# Allosteric amyloid catalysis by coiled coil fibrils

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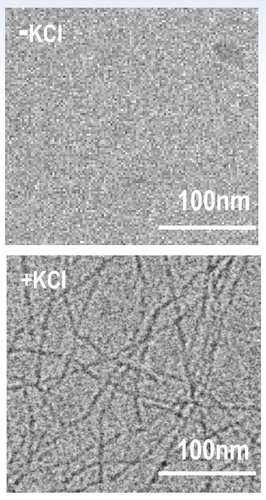
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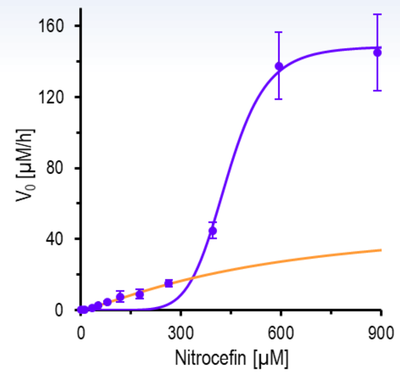
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## Abstract

Amyloid fibrils formed from alternating lysine/phenylalanine β-sheet peptides catalyze the hydrolysis of β-lactam antibiotics, a major contaminant in wastewater linked to antibiotic resistance. Peptide variant analysis, MD simulations, and cryo-EM show that β-lactams dock to fibril surfaces via lysine sidechains, and hydrolysis occurs through an allosteric mechanism in a coiled double-fibril structure that embeds the substrates and enables nucleophilic attack. When displayed on silica beads in a column setup, these catalytic fibrils efficiently degrade and remove β-lactams from water, offering a promising strategy to mitigate antibiotic pollution.

## Fibrillation and catalytic activity

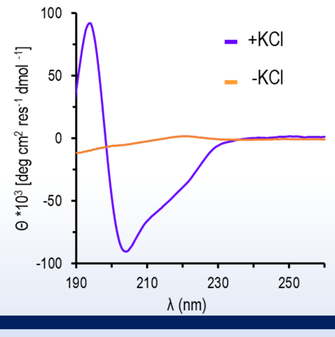



Catalytic parameters

| | Sigmoidal | Hyperbolic |
|---|---|---|
| $V_{max.}$ [μM/h] | 150 [20] | 52.213 [0.005] |
| $K_{cat.}$ *$10^{-4}$ [$s^{-1}$] | 2.5 [0.2] | 0.9 [6*$10^{-5}$]* |
| $K_h$ [μM] | 440 [40] | 600 [300] |
| h | 7 [4] | 1.2 [0.2] |
| ε [$M^{-1}s^{-1}$] | 0.56 [0.04] | 0.14 [0.01] |

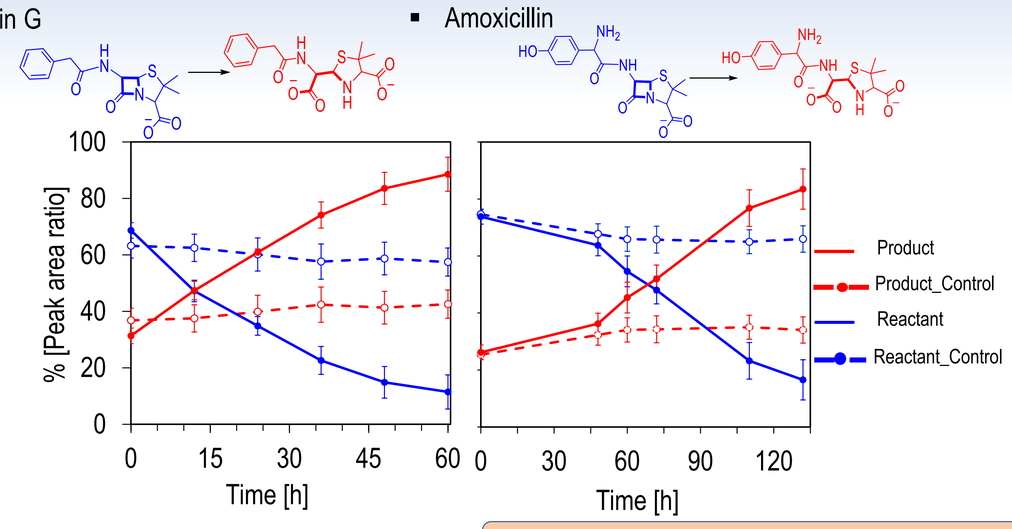
The sigmoidal purple curve corresponds to fitting to the Hill equation. The orange line corresponds to the fitting of only the low nitrocefin concentrations (<300 μM), showing a hyperbolic pattern.



