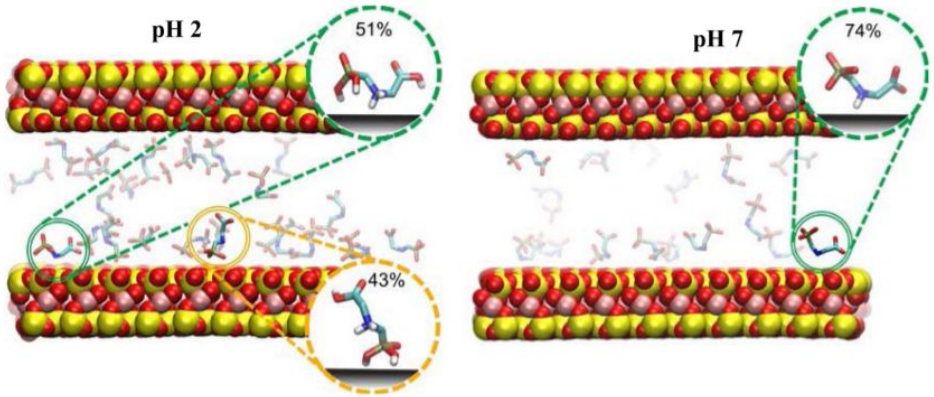
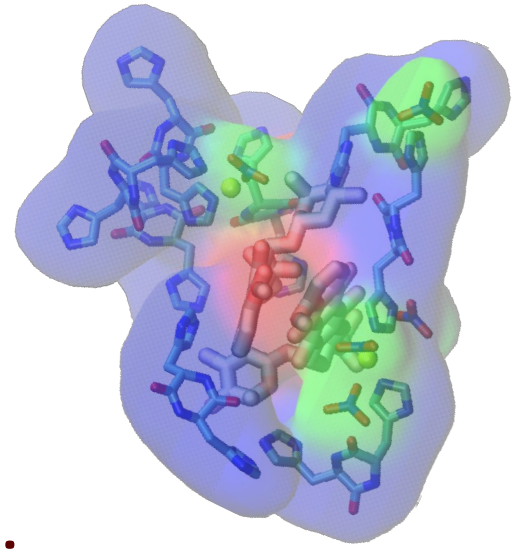
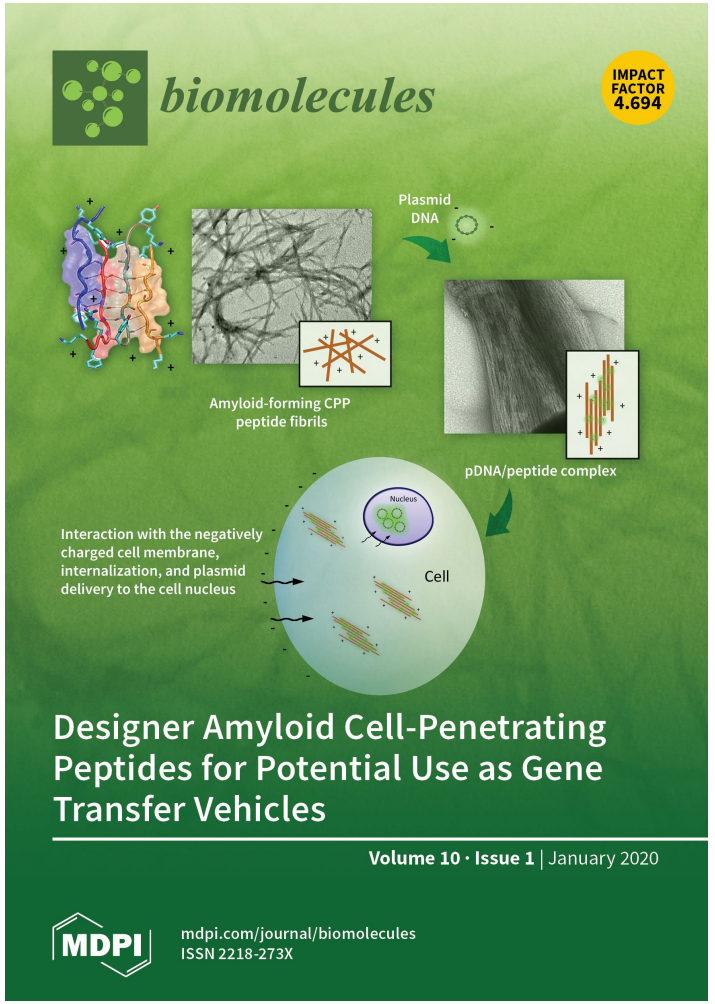
Using computational methods to study, engineer and design

