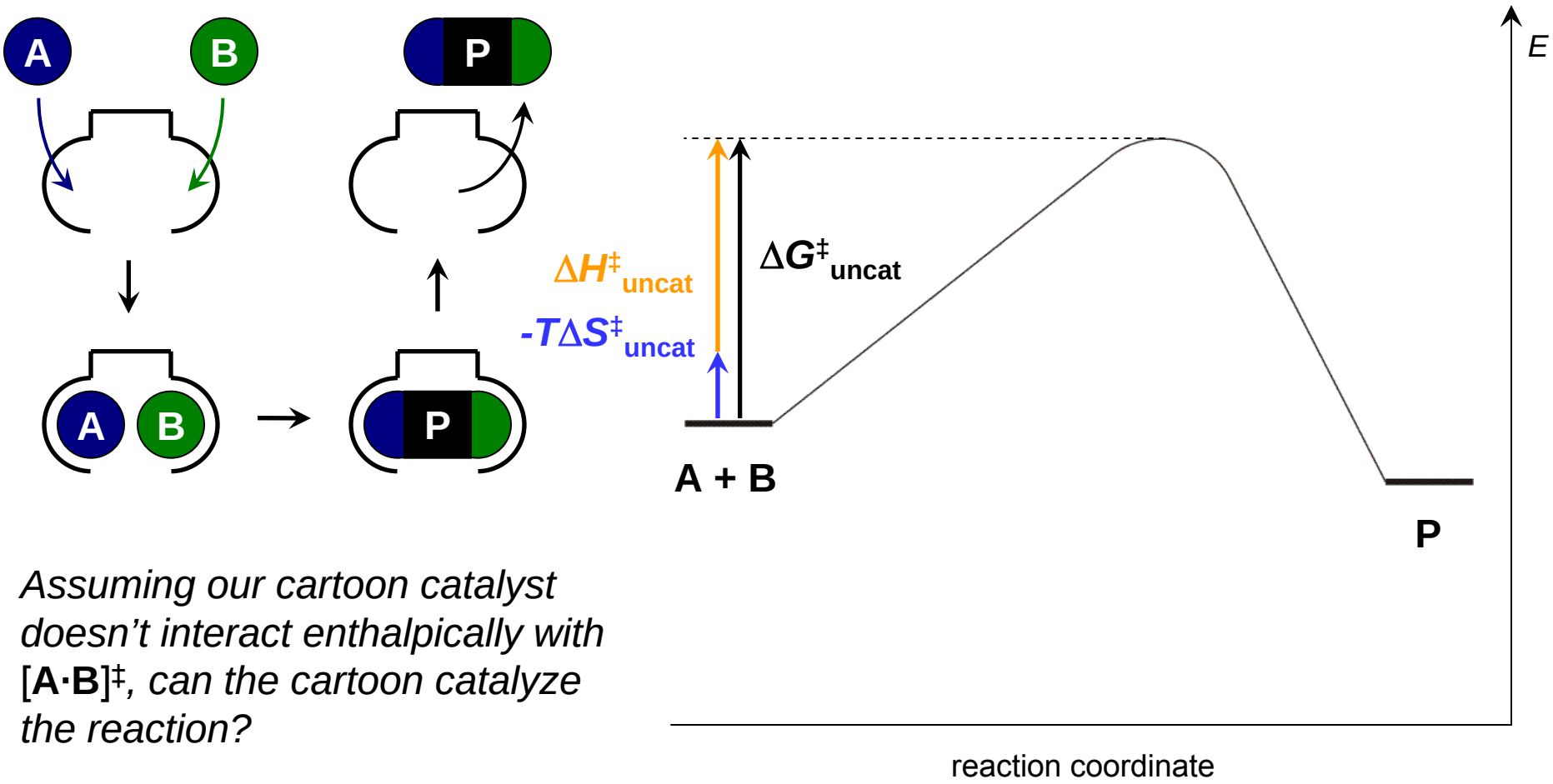
Entropic Catalysis: Bringing Reactants Together

Can catalysts function by improving only $\Delta S^{\ddagger}$?