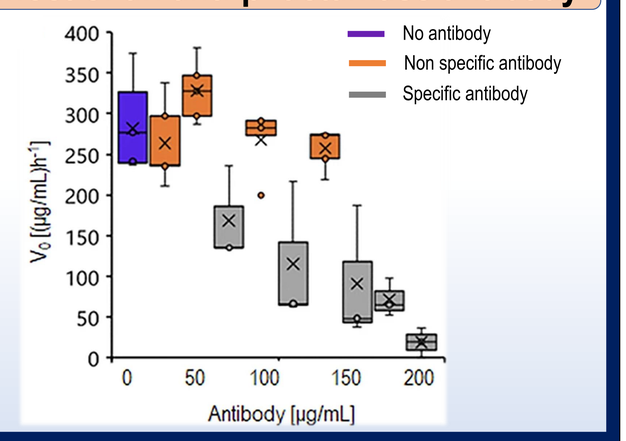

PFK monomers were dissolved in 5 mM Hepes buffer (pH 7.4) with and without added KCl (0.3 M).

## The catalytic activity towards clinical antibiotics

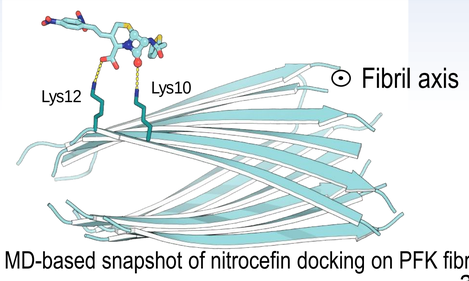
- Penicillin G
- Amoxicillin



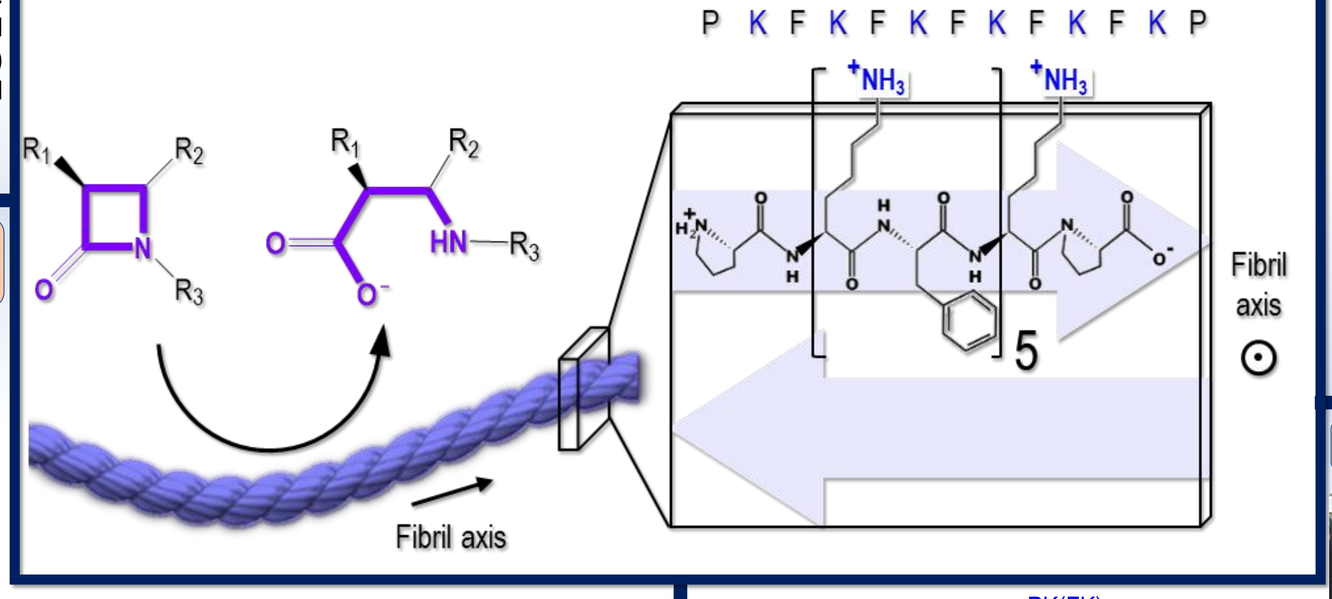

## Effect of an anti-β-lactamase antibody

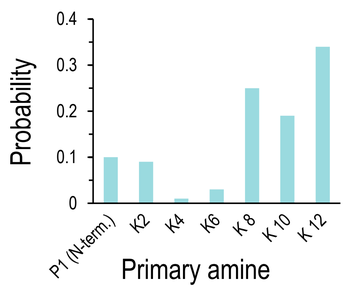



## Structural analysis of the PFK fibril-nitrocefin assembly.

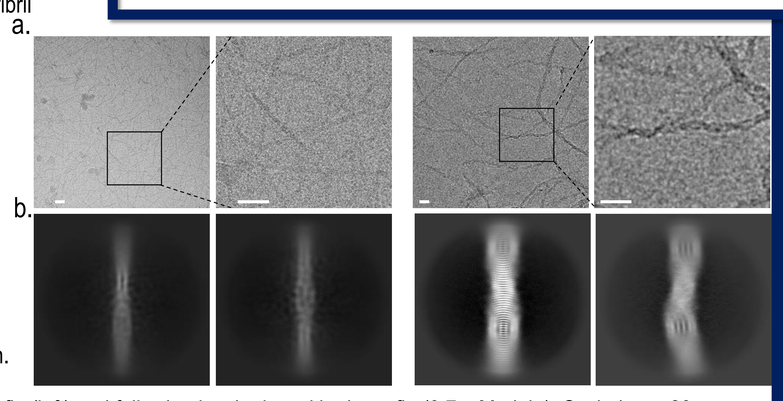