- functional peptide materials
- clay-based sorbents
- proteins binding to RNA modifications and compounds







Phanourios Tamamis

Assistant Professor
Artie Mcferrin Department of Chemical Engineering
Department of Materials Science and Engineering (Affiliated Faculty)
Texas A&M University
tamamis@tamu.edu, http://people.tamu.edu/~tamamis

- Computational research on interactions between peptides, proteins, organic compounds, RNAs/DNAs, clays

We perform MD simulations and free energy calculations CHARMM (Chemistry at HARvard Macromolecular Mechanics). Additional analysis is performed using structure analysis tools, optimization-based design tools which are either primarily developed in our lab, or are available in the literature.

Areas of interest and corresponding applications:

- Self-assembled peptide-or clay-based materials: tissue engineering, sorbents of toxic compounds, drug delivery.
- Amyloid self-assembly: elucidating key aspects of diseases and the design of novel therapeutics.
- Developing novel biophysics tools: elucidating biological axes of compound-protein and RNA-protein interactions and designing novel “modulators”.

Our research is complemented with experiments, strong network of collaborations.

The following slides present an overview of key recent research accomplishments facilitated by HPRC of TAMU.

Montmorillonite Clays as Sorbents of Paraquat and Glyphosate

ACS OMEGA
Article
Cite This: ACS Omega 2019, 4, 17702−17713
http://pubs.acs.org/journal/acsodf

Montmorillonites Can Tightly Bind Glyphosate and Paraquat Reducing Toxin Exposures and Toxicity

Meichen Wang,[†] Asuka A. Orr,[‡] Shujun He,[‡] Chimeddulam Dalaijamts,[†] Weihsueh A. Chiu,[†] Phanourios Tamamis,[‡] and Timothy D. Phillips*[,†]

[†]Veterinary Integrative Biosciences Department, College of Veterinary Medicine and Biomedical Sciences and [‡]Artie McFerrin Department of Chemical Engineering, Texas A&M University, College Station, Texas 77843, United States

- Combination of **in vitro, in vivo, and in silico studies** demonstrated that **montomorillonite clays can potentially be used effective sorbents of paraquat and glyphosate.**

Results from simulations

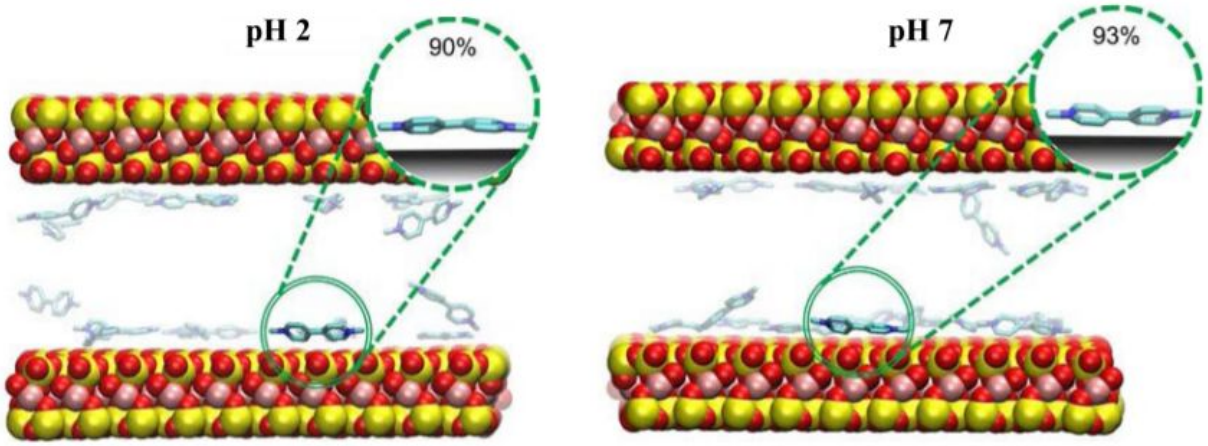
- **Sorption of paraquat: unaffected by pH (2 and 7)**
- Paraquat: binds with both bipyridinium rings parallel to the surface