Assuming our cartoon catalyst doesn't interact enthalpically with **[A·B]**‡*, can the cartoon catalyze the reaction?*

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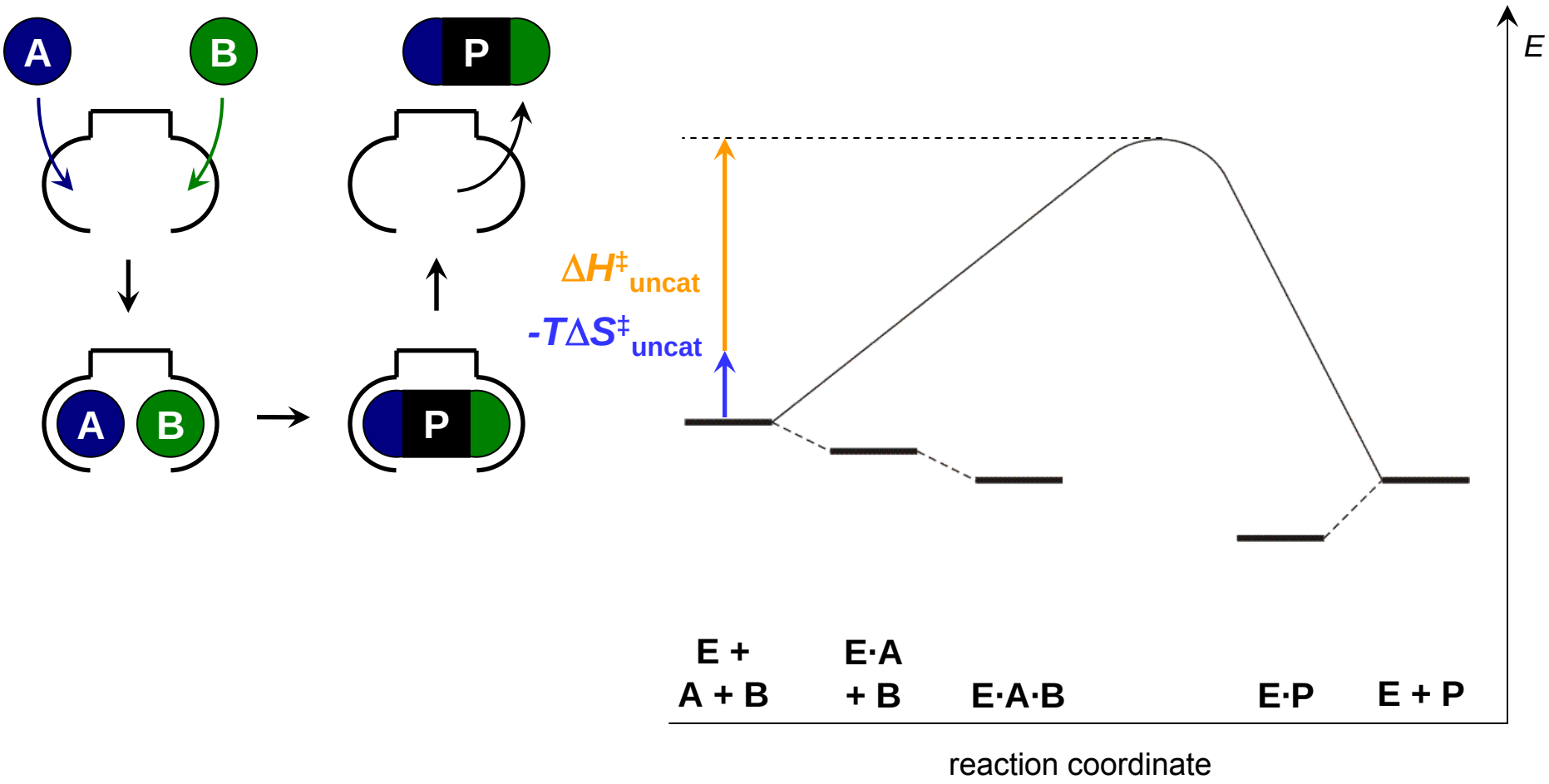