MD-based snapshot of nitrocefin docking on PFK fibril

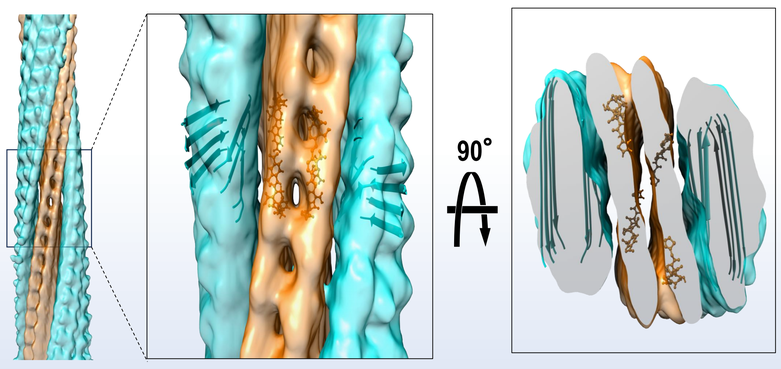



Relative probabilities of lysine binding to Nitrocefin.




a. Cryo-EM micrographs of PFK fibrils without nitrocefin (left) and following incubation with nitrocefin (0.7 mM; right). Scale bars -20 nm.
b. Representative 2D class averages of PFK amyloid fibrils without (two left images) and after incubation with nitrocefin (right images). Scale bars -5 nm.