- **Glyphosate: binds via its positive amide group at pH 2 and 7.**
- **At pH 2**, glyphosate also binds via **hydrogen bond interactions between its phosphate group** and the oxygens of the clay

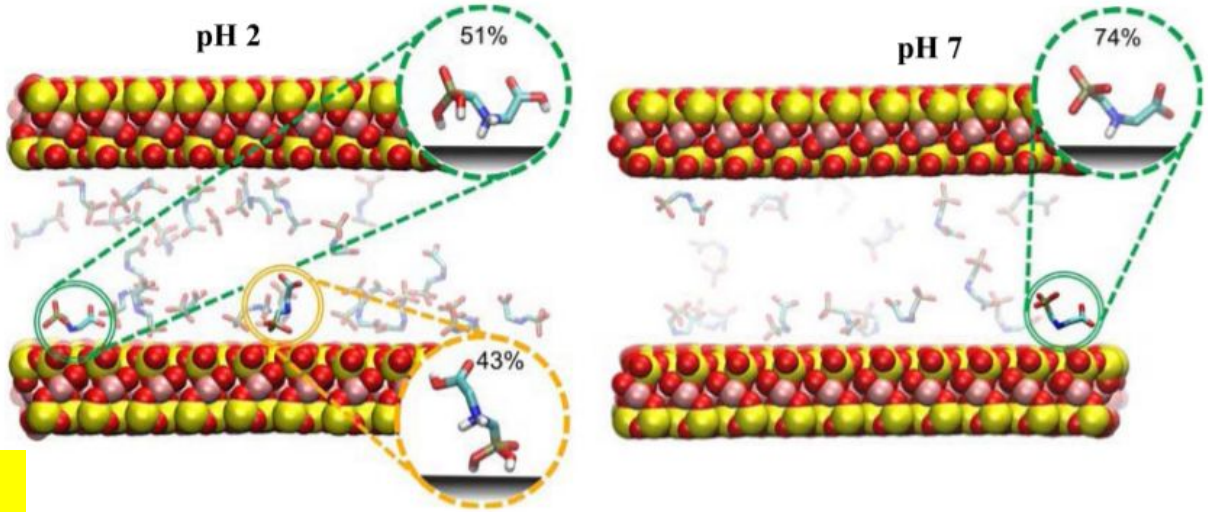
Experimental Collaborator: Tim Phillips (Texas A&M University)

Clays: Effective Sorbents for Both

Paraquat



Glyphosate



Montmorillonite Clays as Sorbents of Bisphenols

ELSEVIER

Computers & Chemical Engineering
Volume 143, 5 December 2020, 107063

Insights into the interactions of bisphenol and phthalate compounds with unamended and carnitine-amended montmorillonite clays

Asuka A. Orr [a, 1], Shujun He [a, 1], Meichen Wang [b, 1], Alicia Goodall [a], Sara E. Hearon [b], Timothy D. Phillips [b] ✉, Phanourios Tamamis [a, c] ✉

[a] Artie McFerrin Department of Chemical Engineering, Texas A&M University, College Station, TX, 77843, USA
[b] Veterinary Integrative Biosciences Department, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, 77843, USA
[c] Department of Materials Science and Engineering, Texas A&M University, College Station, TX, 77843, USA

