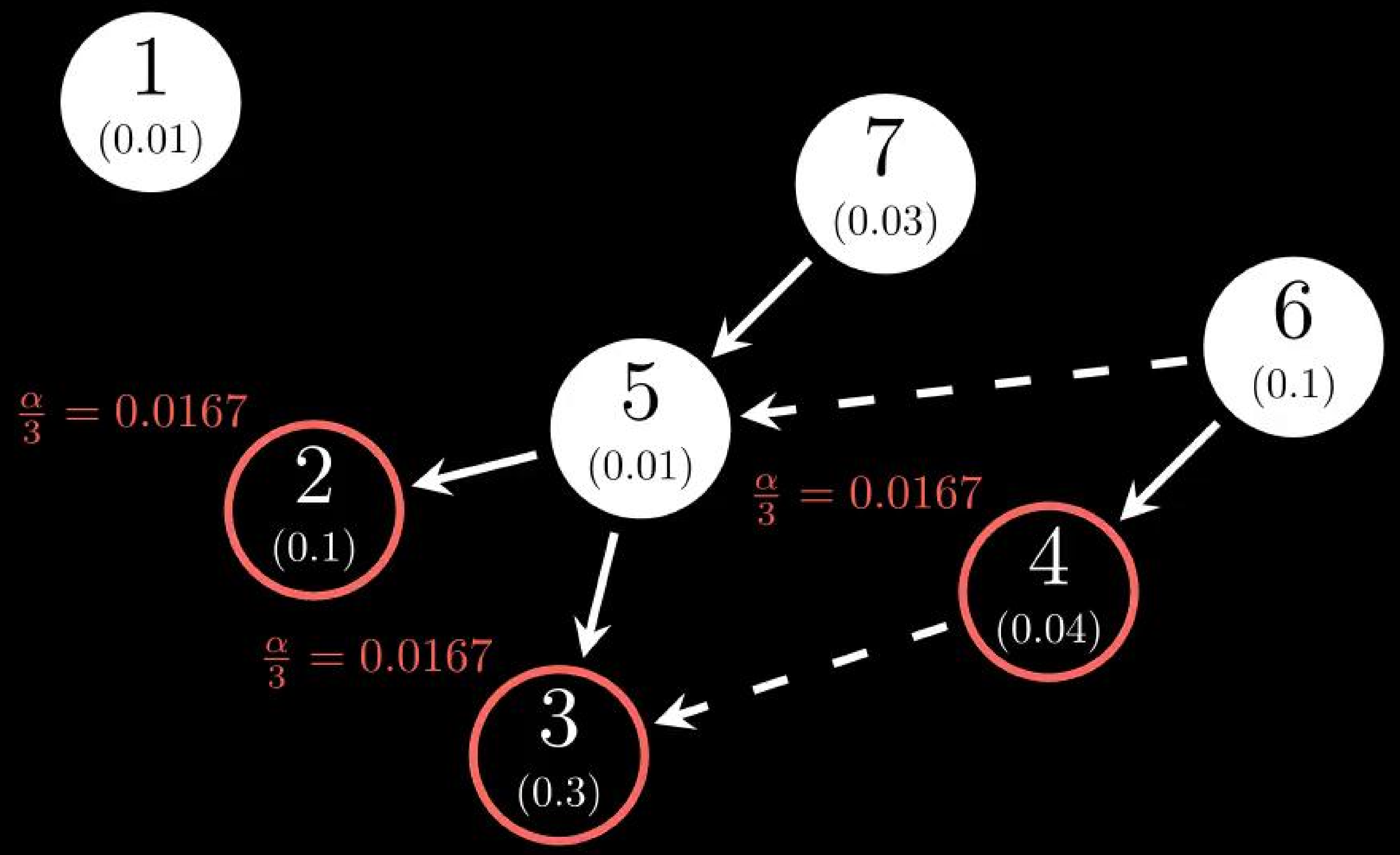

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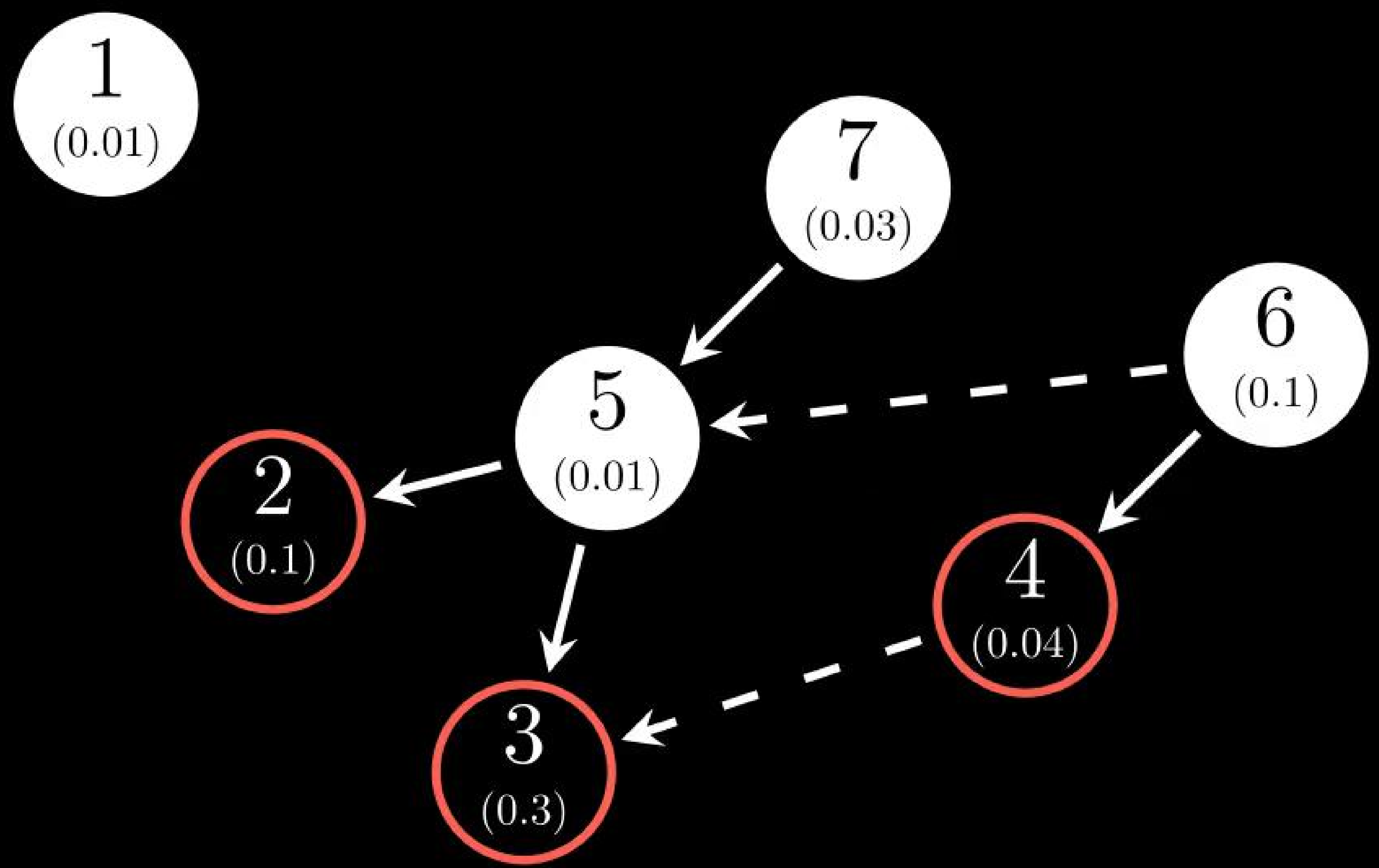

Here: $\alpha = 0.05$. The procedure terminates with $\mathcal{R}_\alpha = \{1, 5, 6, 7\}$.

Further conditions are needed for power

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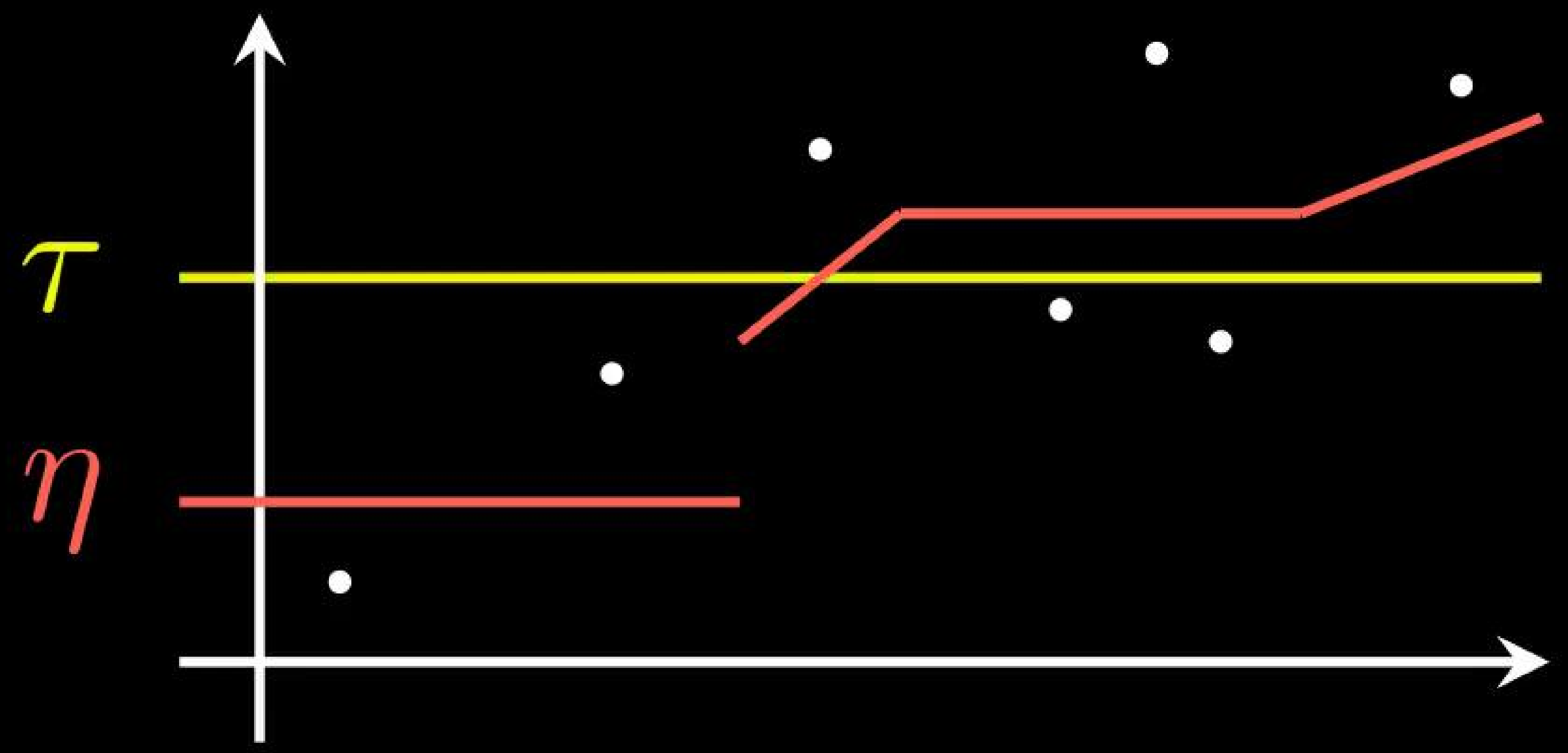