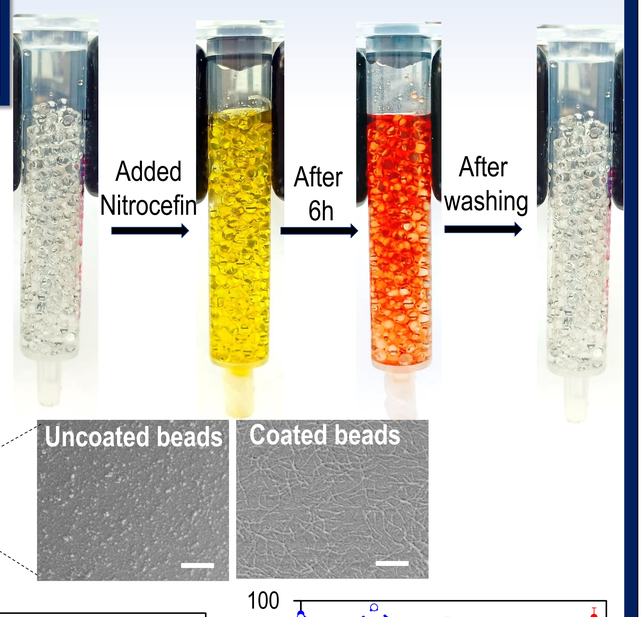


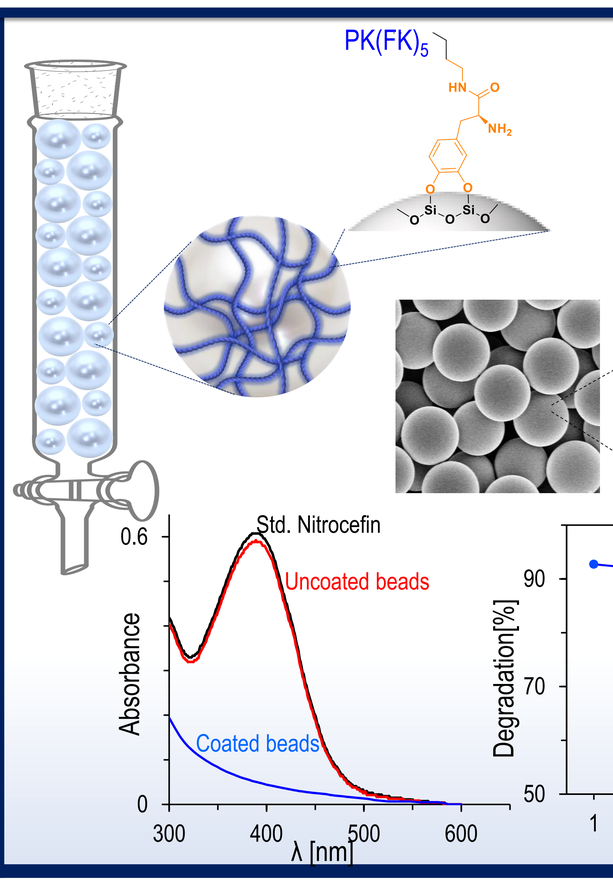

3D cryo-EM map of PFK fibrils incubated with nitrocefin.

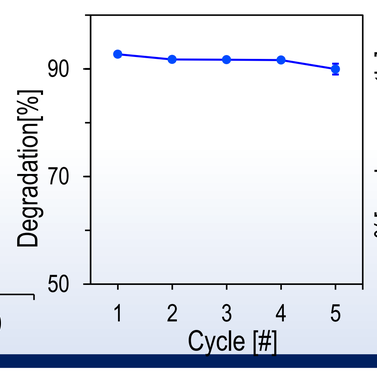
Zoomed-in are the side (center) and radial (right)

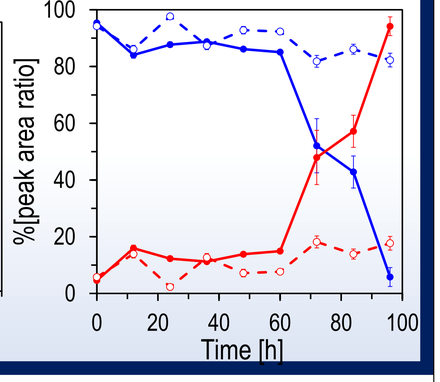
Views of a manually fitted MD-based model to the 3D cryo-EM map.

## PFK fibrils on beads




## Conclusion

- PFK fibrils form at low concentration with salt.
- Catalytically degrade β-lactam antibiotics.
- Activity via a unique allosteric coiled double fiber mechanism.
- Lysine residues enable nucleophilic attack on β-lactams.
- Active against Penicillin G and Amoxicillin.
- Bead-attached fibrils usable in filtration for antibiotic removal.

## References

- Kunnath, Sisira Mambram, et al. "Allosteric amyloid catalysis by coiled coil fibrils." *Nature Communications* 16.1 (2025): 5071.
- Arad, Elad, et al. "Staphylococcus aureus functional amyloids catalyze degradation of β-lactam antibiotics." *Nature Communications* 14.1 (2023): 8198.