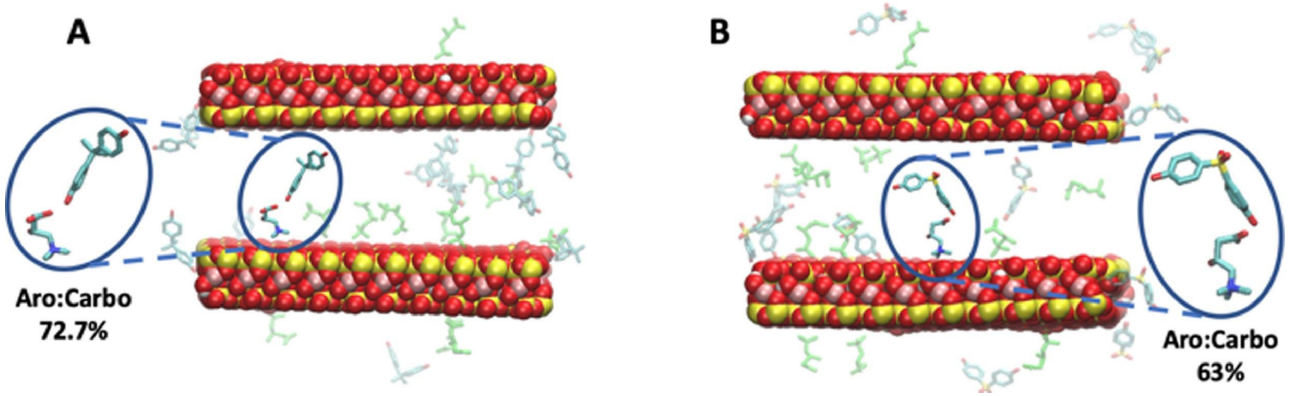
- **Simulations predicted that**
- **Parent, unamended, clay has higher binding propensity for BPA and BPS (bisphenols) than for DBP and DEHP (phthalates).**
- **Carnitine-amended clay improved BPA and BPS binding.**

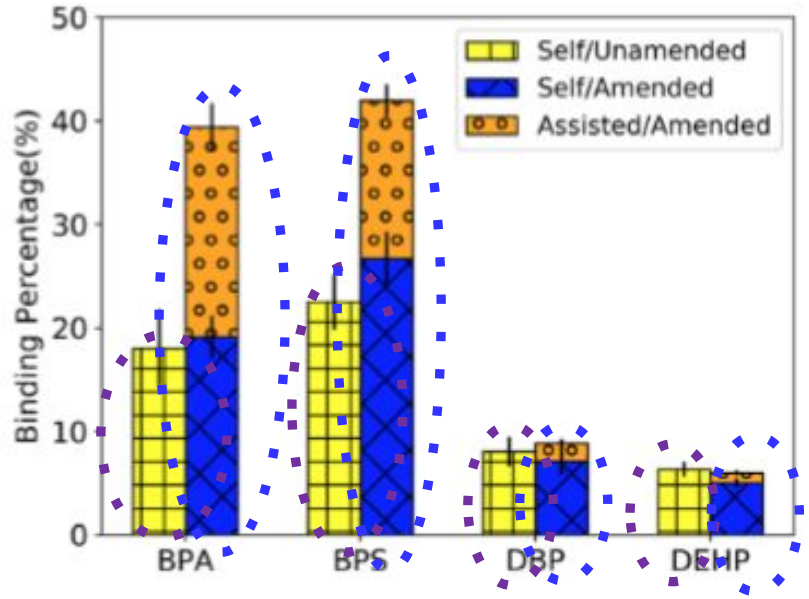
- **Experimental isothermal analysis confirmed that carnitine- amended clay has enhanced BPA binding capacity, affinity and enthalpy.**

Experimental Collaborator: Tim Phillips (Texas A&M University)

Carnitine Amendment Improves BPA/BPS binding

Snapshots from simulations showing how carnitine can enhance binding of BPA and BPS to clays





Montmorillonite Clays as Sorbents of PFAS (Per- and polyfluoroalkyl substances)