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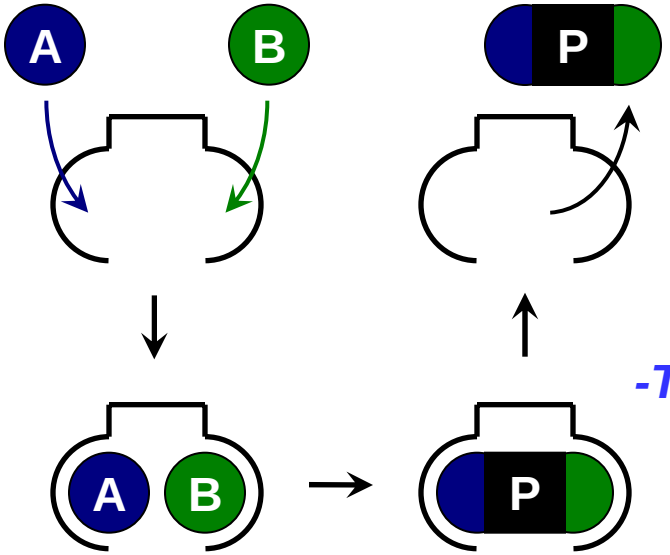
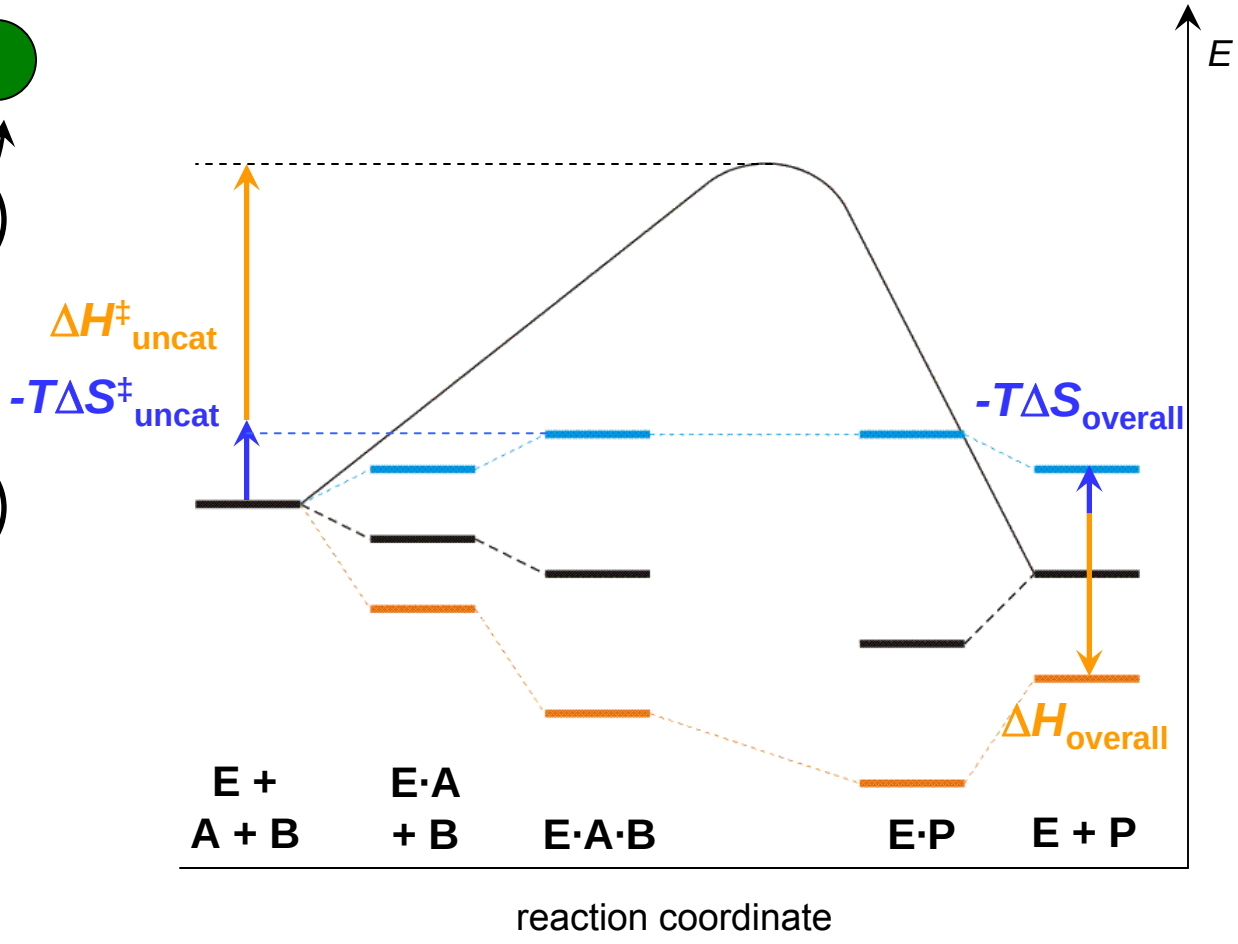


At **E·A·B**, enzyme has countered
all of negative entropy
with negative enthalpy.