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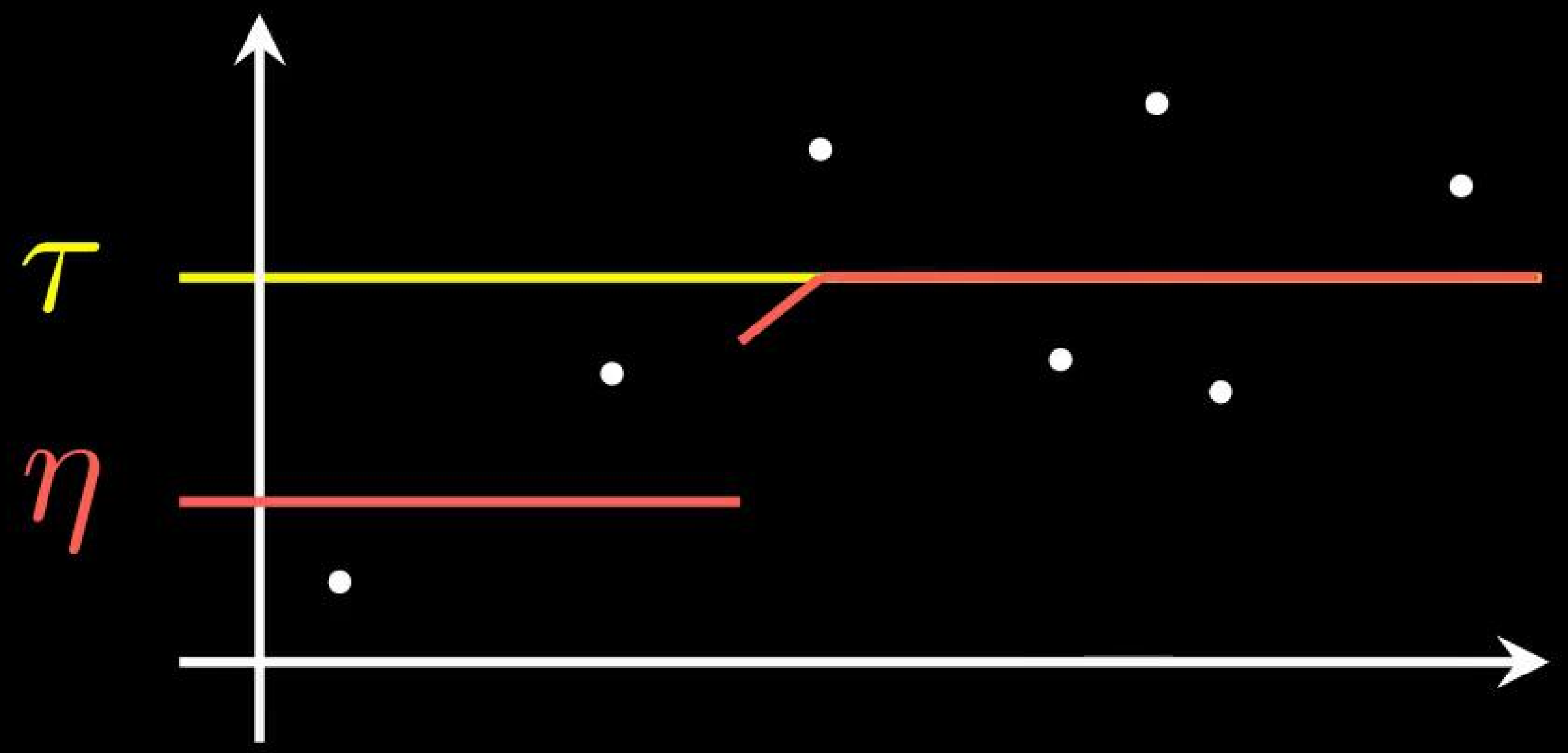

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$$\sup_{P \in \mathcal{P}_{\mathrm{MonReg},d}(\sigma,\tau,\gamma,\lambda,\theta)} R_\tau(\hat{A}^{\mathrm{ISS}}) \leq 1 \wedge C \Bigg\{ \bigg(\frac{\sigma^2}{n\lambda^2} \log_+\Big(\frac{n \log_+ n}{\alpha} \Big) \bigg)^{1/(2\gamma+d)} + \bigg(\frac{\log_+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

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

Heterogeneous treatment effects

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

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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 $t \in (0, 1)$.

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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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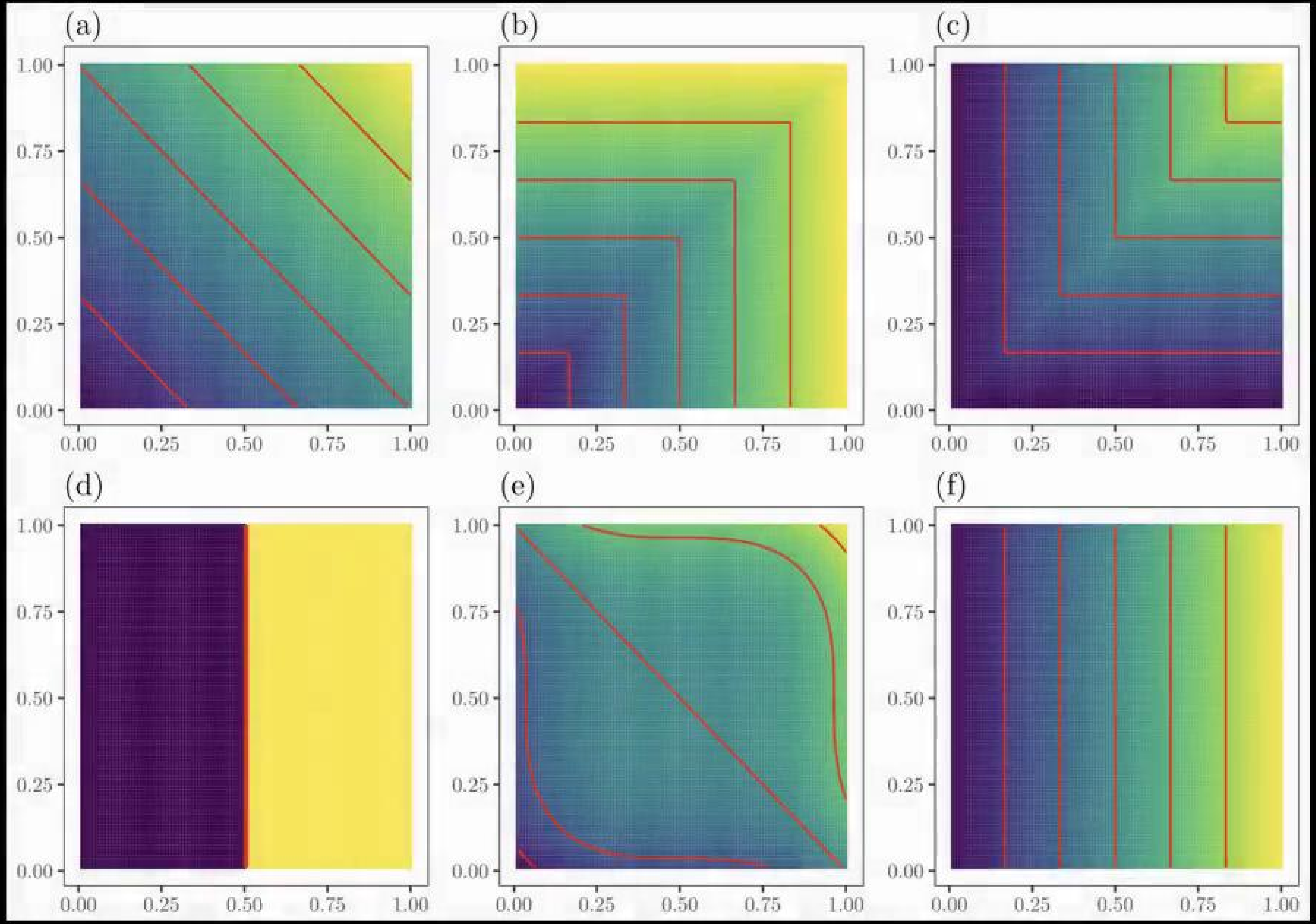

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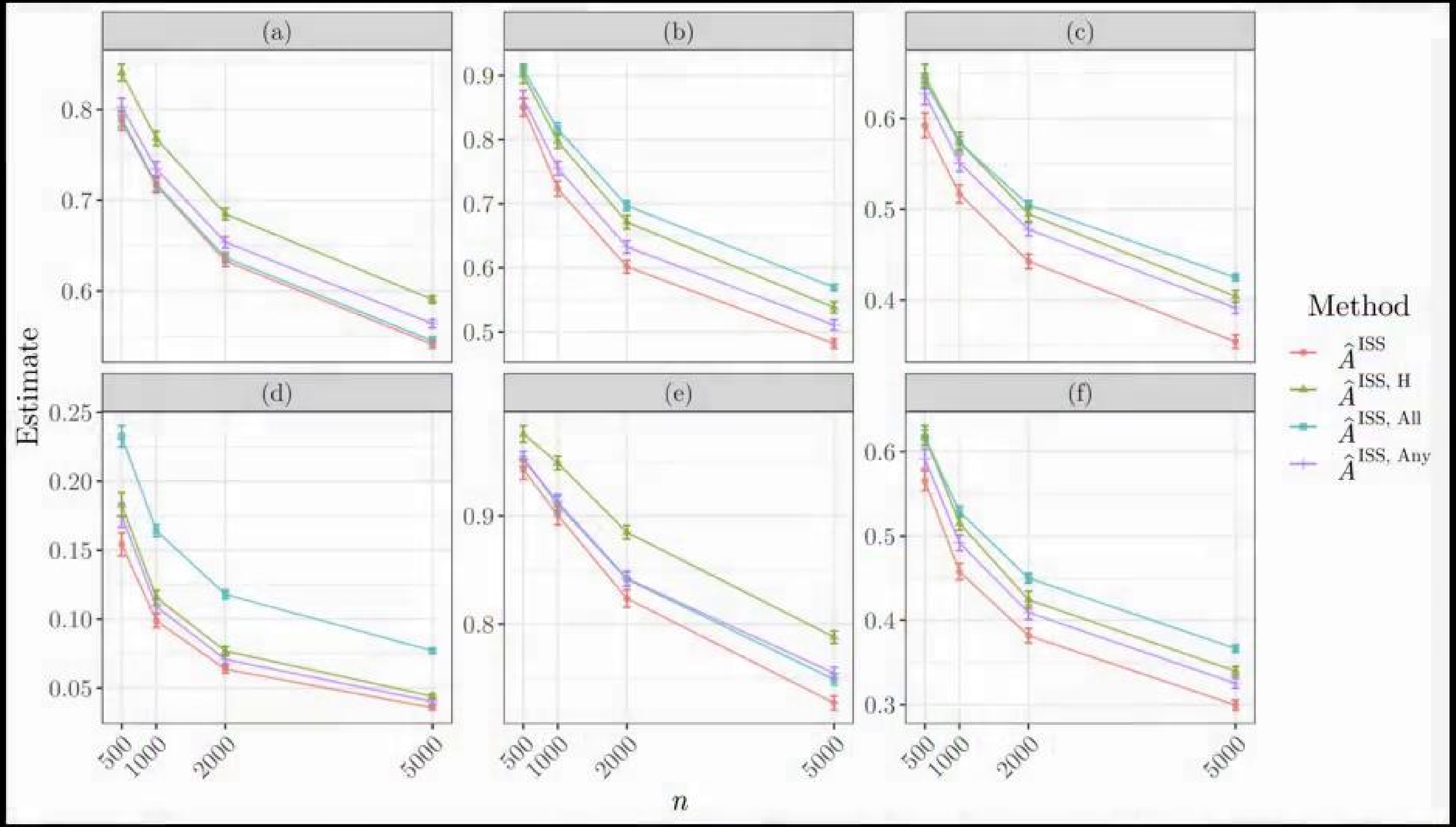
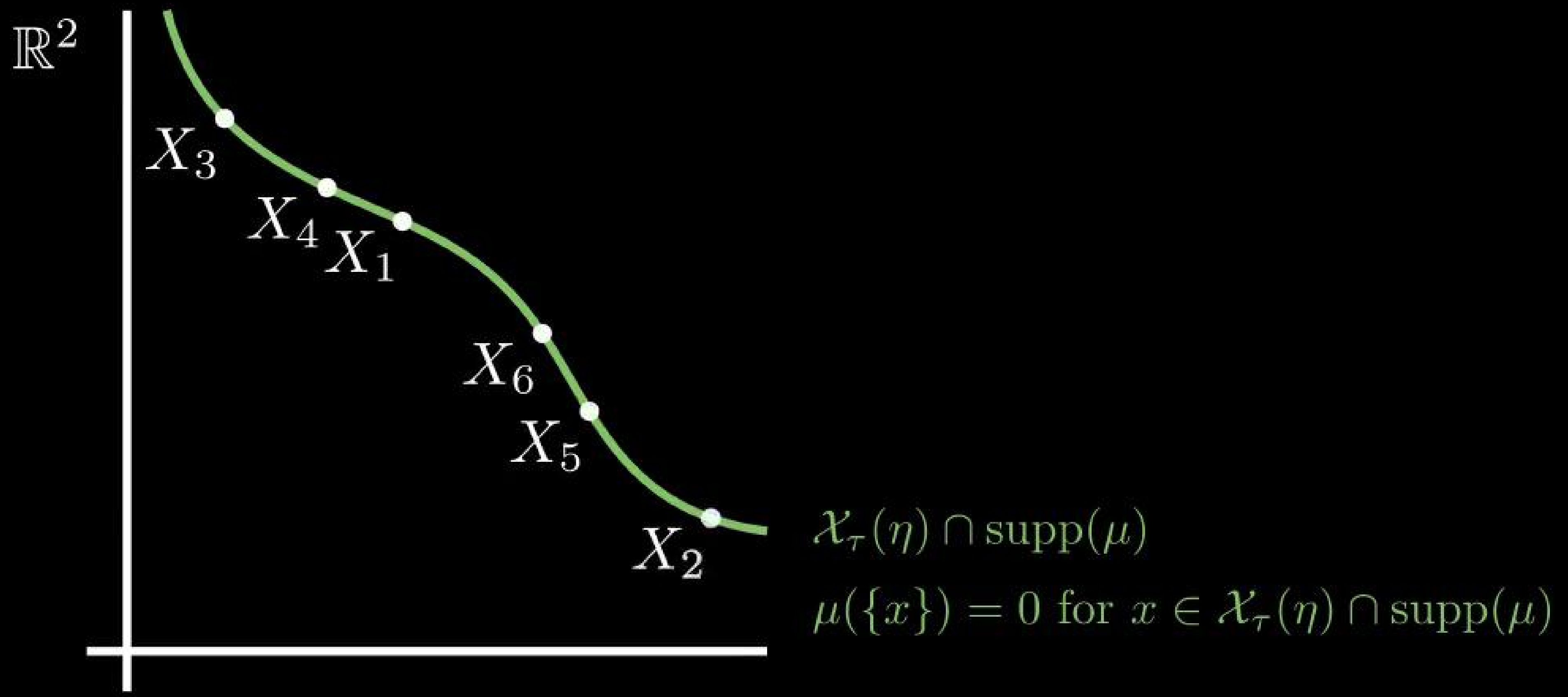


Here, $d = 2$, $\sigma = 1/4$.
See also Meijer and Goeman (2015).