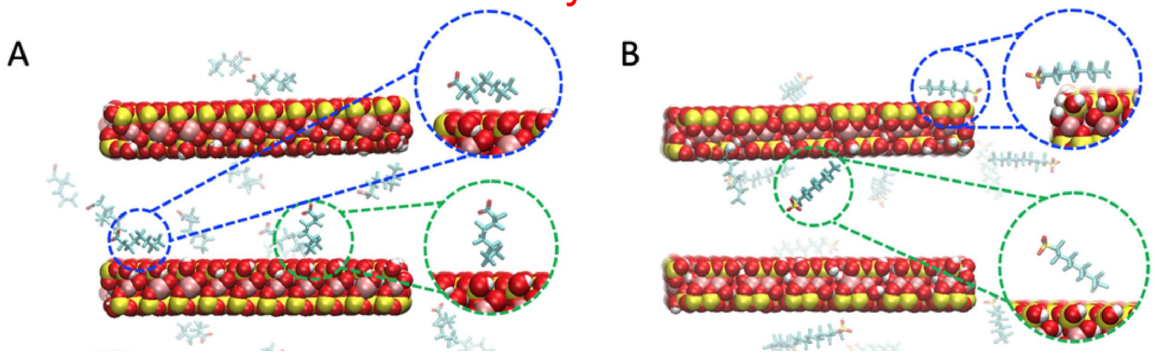
Simulaitions were used to study Interactions of PFOA, PFOS, GenX, PFBS with montmorillonite clays

Major routes for human exposures to PFAS include the ingestion of PFAS-contaminated drinking water, fish, food packaged or processed with PFAS-containing materials, and crops grown in contaminated soil or water.

Objective: To identify the optimal mitigating sorbents for PFAS, delineating mechanisms, and investigate efficacy of sorbents in reducing PFAS through ingestion by simulating gastrointestinal conditions.

Molecular dynamics (MD) simulations suggested the key mode of interaction of PFAS was through fluorinated carbon chains, and confirmed that PFOA and PFOS had enhanced binding to amended clays compared to GenX and PFBS.

Our studies suggest that the inclusion of edible, nutrient-amended clays with optimal affinity, capacity, and enthalpy can be used to decrease the bioavailability of PFAS from contaminated drinking



Water Research
Volume 188, 1 January 2021, 116534

Enhanced adsorption of per- and polyfluoroalkyl substances (PFAS) by edible, nutrient-amended montmorillonite clays

Meichen Wang [a], Asuka A. Orr [b], Joseph M. Jakubowski [b], Kelsea E. Bird [b], Colleen M. Casey [b], Sara E. Hearon [a], Phanourios Tamamis [b, c], Timothy D. Phillips [a]

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https://doi.org/10.1016/j.watres.2020.116534

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Highlights

- Nutrient-amended montmorillonite clays were shown to strongly bind PFAS.
- PFOA, PFOS, and mixtures of PFAS were tightly adsorbed within interlayers of clays.
- Hydrophobic/electrostatic interactions and hydrogen bonds were involved in sorption.
- Computer modeling and MD simulations validated our experimental results.
- Low doses of sorbents protected a *PFAS-sensitive organism* from toxicity of PFAS.

Experimental Collaborator: Tim Phillips (Texas A&M University)

Cyclic-Dihistidine Peptide Materials

Self-Assembly of Fluorescent Biomaterials for Cancer Drug Carriers

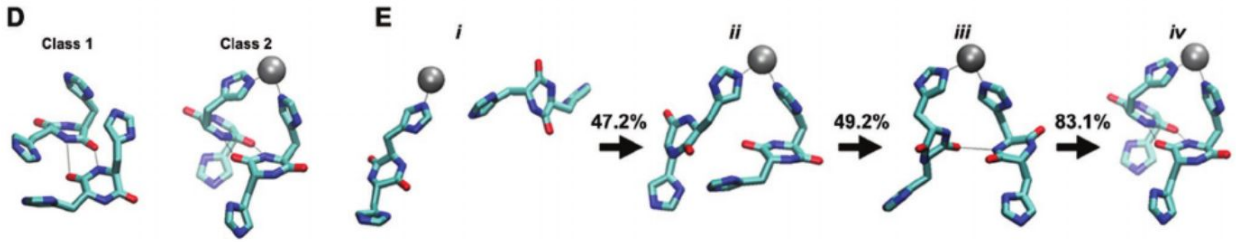
ADVANCED FUNCTIONAL MATERIALS

Full Paper | Full Access

Enhanced Fluorescence for Bioassembly by Environment-Switching Doping of Metal Ions

Kai Tao, Yu Chen, Asuka A. Orr, Zhen Tian, Pandeeswar Makam, Sharon Gilead, Mingsu Si, Sigal Rencus-Lazar, Songnan Qu, Mingjun Zhang, Phanourios Tamamis, Ehud Gazit