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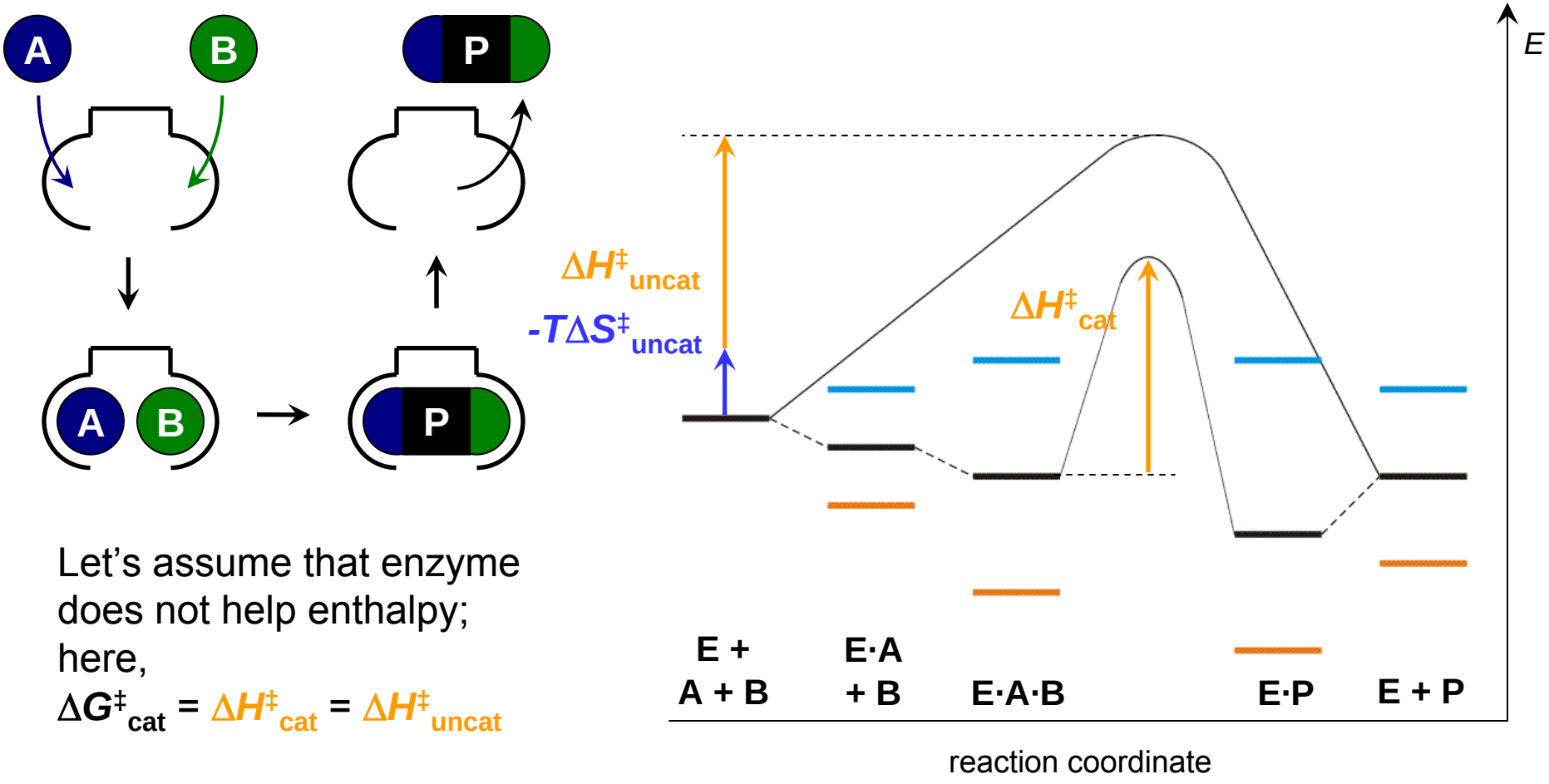

Let's assume that enzyme does not help enthalpy; here,

$\Delta G^{\ddagger}_{cat} = \Delta H^{\ddagger}_{cat} = \Delta H^{\ddagger}_{uncat}$