Density condition



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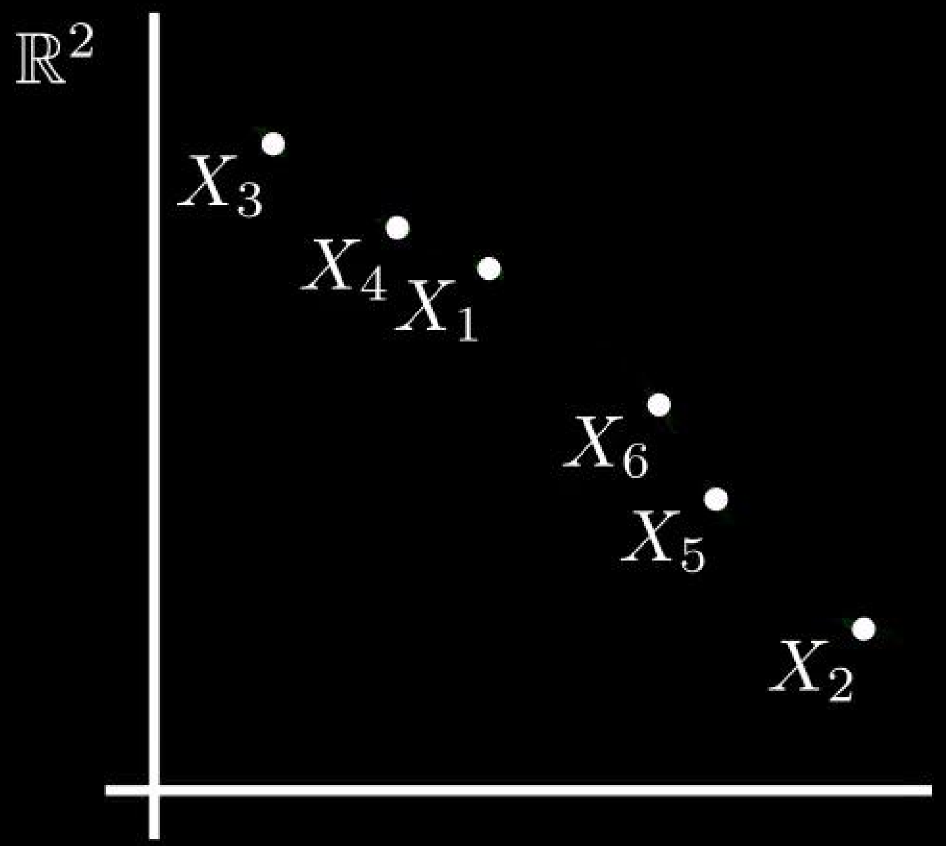

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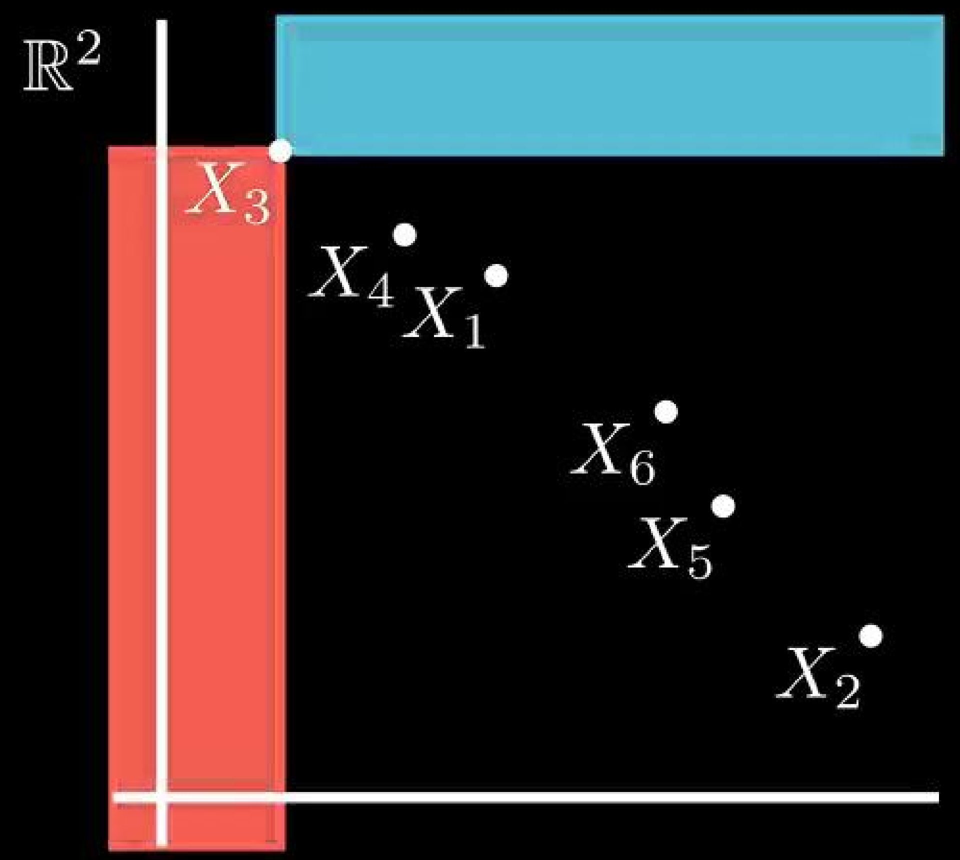

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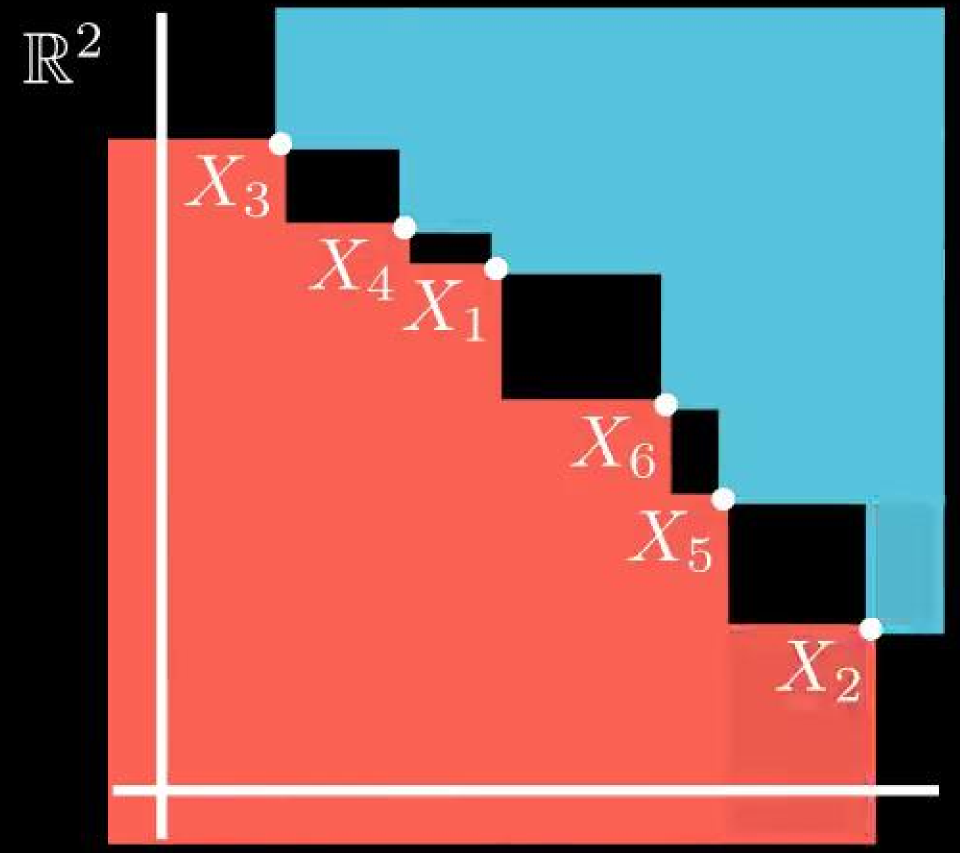

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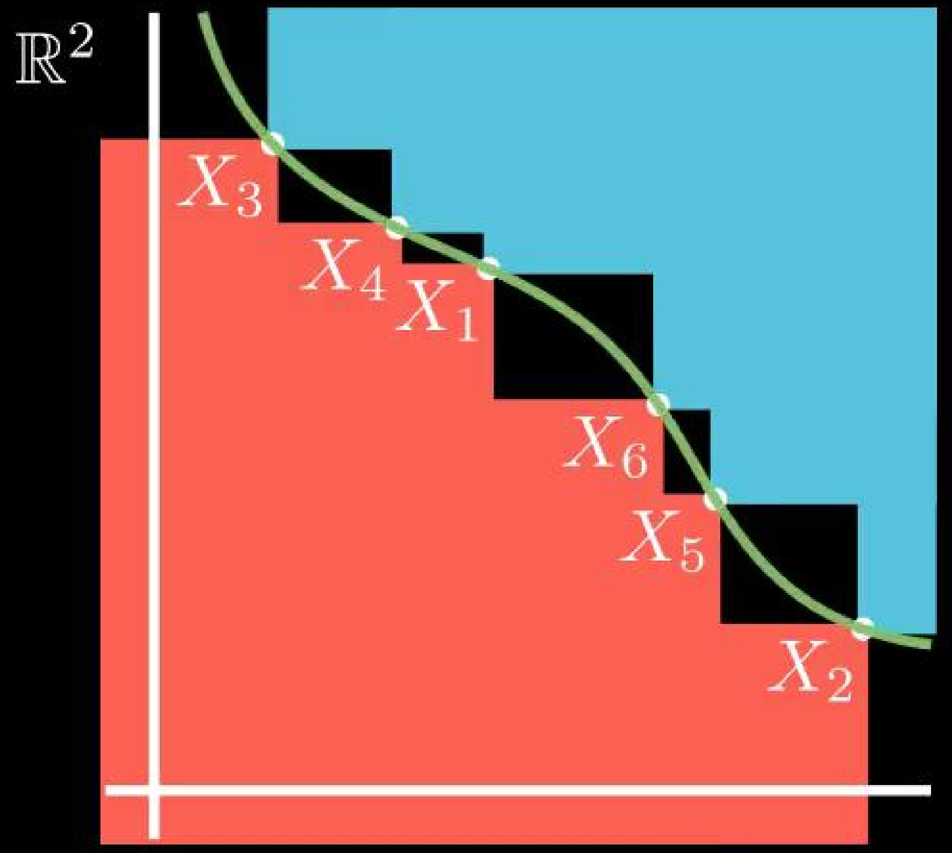

$\mathcal{X}_\tau(\eta) \cap \mathrm{supp}(\mu)$

$\mu(\{x\}) = 0$ for $x \in \mathcal{X}_\tau(\eta) \cap \mathrm{supp}(\mu)$

Proof of the upper bound (for $m \in [n]$)

Theorem. There exists $C \geq 1$, depending only on (d, θ), such that for any $P \in \mathcal{P}_{\mathrm{MonReg},d}(\sigma, \tau, \gamma, \lambda, \theta)$, $\alpha \in (0,1)$ and $m \in [n]$,