First published: 07 January 2020 | https://doi.org/10.1002/adfm.201909614 | Citations: 8



Cyclo-HH self-assembly doping by Zn^{2+}

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High-Efficiency Fluorescence through Bioinspired Supramolecular Self-Assembly

Yu Chen, Asuka A. Orr, Kai Tao, Zhibin Wang, Antonella Ruggiero, Linda J. W. Shimon, Lee Schnaider, Alicia Goodall, Sigal Rencus-Lazar, Sharon Gilead, Inna Slutsky, Phanourios Tamamis*, Zhan'ao Tan*, and Ehud Gazit*

Cite this: *ACS Nano* 2020, 14, 3, 2798–2807
Publication Date: February 4, 2020
https://doi.org/10.1021/acsnano.9b10024

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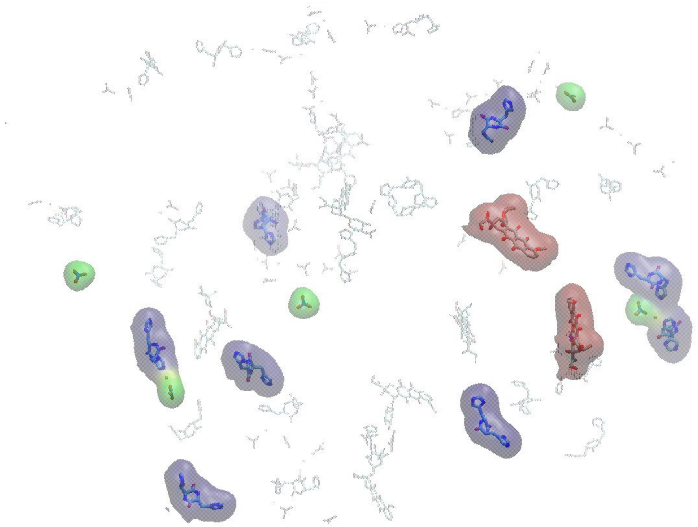
SUBJECTS: Self organization,



Movie from a simulation depicting an example case of cancer drug epirubicin encapsulated by Cyclo-HH peptides and NO_3^-

We used a combination of computational methods and experimental methods in collaboration with Dr. Ehud Gazit's lab (Tel Aviv University), and designed a novel generation of cancer drug nanocarrier with enhanced fluorescence properties, and with the ability to self-encapsulate a particular cancer drug epirubicin with in situ monitoring properties.

Experimental collaborator: Ehud Gazit (Tel Aviv University)

Amyloid Materials

Simulations of Cell-Penetrating Peptides for Potential Use as Gene Transfer Vehicles

Open Access | Feature Paper | Article

Designer Amyloid Cell-Penetrating Peptides for Potential Use as Gene Transfer Vehicles

by Chrysoula Kokotidou [1,2], Sai Vamshi R. Jonnalagadda [3], Asuka A. Orr [3], George Vrentzos [4], Androniki Kretsovali [4], Phanourios Tamamis [3,*] and Anna Mitraki [1,2,*]

[1] Department of Materials Science and Technology, University of Crete, 70013 Heraklion, Grete, Greece
[2] Institute of Electronic Structure and Laser (IESL) FORTH, 70013 Heraklion, Crete, Greece
[3] Artie McFerrin Department of Chemical Engineering, Texas A&M University College Station, TX 77843-3251, USA
[4] Institute of Molecular Biology and Biotechnology (IMBB) FORTH, 70013 Heraklion, Crete, Greece
* Authors to whom correspondence should be addressed.

Biomolecules **2020**, *10*(1), 7; https://doi.org/10.3390/biom10010007

Received: 25 November 2019 / Revised: 15 December 2019 / Accepted: 16 December 2019 / Published: 18 December 2019

(This article belongs to the Special Issue 2019 Feature Papers by Biomolecules' Editorial Board Members)