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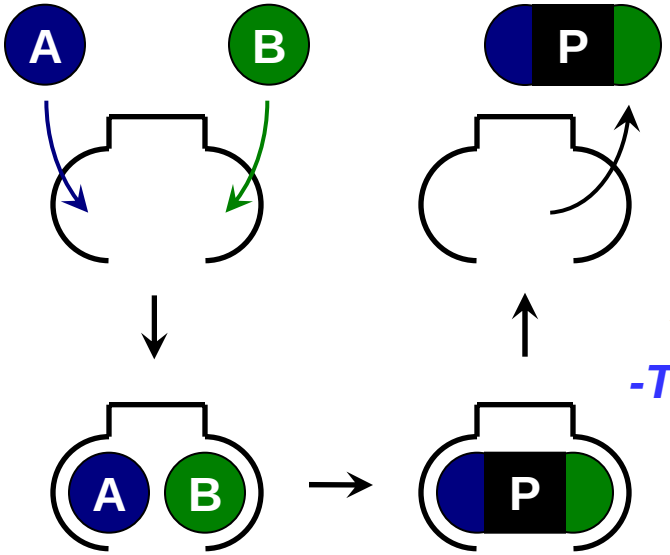
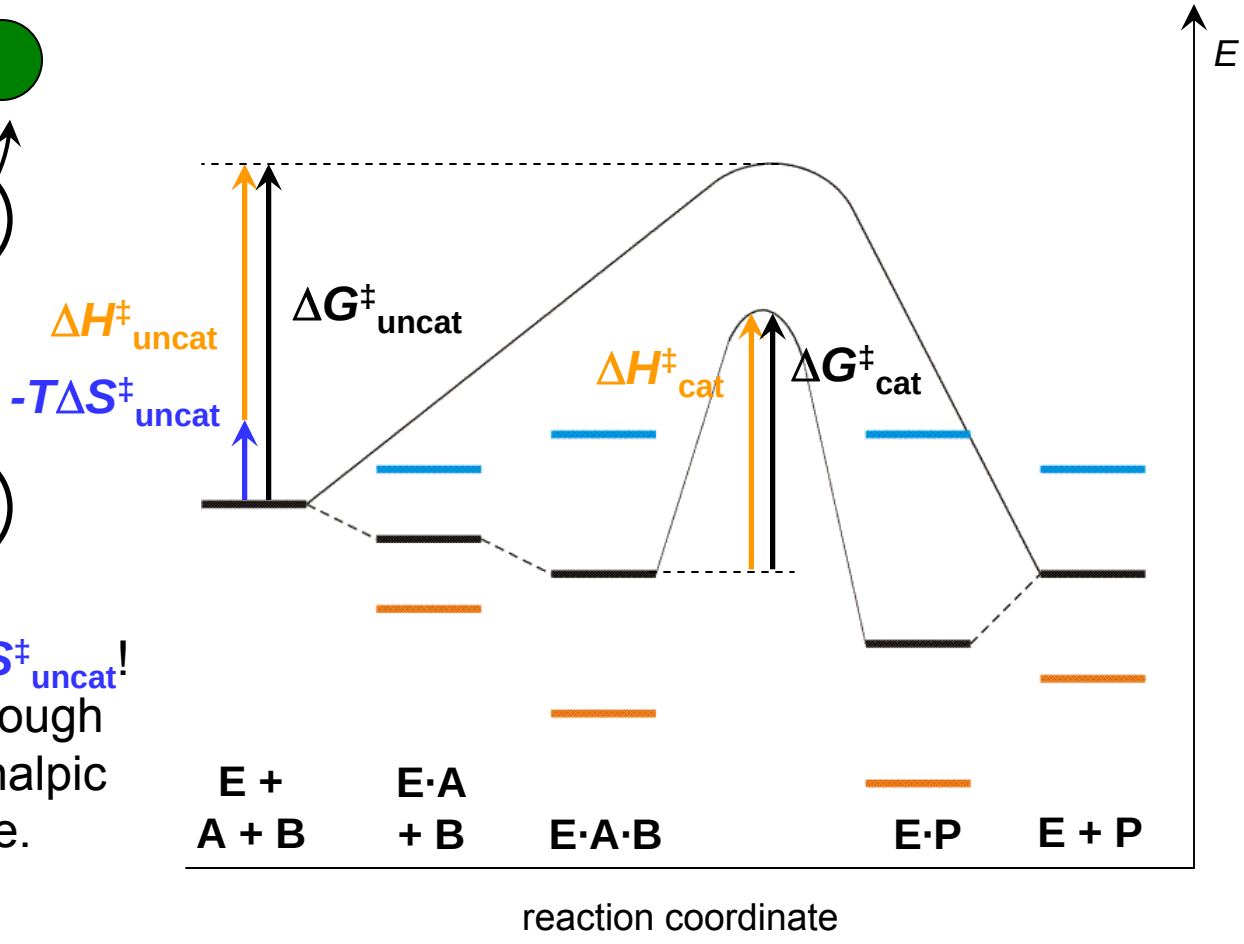
Can catalysts function by improving only $\Delta S^{\ddagger}$?
Yes. (To an extent.)

