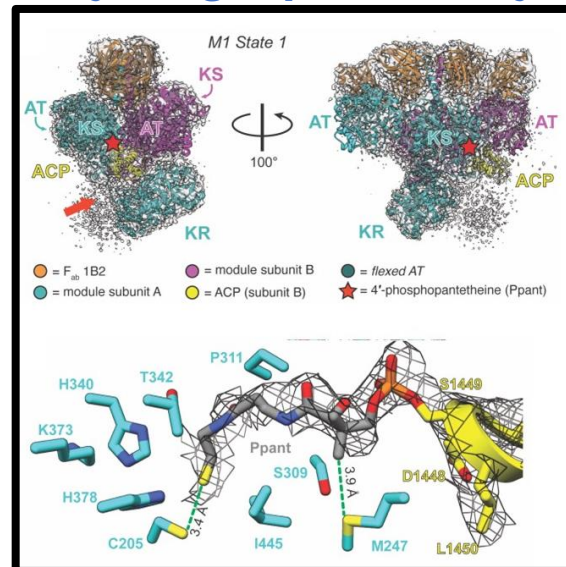




## CryoEM Current Practices Webinar

### *Mapping the catalytic conformations of an assembly-line polyketide synthase module by single-particle cryo-EM*



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Assembly-line polyketide synthases, such as the 6-deoxyerythronolide B synthase (DEBS), are large multienzyme systems prized for their ability to produce specific and complex polyketide products. By transferring protein-tethered substrates across multiple active sites in a defined linear sequence, these enzymes facilitate programmed small molecule syntheses that could theoretically be harnessed to access countless polyketide product structures. Using single particle cryogenic electron microscopy (cryo-EM) to study DEBS module 1, we present the structural basis for inter-polypeptide substrate channelling as well as a model for structural dynamics during its catalytic cycle. Multiple near-atomic resolution structures (3.2–4.1 Å) reveal key domain-domain interfaces and an unexpected module asymmetry. We present an additional structure of DEBS module 1 in its product-bound state (4.3 Å) to rationalize a recently described “turnstile” mechanism that underlies vectorial biosynthesis by these assembly lines. Finally, we report on site- and domain-specific crosslinking to validate the observed structures as well as to unlock previously unknown conformations by single particle cryo-EM.

All are welcome to attend. Registration is at no-cost, but sign-up is required:

[https://us02web.zoom.us/webinar/register/WN\\_TKM1Hak8S-yFUOXyXPiQZw](https://us02web.zoom.us/webinar/register/WN_TKM1Hak8S-yFUOXyXPiQZw)

This webinar series is jointly hosted by the NIH Transformative High Resolution CryoEM Program Service Centers: the National Center for CryoEM Access and Training (NCCAT), the Pacific Northwest Center for CryoEM (PNCC), and the Stanford-SLAC CryoEM Center (S2C2) who provide no-cost access to cryoEM instrumentation and training. In this monthly series, we will highlight cryoEM methods and use the Q&A session after the seminar to stimulate discussion of best practices and interesting challenges that will be helpful to researchers new to the field. Representatives from all three service centers will also be on hand to answer questions about the cryoEM resources available to biomedical researchers and how to access them.