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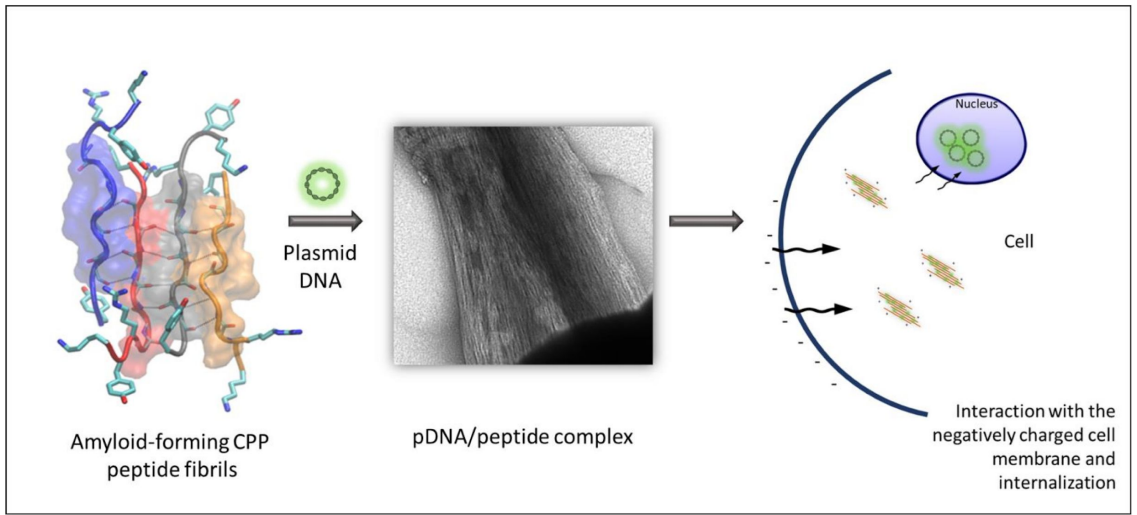

- We used a combination of computational and experimental methods to design two peptides comprised of β-sheet cores derived from naturally occurring protein sequences and designed positively charged and aromatic residues exposed at key residue positions.

- The introduction of positively charged and aromatic residues additionally promotes DNA condensation and cell internalization by the self-assembled material formed by the designed peptides.

- Our results demonstrate that these designer peptide fibrils can efficiently enter mammalian cells while carrying packaged luciferase-encoding plasmid DNA, and they can act as a protein expression enhancer. Interestingly, the peptides additionally exhibited strong antimicrobial activity against the enterobacterium *Escherichia coli.*

Potential Future Directions-Applications:

- Transfer of small interfering RNAs and protein therapeutic cargos.
- Examining and improving their antimicrobial activity for different bacteria and microbes.

Experimental collaborator: Anna Mitraki (University of Crete)

Protein Interactions with modified RNAs

Using “computational evolution” to redesign proteins

Computational and Structural Biotechnology Journal
Volume 18, 2020, Pages 137-152

Computational evolution of an RNA-binding protein towards enhanced oxidized-RNA binding

Juan C. Gonzalez-Rivera [a, 1], Asuka A. Orr [c, 1], Sean M. Engels [a], Joseph M. Jakubowski [c], Mark W. Sherman [b], Katherine N. O'Connor [a], Tomas Matteson [b], Brendan C. Woodcock [c], Lydia M. Contreras [a, b], Phanourios Tamamis [c]

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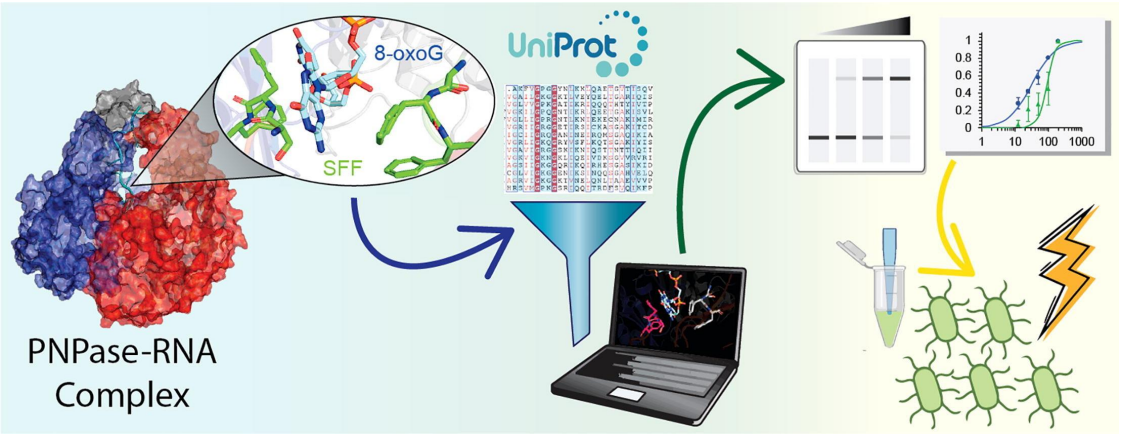
https://doi.org/10.1016/j.csbj.2019.12.003