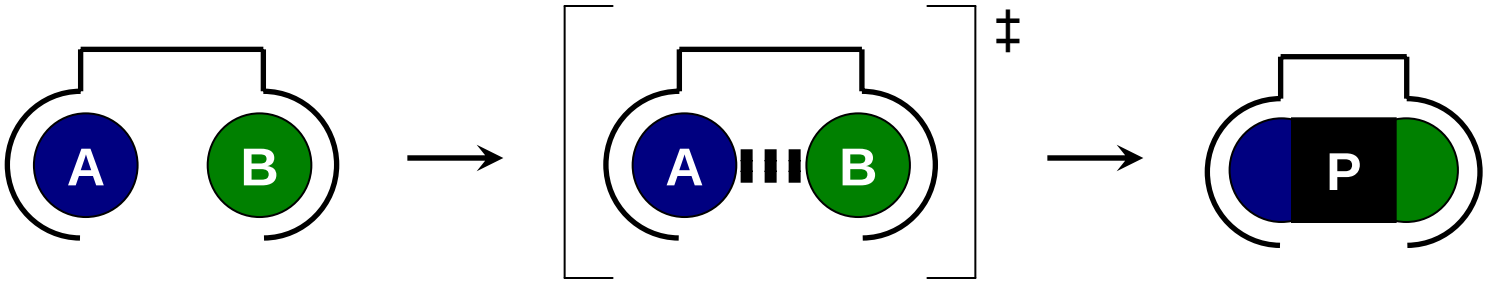


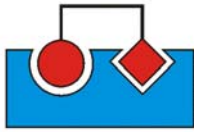


Enzyme eliminated all of $-T\Delta S^{\ddagger}_{uncat}$!
Reaction is catalyzed even though active site has no unique enthalpic interaction with transition state.

Entropic Catalysis: Cooperativity and Effective Molarity

How can entropy alone stabilize transition state?
Chelate effect (cooperativity).