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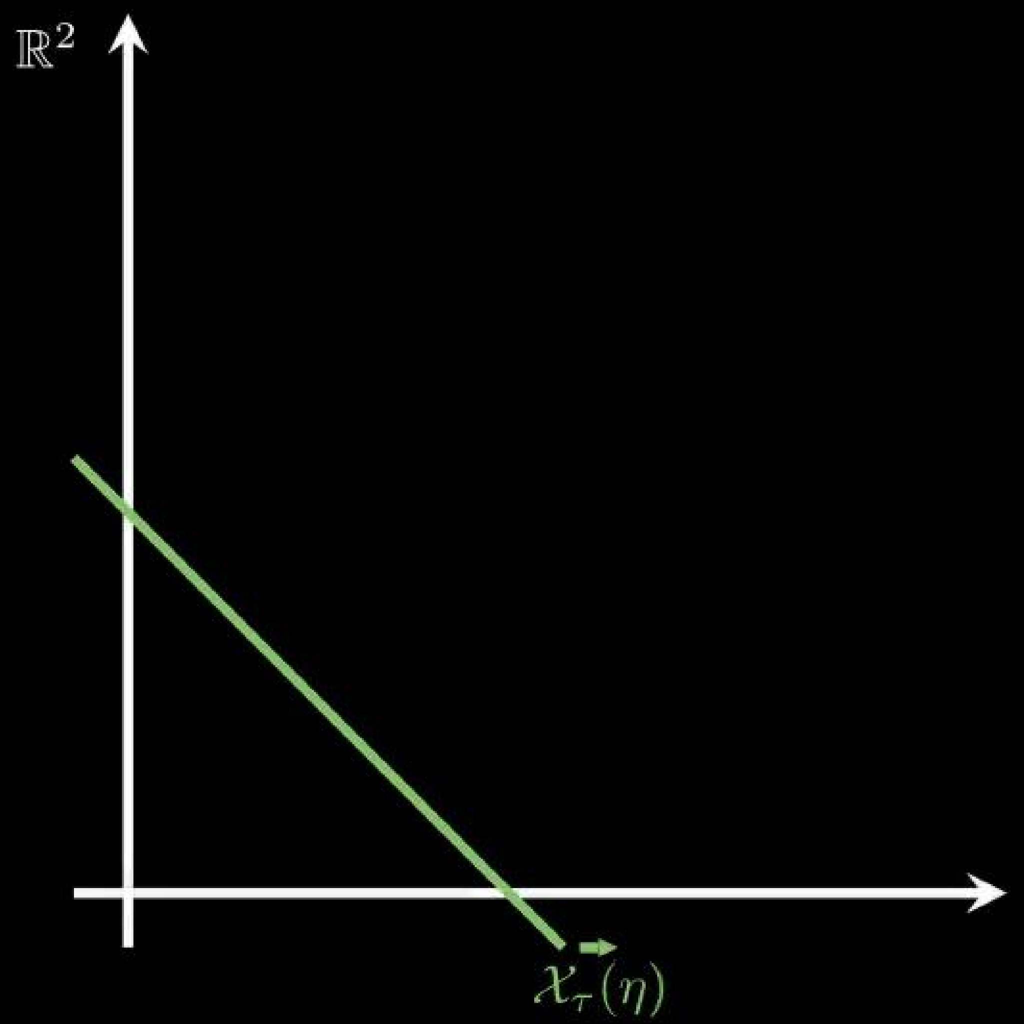

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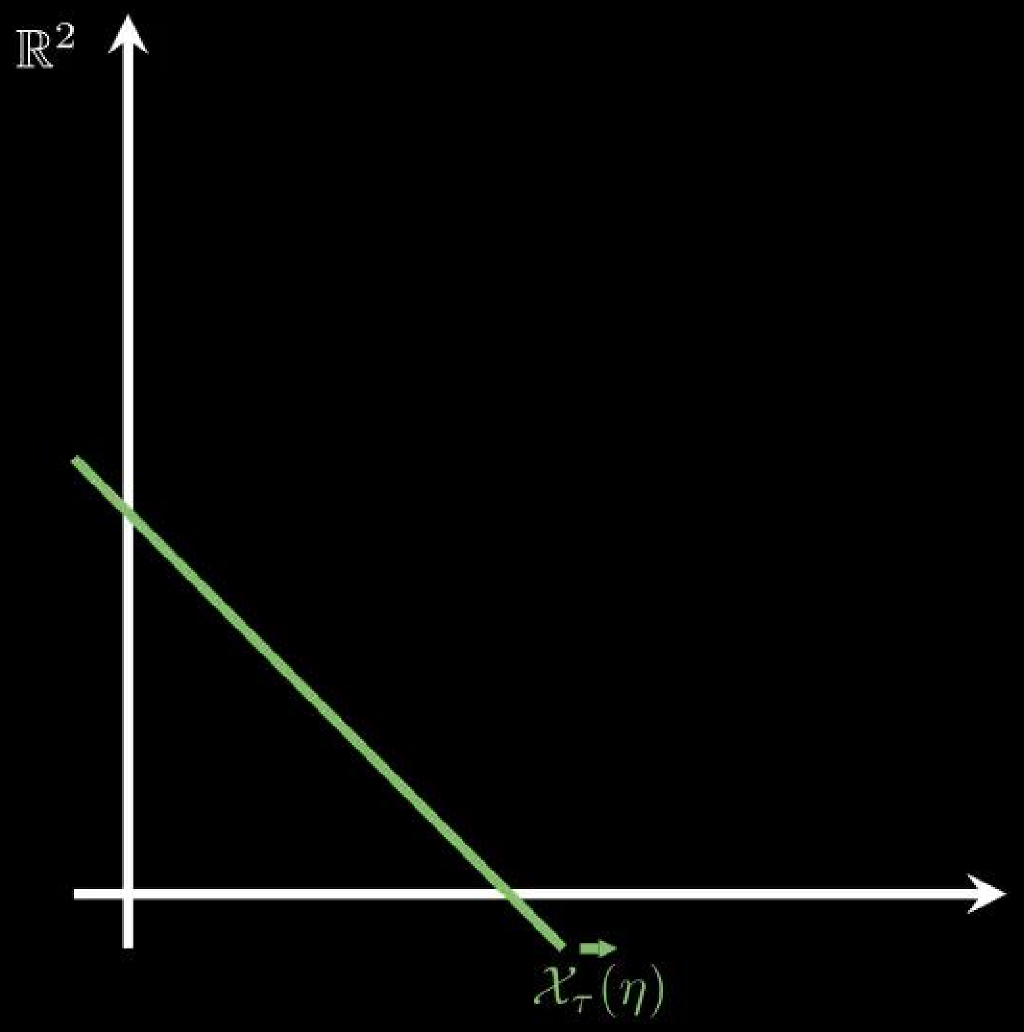

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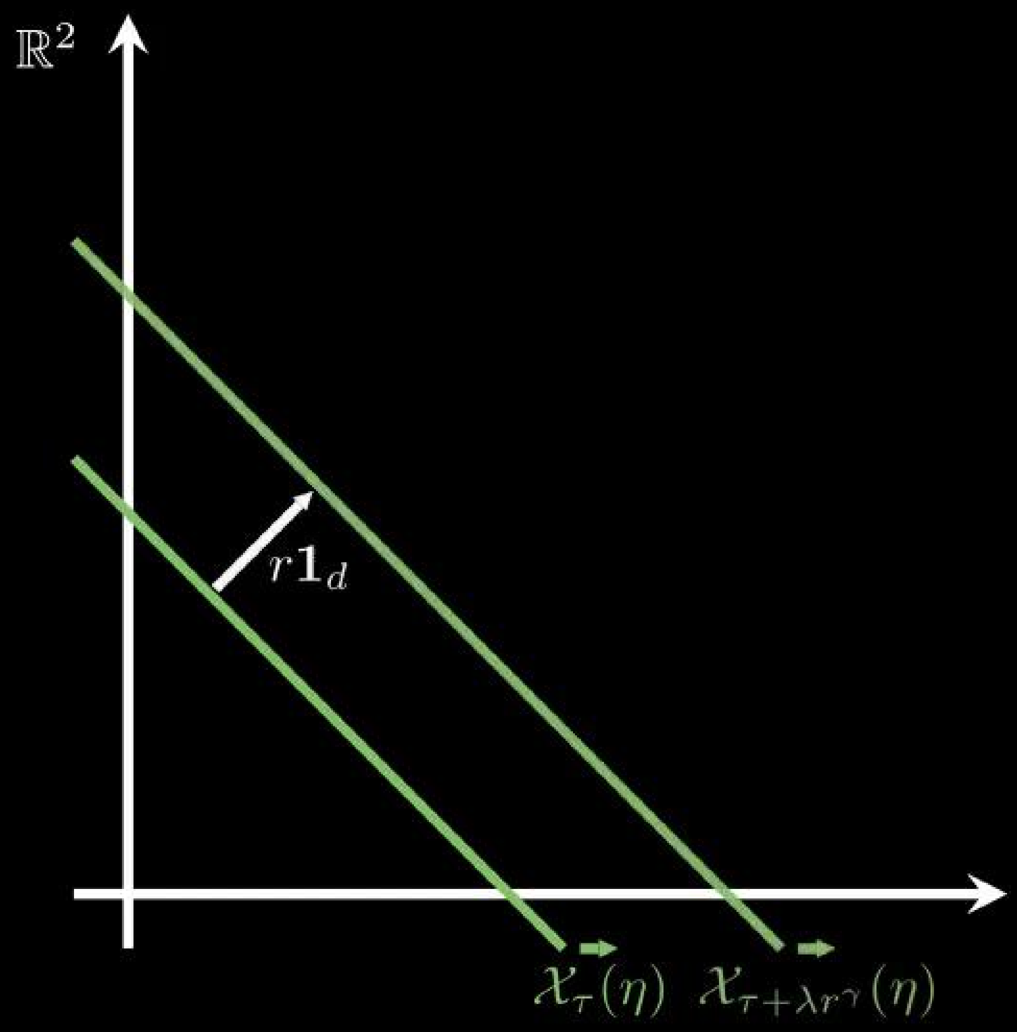

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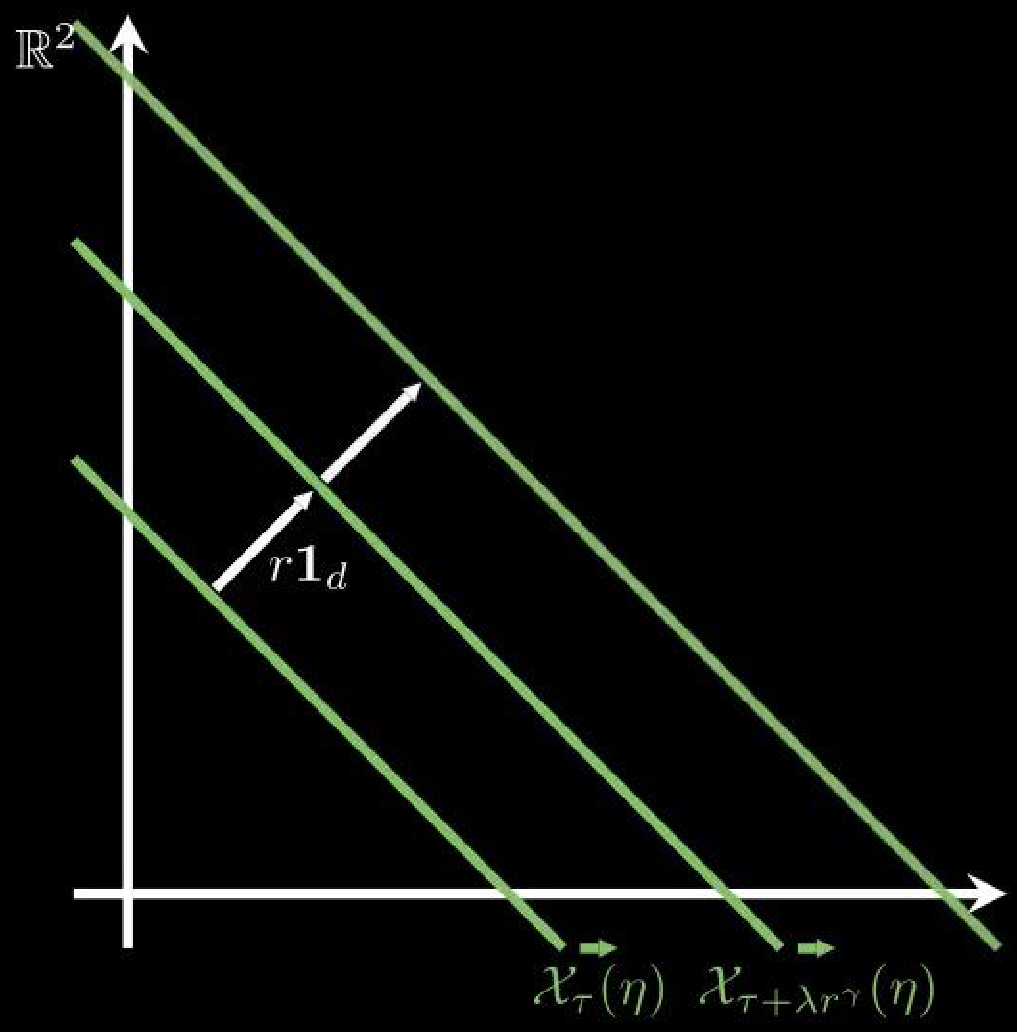

