

## Syllabus for MCB 335: Protein Folding

**Instructors:** Alexandrescu & Teschke (contact information below)

**Class times:** 11:00-12:15 pm Tuesday/Thursday BSP 201

### **Part 1: Protein physics and the folding code.**

1	Jan 17	AA	Class Organization / The thermodynamic hypothesis.
2	19	AA	Survey of protein structure and folds I
3	24	AA	Survey of protein structure and folds II
4	26	AA	<u>Student Presentation 1</u> – Negative design
5	Jan 31	AA	Protein physics / cooperativity / random coils /uniqueness of native state
6	Feb 2	AA	<u>Student Presentation 2</u> – Intrinsically unfolded proteins
7	7	AA	Structural approaches to understanding protein folding
8	Feb 9	AA	<u>Student Presentation 3</u> – Single molecule unfolding

### **Part 2: Intermediates**

9	Feb 14	CT	Mutagenic approaches: thermodynamics, kinetics and transition states
10	16	CT	<u>Student Presentation 4</u>
11	21	CT	Proline isomerization and isomerases.
12	23	CT	<u>Student Presentation 5</u>
13	Feb 28	CT	Early stages in protein folding
14	Mar 2	CT	<u>Student Presentation 6</u>

**March 2 – have your proposal topic approved.**

←-----SPRING BREAK (March 4 to 12) -----→

### **Part 3: Protein structure prediction and design**

14	Mar14	AA	Protein folding hierarchy: domains, sub-domains, structure elements
15	16	AA	Student Presentation 7 – Free energy landscapes
16	21	AA	<b>Special seminar: TBA</b>
17	23	AA	Student Presentation 8 – Evolution of protein structures
18	28	AA	Protein structure prediction: methods and challenges
19	Mar30	AA	Student Presentation 9 – Protein modeling & design

### **Part 4: Chaperones**

20	Apr 4	CT	Aggregation / Inclusion bodies
21	6	CT	Student Presentation 10
22	11	CT	GroEL/S and CCT
23	13	CT	Student Presentation 11
24	18	CT	DnaK/Hsp70 and co-chaperones
25	20	CT	Student Presentation 12
26	25	CT	Chaperones and protein synthesis.
27	Apr 27	CT	Student Presentation 13

**Final Exam – Proposals are due APRIL 27 !!!**

**Recommended Books (not required):** 'Protein Physics' by Finkelstein & Ptitsyn; Structure and Mechanism in Protein Science by Alan Fersht. Some additional readings will be in the MCB office BSP 104 or will be posted on WebCT.

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### Student Presentations

#### Jan 26 **SP1 Negative Design**

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Richardson JS, Richardson DC: **Natural beta-sheet proteins use negative design to avoid edge-to-edge aggregation.** *Proc Natl Acad Sci U S A* 2002, **99**:2754-2759.

Wang W, Hecht MH: **Rationally designed mutations convert de novo amyloid-like fibrils into monomeric beta-sheet proteins.** *Proc Natl Acad Sci U S A* 2002, **99**:2760-2765.

#### Feb 2 **SP2 Intrinsically Disordered Proteins**

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Dyson HJ, Wright PE: **Intrinsically unstructured proteins and their functions.** *Nat Rev Mol Cell Biol* 2005, **6**:197-208.

Fernandez CO, Hoyer W, Zweckstetter M, Jares-Erijman EA, Subramaniam V, Griesinger C, Jovin TM: **NMR of alpha-synuclein-polyamine complexes elucidates the mechanism and kinetics of induced aggregation.** *Embo J* 2004, **23**:2039-2046.

#### Feb 9 **SP3 Single Molecule Unfolding**

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Carrion-Vazquez M, Oberhauser AF, Fowler SB, Marszalek PE, Broedel SE, Clarke J, Fernandez JM: **Mechanical and chemical unfolding of a single protein: a comparison.** *Proc Natl Acad Sci U S A* 1999, **96**:3694-3699.

Oesterhelt F, Oesterhelt D, Pfeiffer M, Engel A, Gaub HE, Muller DJ: **Unfolding pathways of individual bacteriorhodopsins.** *Science* 2000, **288**:143-146.

Feb 16 **SP4** \_\_\_\_\_

Feb 23 **SP5** \_\_\_\_\_

Mar 2 **SP6** \_\_\_\_\_

#### Mar16 **SP7 Free Energy Landscapes**

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Dill KA, Chan HS: **From Levinthal to pathways to funnels.** *Nat Struct Biol* 1997, **4**:10-19.

Chamberlain AK, Marqusee S: **Touring the landscapes: partially folded proteins examined by hydrogen exchange.** *Structure* 1997, **5**:859-863.

#### Mar23 **SP8 Evolution of protein structures**

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Orengo CA, Thornton JM: **Protein families and their evolution-a structural perspective.** *Annu Rev Biochem* 2005, **74**:867-900.

Riechmann L, Winter G: **Novel folded protein domains generated by combinatorial shuffling of polypeptide segments.** *Proc Natl Acad Sci U S A* 2000, **97**:10068-10073.

**Mar30 SP9 Protein Modeling & design**

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Kuhlman B, Dantas G, Ireton GC, Varani G, Stoddard BL, Baker D: **Design of a novel globular protein fold with atomic-level accuracy.** *Science* 2003, **302**:1364-1368.

Schueler-Furman O, Wang C, Bradley P, Misura K, Baker D: **Progress in modeling of protein structures and interactions.** *Science* 2005, **310**:638-642.

Apr 6 **SP10**\_\_\_\_\_

Apr 13 **SP11**\_\_\_\_\_

Apr 20 **SP12**\_\_\_\_\_

Apr 20 **SP12**\_\_\_\_\_