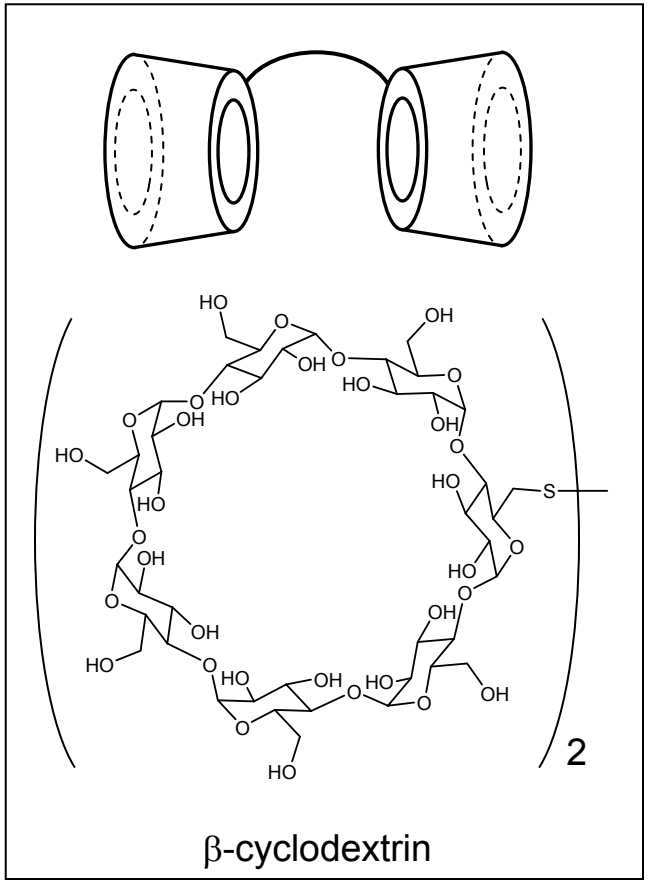


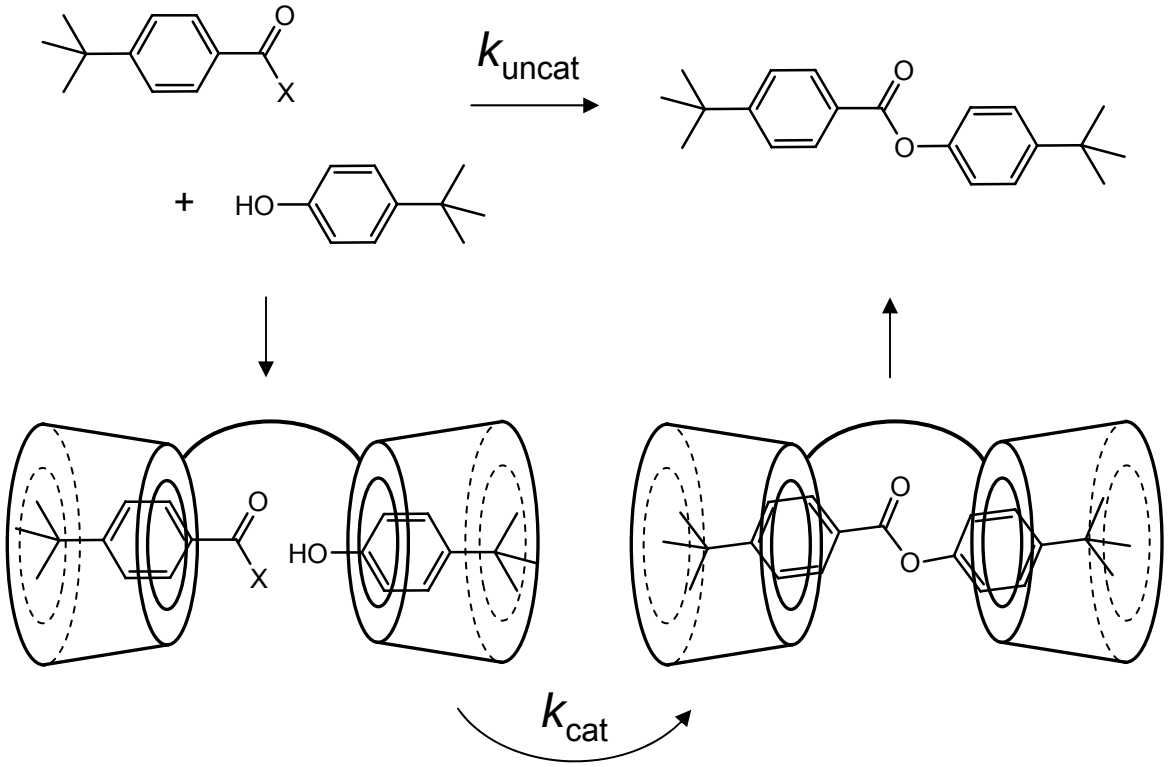
Developing connection between A & B pre-orients them. (like  .)

In this case, for bimolecular reaction, k_{cat} measured in **sec^{-1}**,
k_{uncat} measured in **M^{-1} sec^{-1}**,

So k_{cat}/k_{uncat} is expressed in **M**; is "effective molarity".

Entropic Catalysis: Bringing Reactants Together



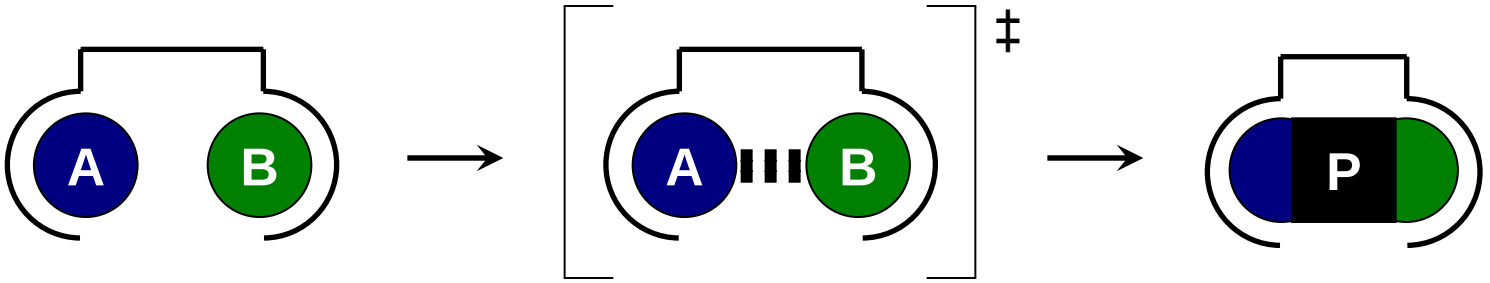


Catalyst just brings two reactants together.
Binds transition state better than starting materials, so
$k_{cat}/k_{uncat} \approx 50$ M.