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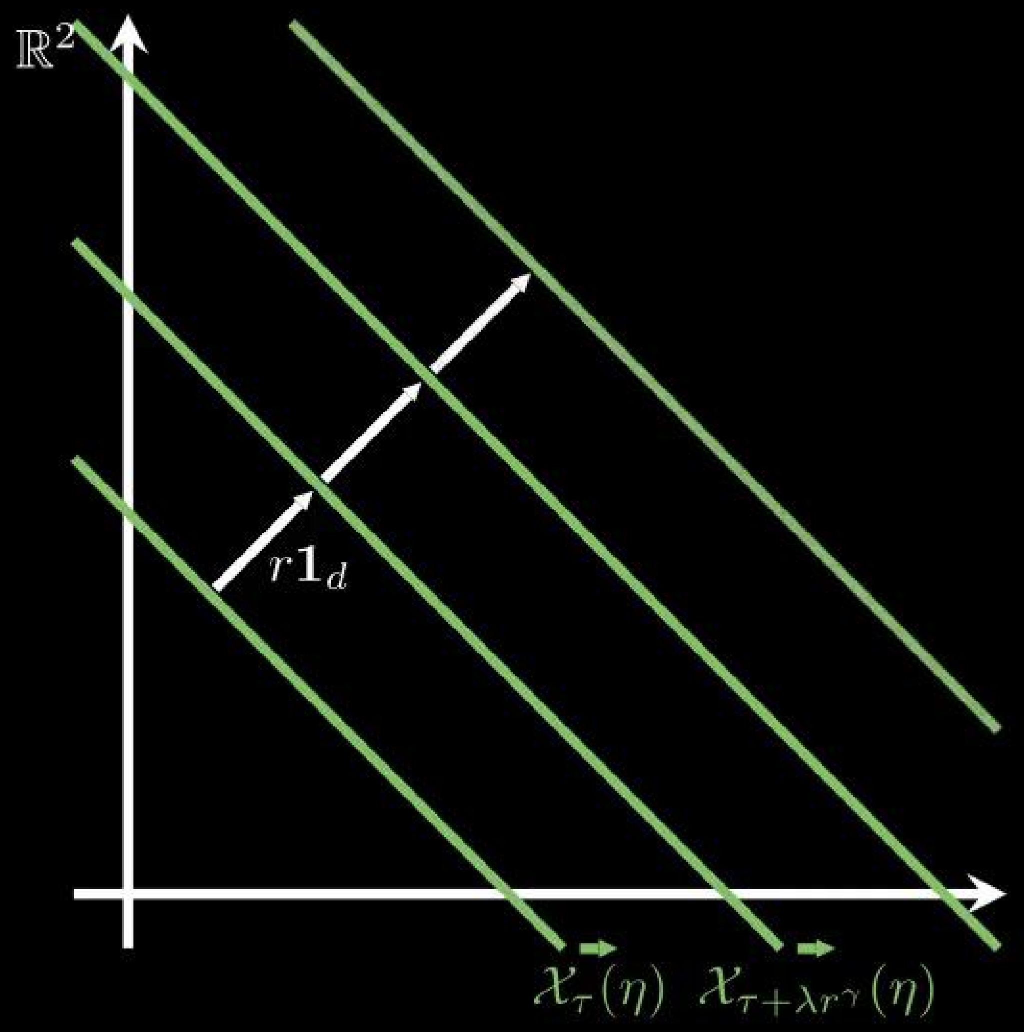

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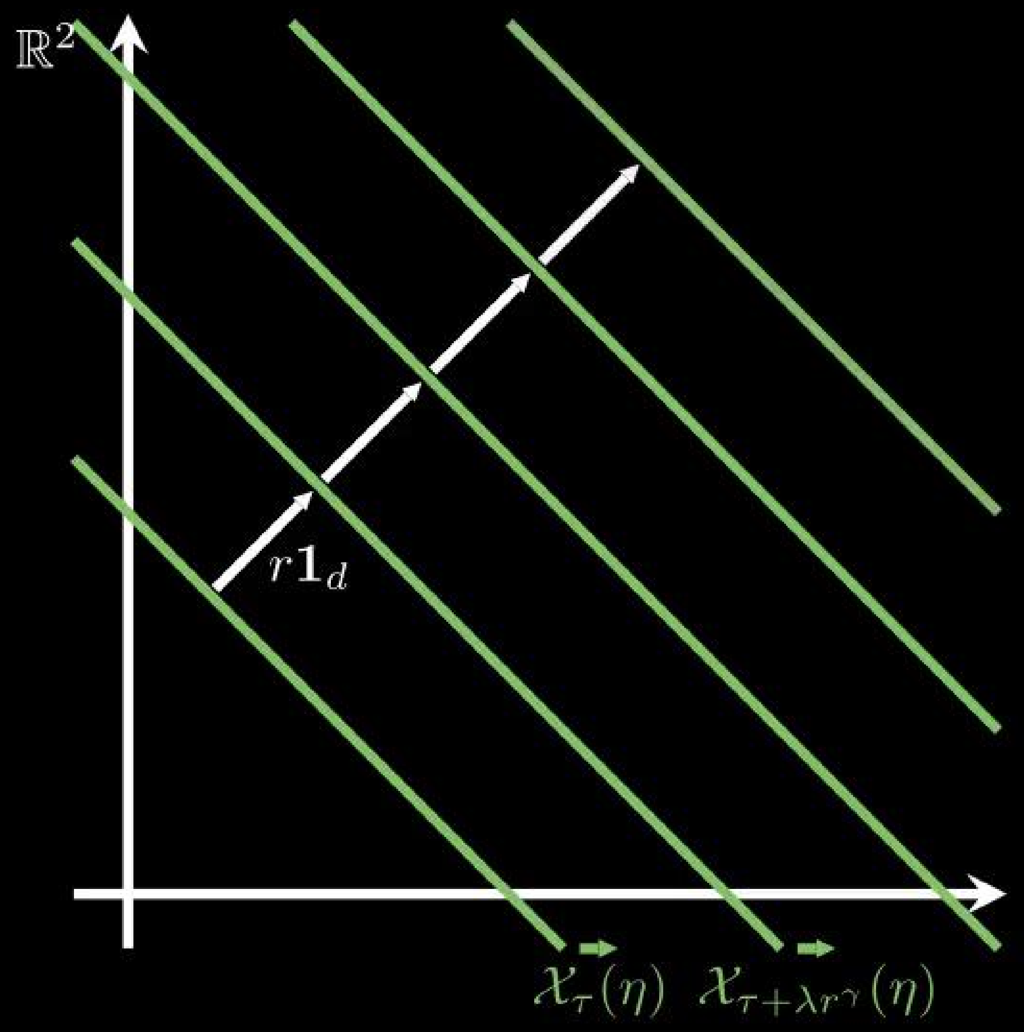

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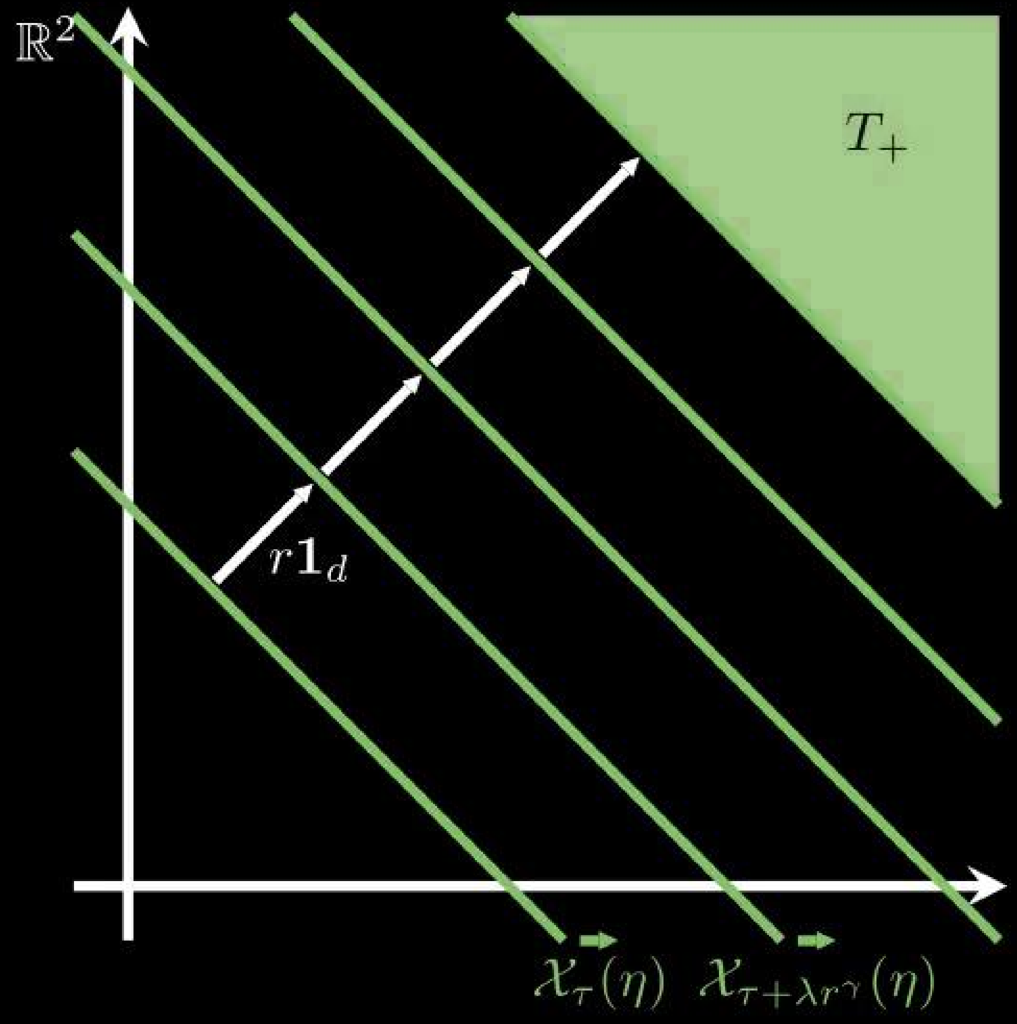

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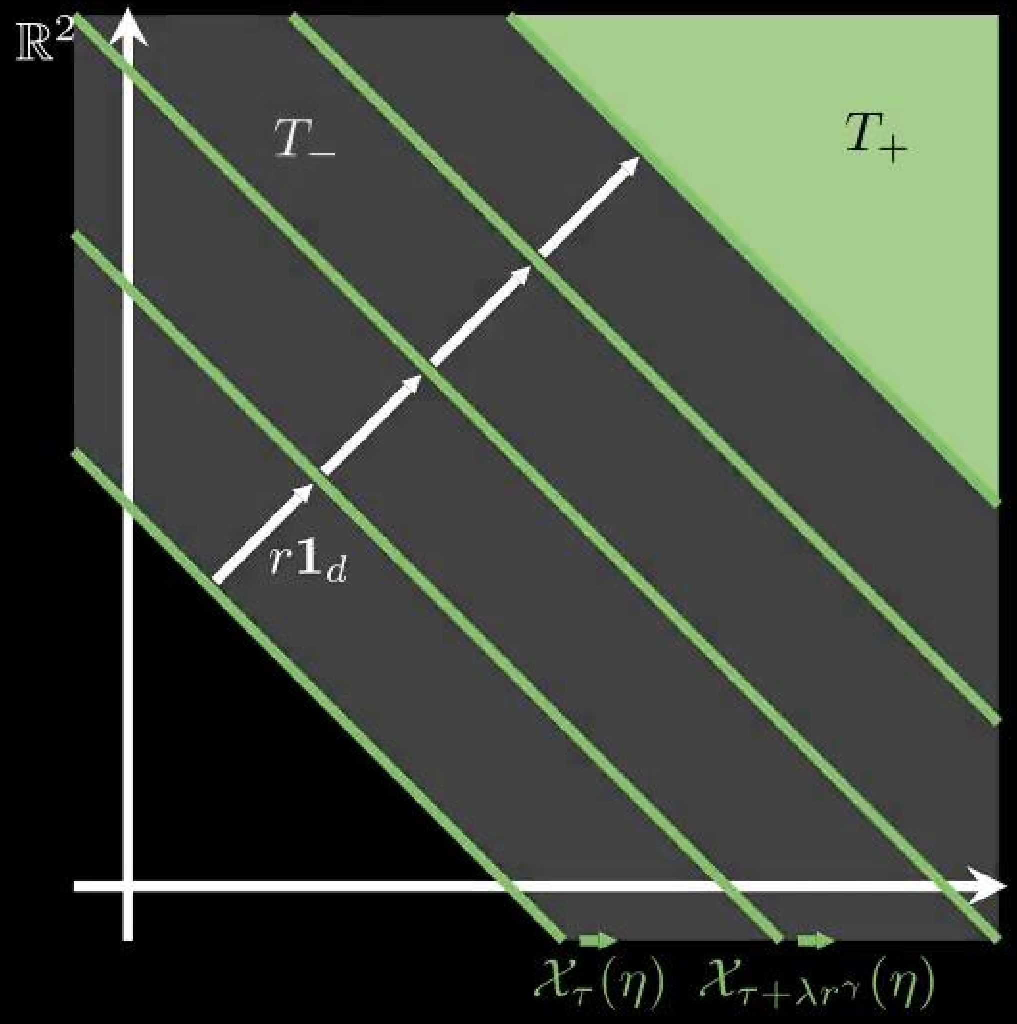