We have examined the interaction of PNPase with 8-oxoG in atomic detail to provide insights into the mechanism of 8-oxoG discrimination.

We hypothesized that PNPase subunits cooperate to form a binding site using the dynamic SFF loop within the central channel of the PNPase homotrimer.

We evolved this site using a novel approach that initially screened mutants from a library of beneficial mutations and assessed their interactions using multi-nanosecond Molecular Dynamics simulations.

We found that evolving this single site resulted in a fold change increase in 8-oxoG affinity between 1.2 and 1.5 and/or selectivity between 1.5 and 1.9.

In addition to the improvement in 8-oxoG binding, complementation of K12 Δ*pnp* with plasmids expressing mutant PNPases caused increased cell tolerance to H_2O_2.

This observation provides a clear link between molecular discrimination of RNA oxidation and cell survival. Moreover, this study provides a framework for the manipulation of modified RNA protein reac

Experimental collaborator: Lydia Contreras (UT Austin)

Interactions between Curcumin Derivatives and Amyloid-β Fibrils

Interactions between Curcumin Derivatives and Amyloid-β Fibrils: Insights from Molecular Dynamics Simulations

Joseph M. Jakubowski, Asuka A. Orr, Doan A. Le, and Phanourios Tamamis*

Cite this: *J. Chem. Inf. Model.* 2020, 60, 1, 289–305
Publication Date: December 6, 2019
https://doi.org/10.1021/acs.jcim.9b00561

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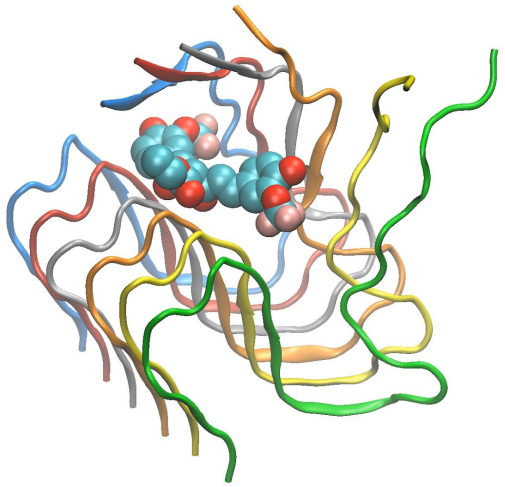
SUBJECTS: Binding modes, Nanofibers,

- In a small subset of these simulations, curcumin derivatives partly dissociate the outermost peptide of the $A\beta_{1-42}$ fibril by disrupting β-sheets within the residue domain $_{12}$VHHQKLVFF$_{20}$.

- A comparison between binding modes leading or not leading to partial dissociation of the outermost peptide suggests that the latter is attributed to a few subtle key structural and energetic interaction-based differences.

- Interestingly, partial dissociation appears to be either an outcome of high affinity interactions or a cause leading to high affinity interactions between the molecules and the fibril, which could partly serve as a compensation for the energy loss in the fibril due to partial dissociation.



Acknowledgement: Computational Facilities and Funding Resources

Ada

Ada is a 874-node hybrid cluster from IBM/Lenovo with Intel Ivy Bridge processors and a Mellanox FDR-10 Infiniband interconnect. Ada includes 68 NVIDIA K20 GPUs supporting applications already ported to GPUs, and 24 Intel Xeon Phi 5110P co-processors supporting applications benefiting from Knights Corner Phi cards.

Artie McFerrin Department of CHEMICAL ENGINEERING TEXAS A&M UNIVERSITY

TEES TEXAS A&M ENGINEERING EXPERIMENT STATION

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