Breslow, R. et al. *J. Am. Chem. Soc.* **1989**, *111*, 8296-8297.

Entropic Catalysis Alone Is Not Very Effective

How can entropy alone stabilize transition state?
Chelate effect (cooperativity).



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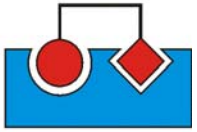
(like  .)

But entropy isn't worth much.

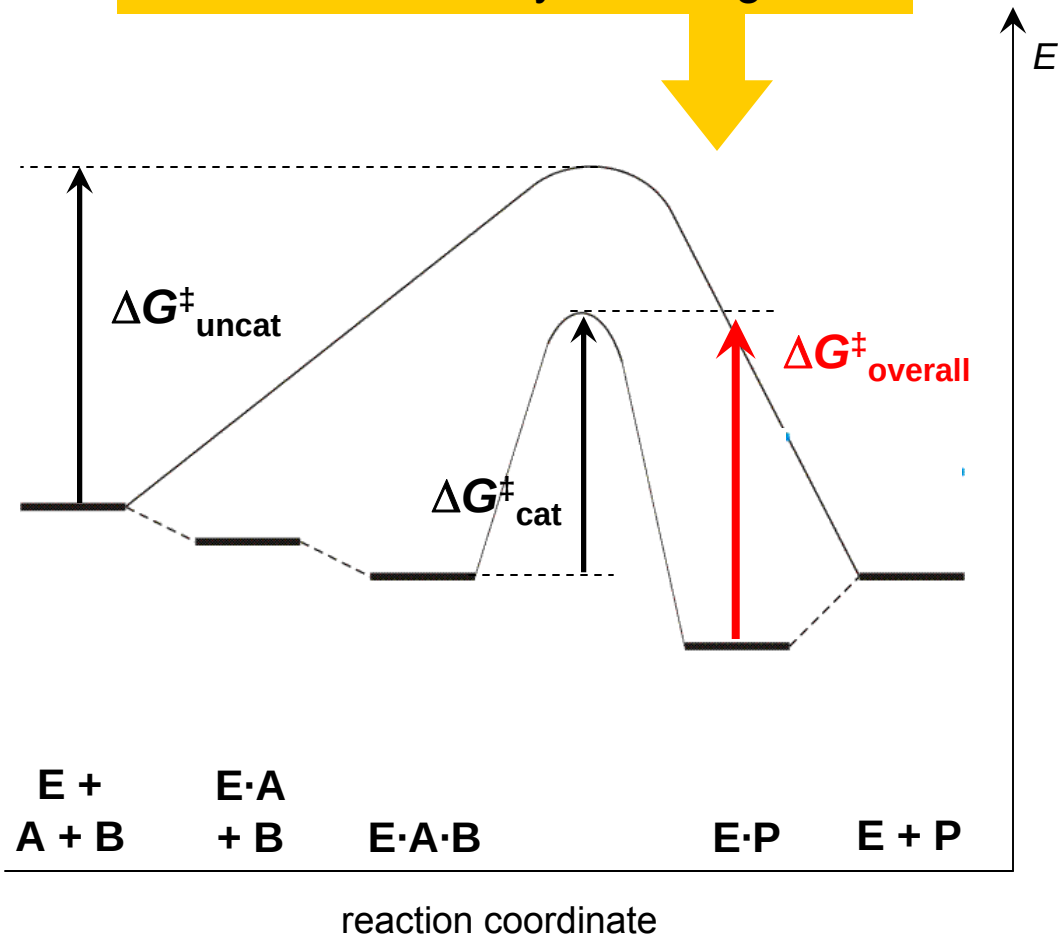
Potential Problem:

Product chelates catalyst even better.

Product may inhibit catalyst, decrease turnover.

Entropic Catalysis Alone Is Not Very Effective

Under product inhibition,
this becomes catalytic resting state!



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