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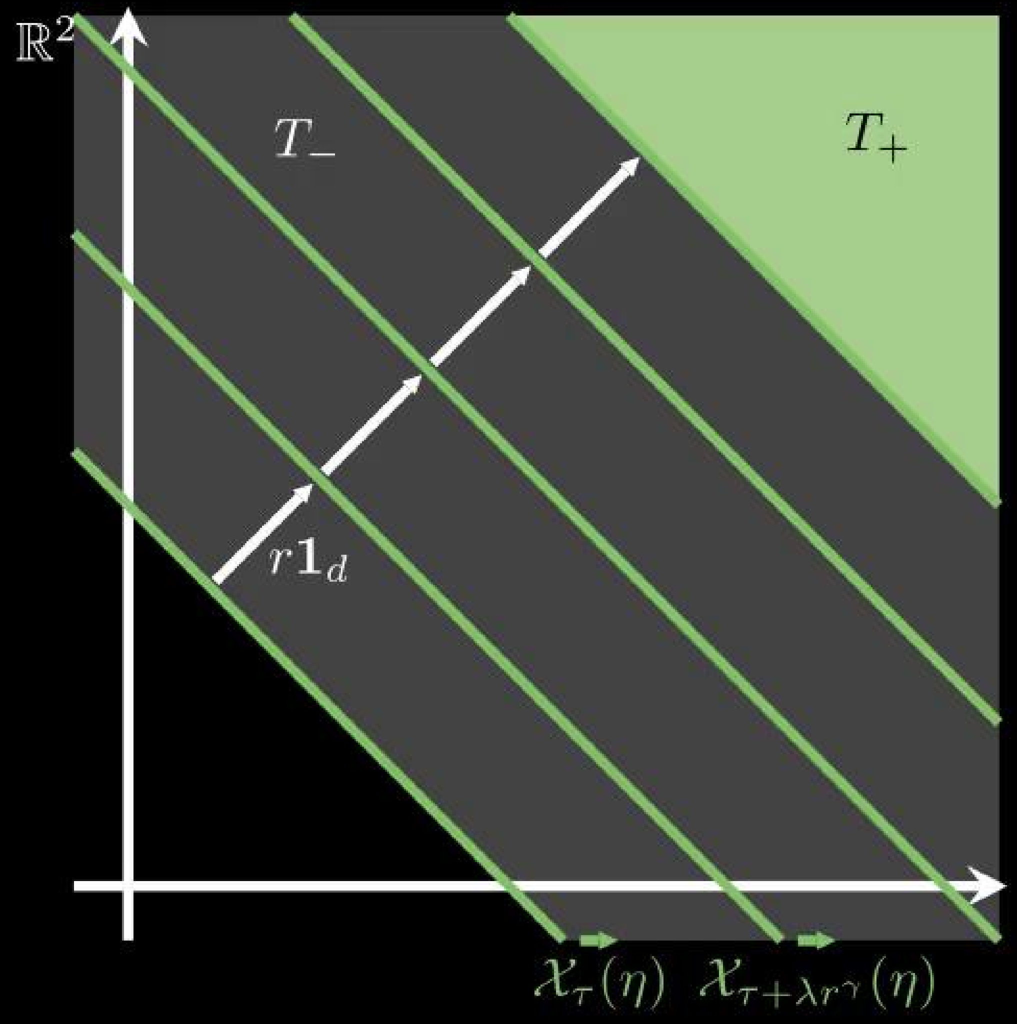

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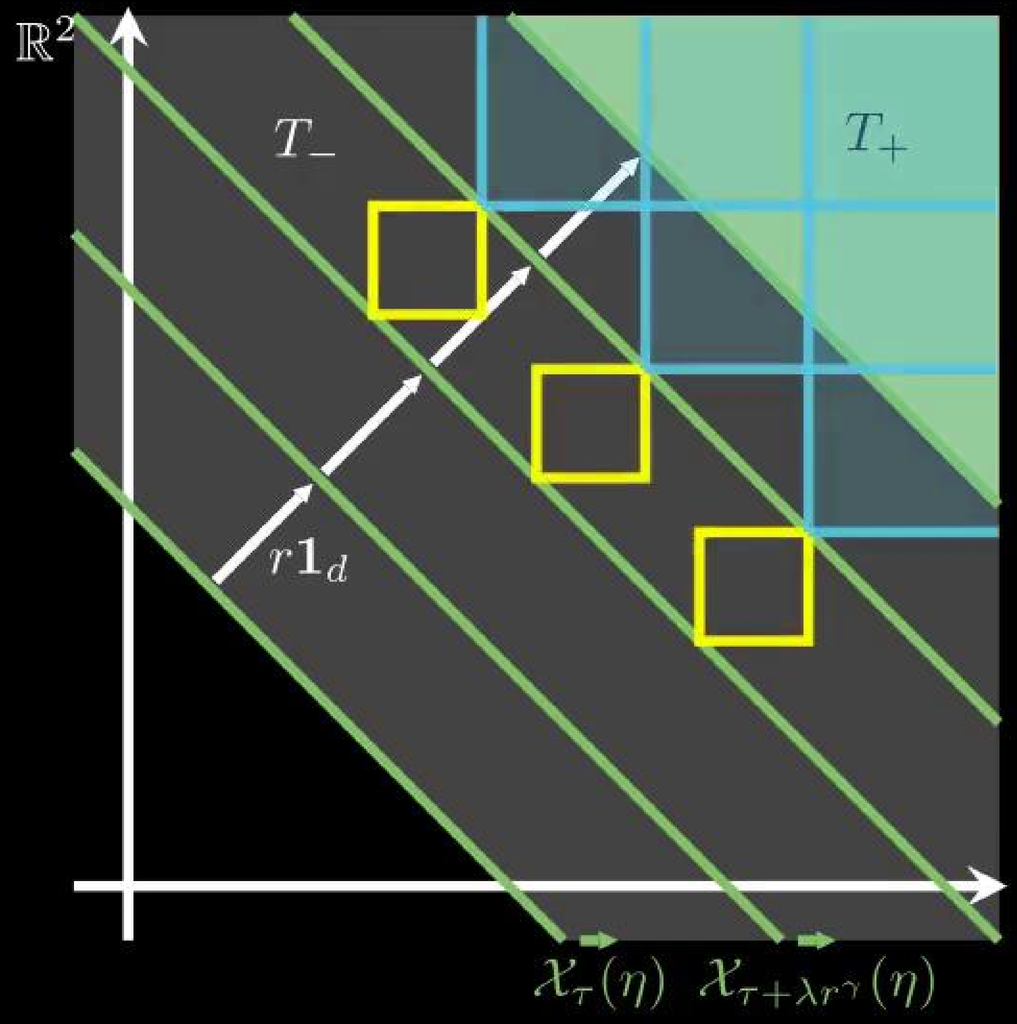

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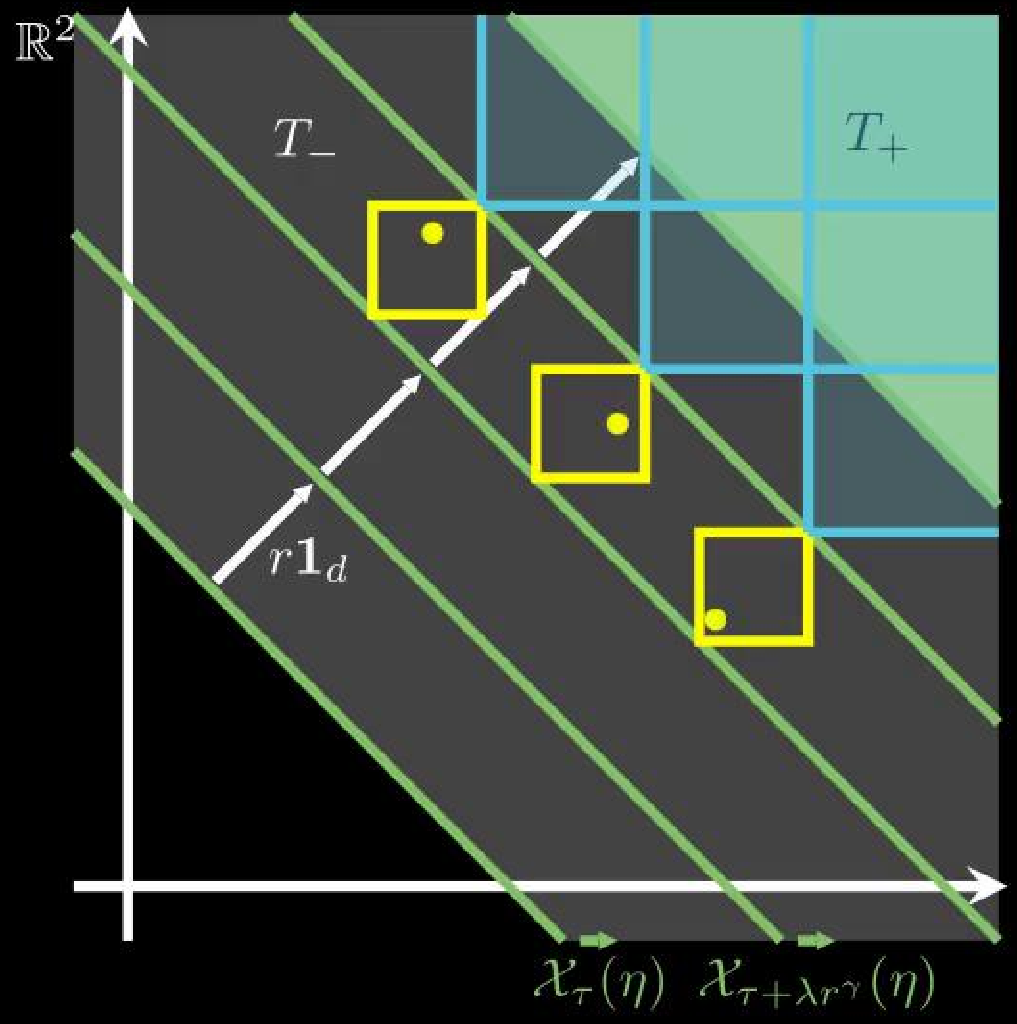

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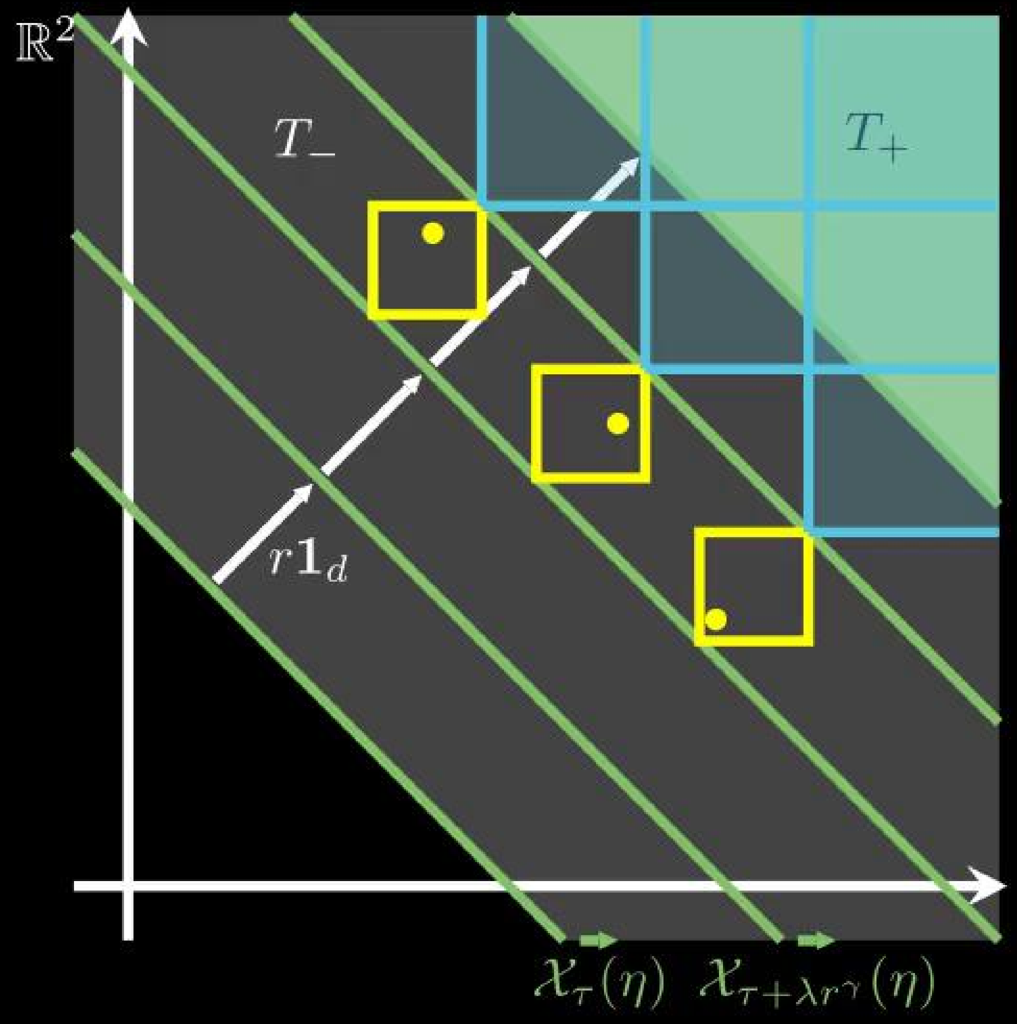

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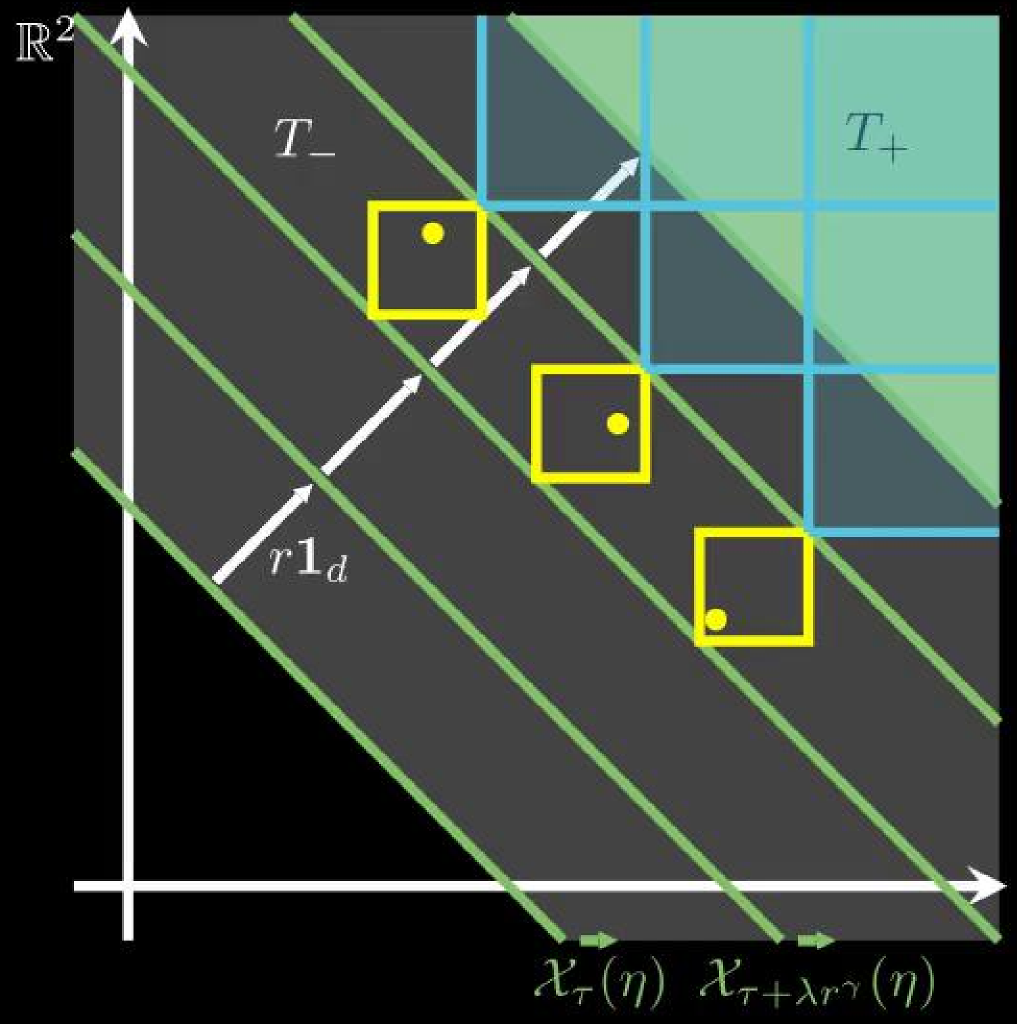

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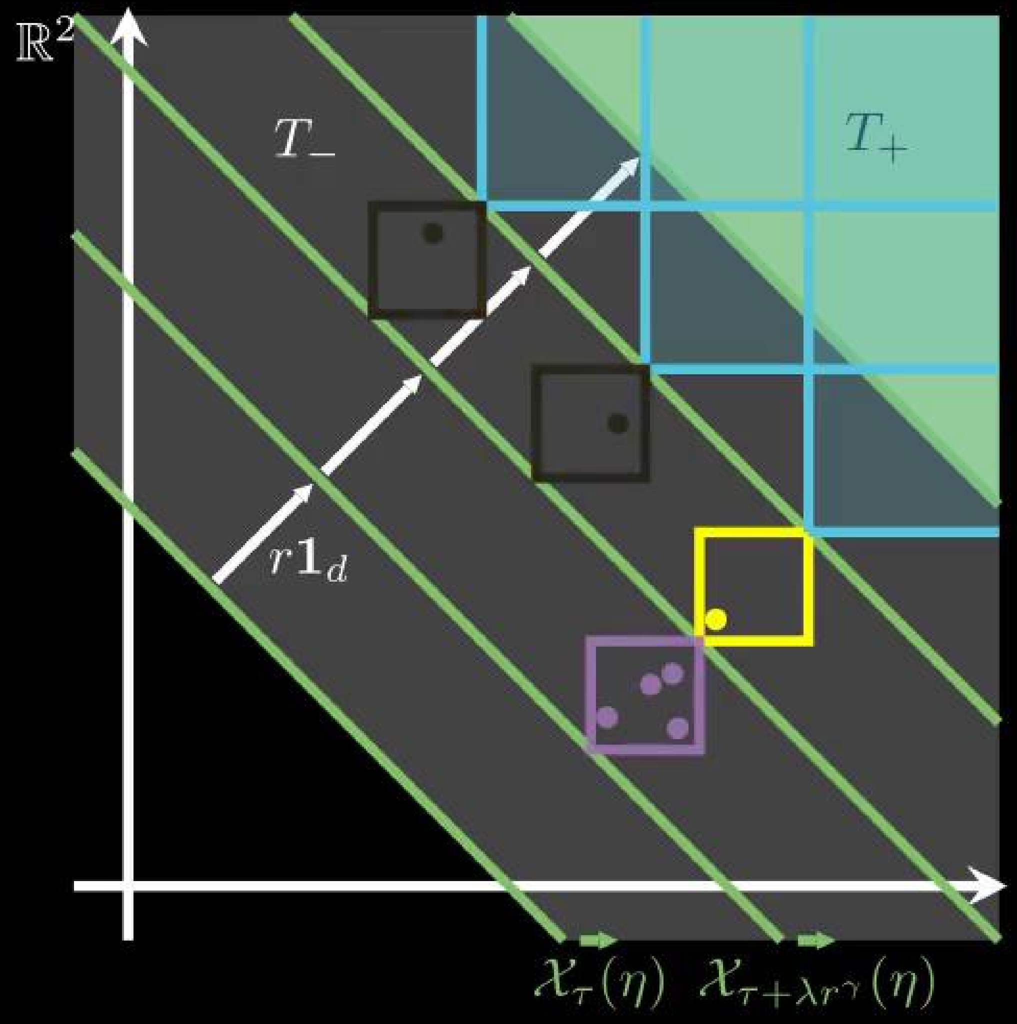

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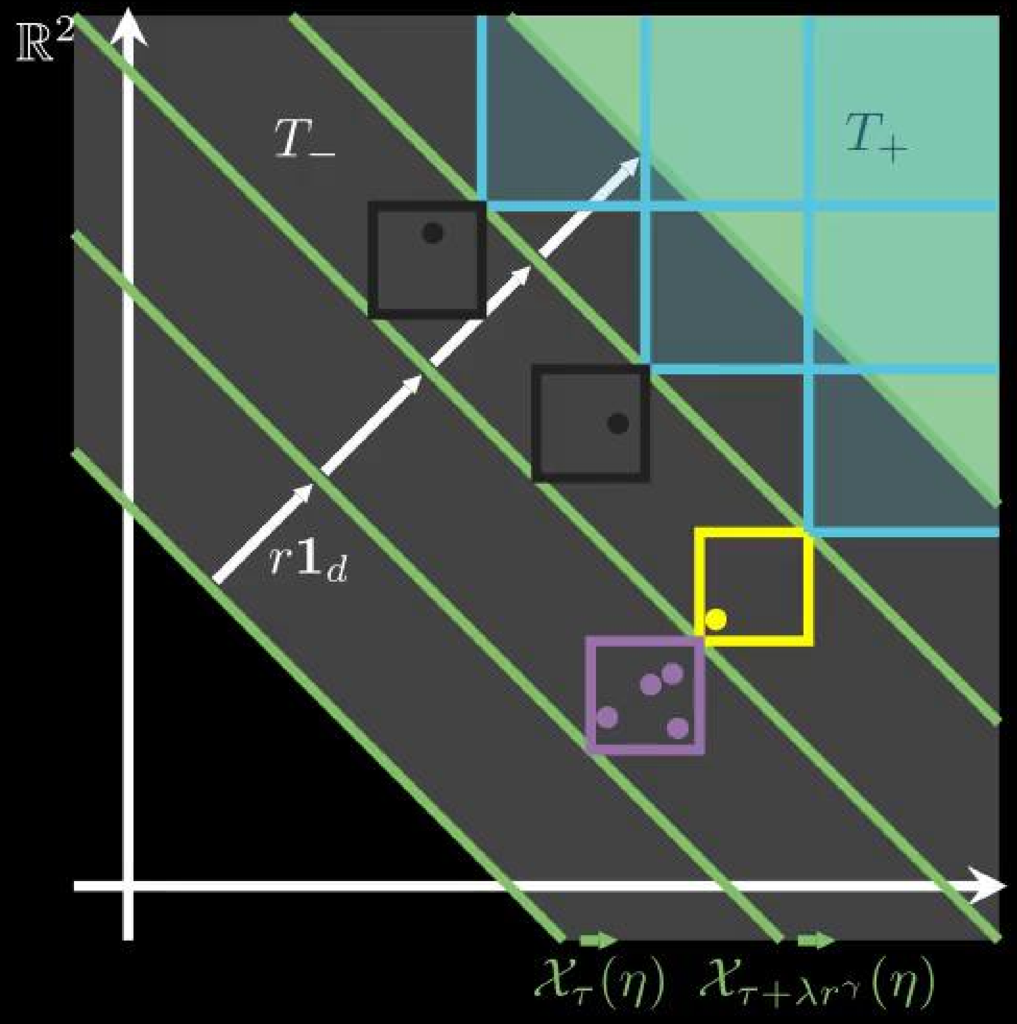

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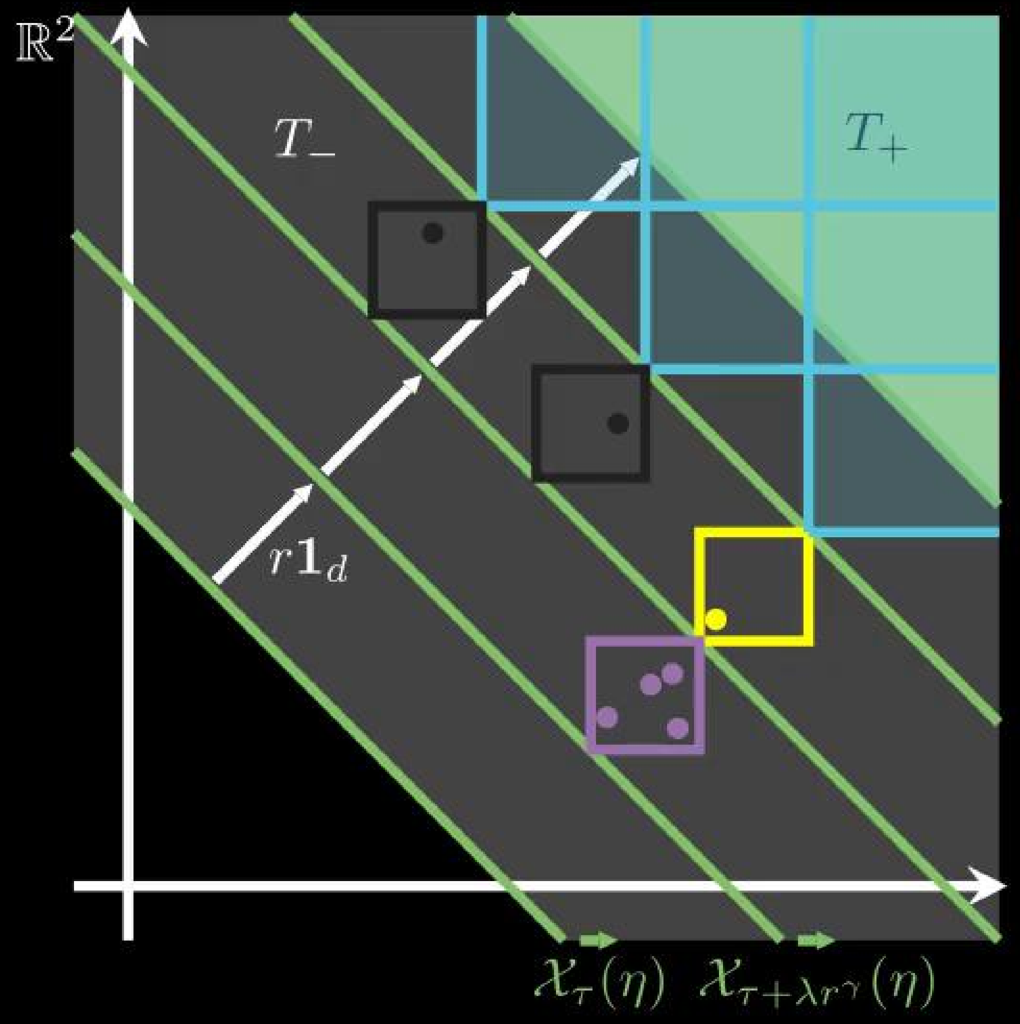

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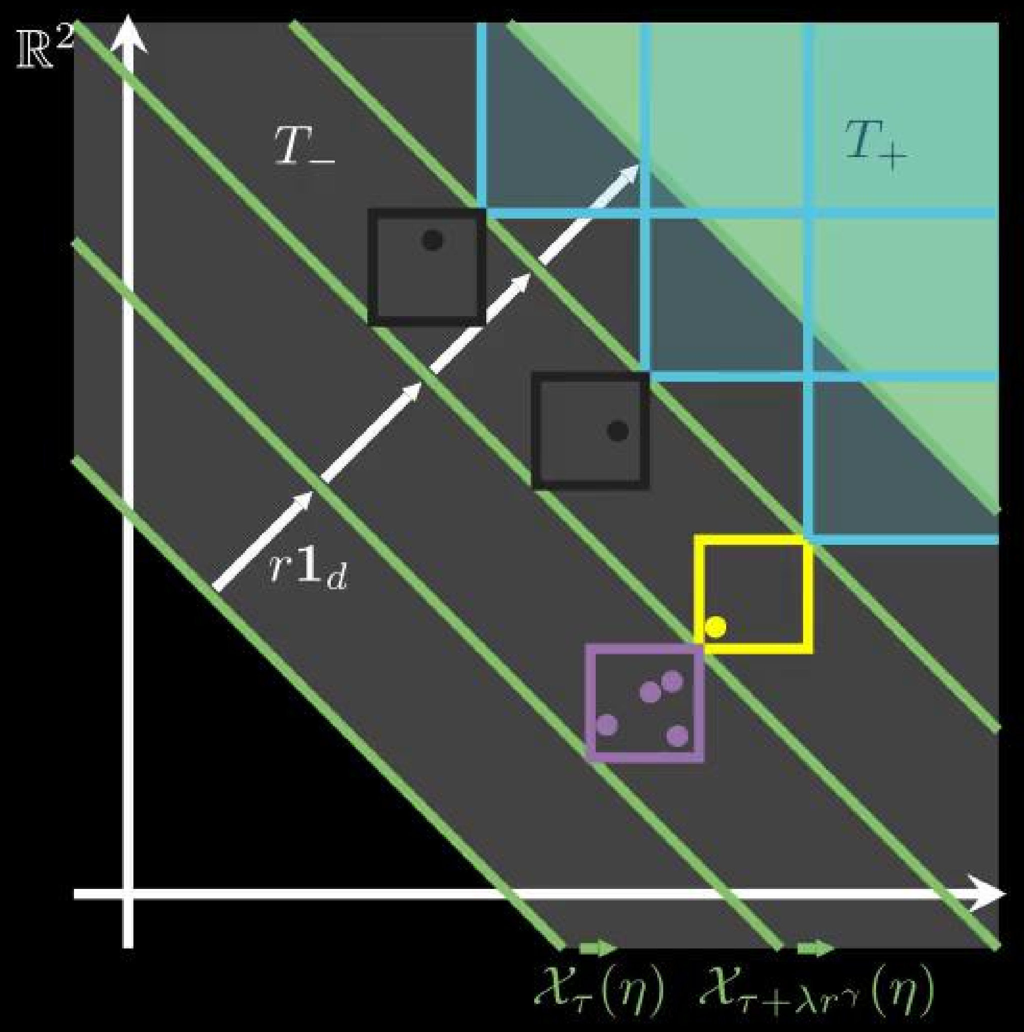

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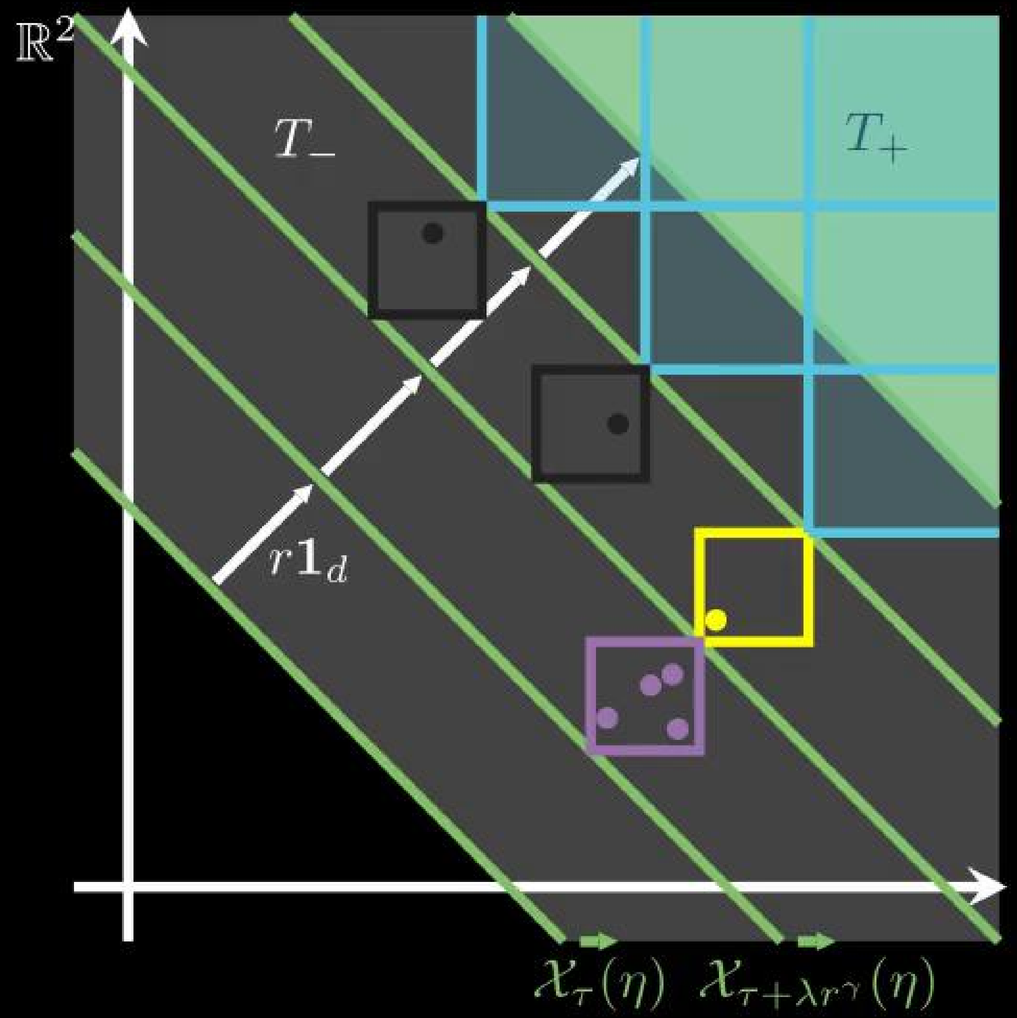

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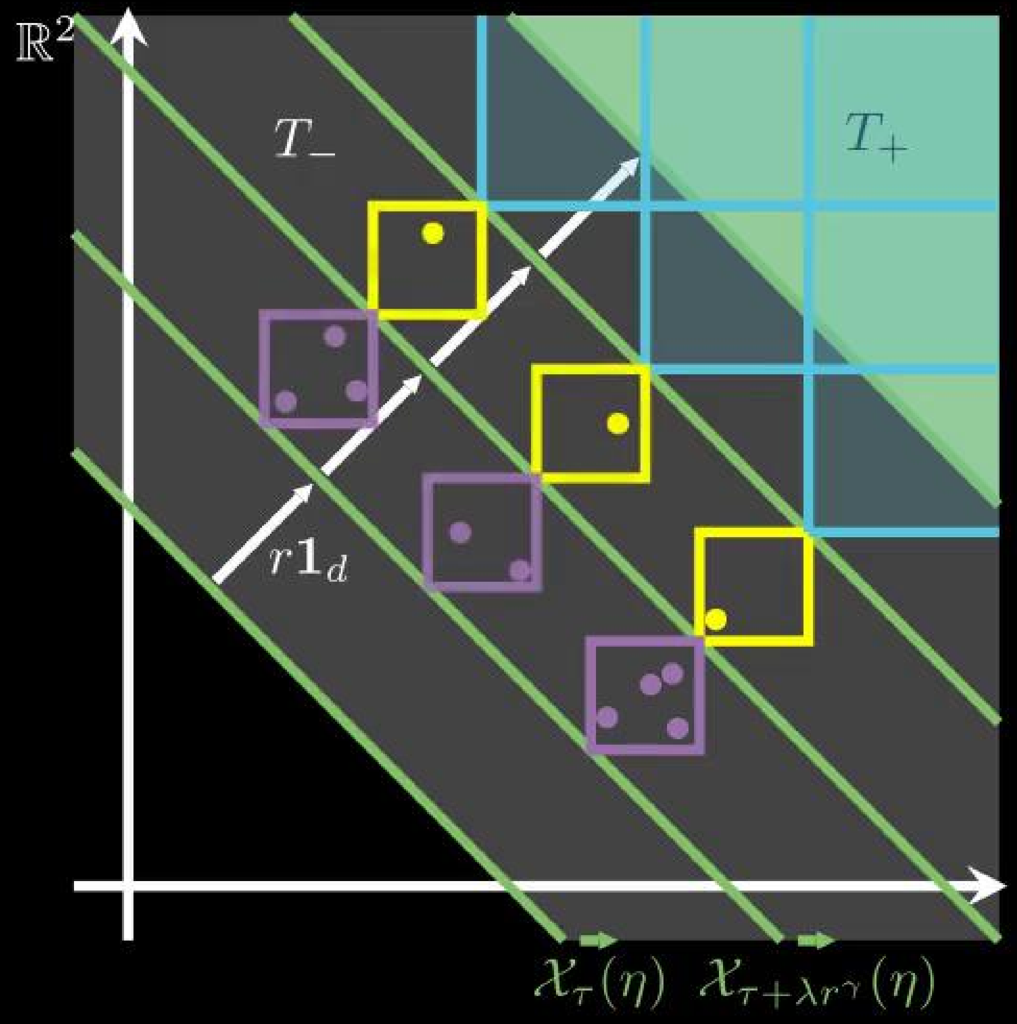

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