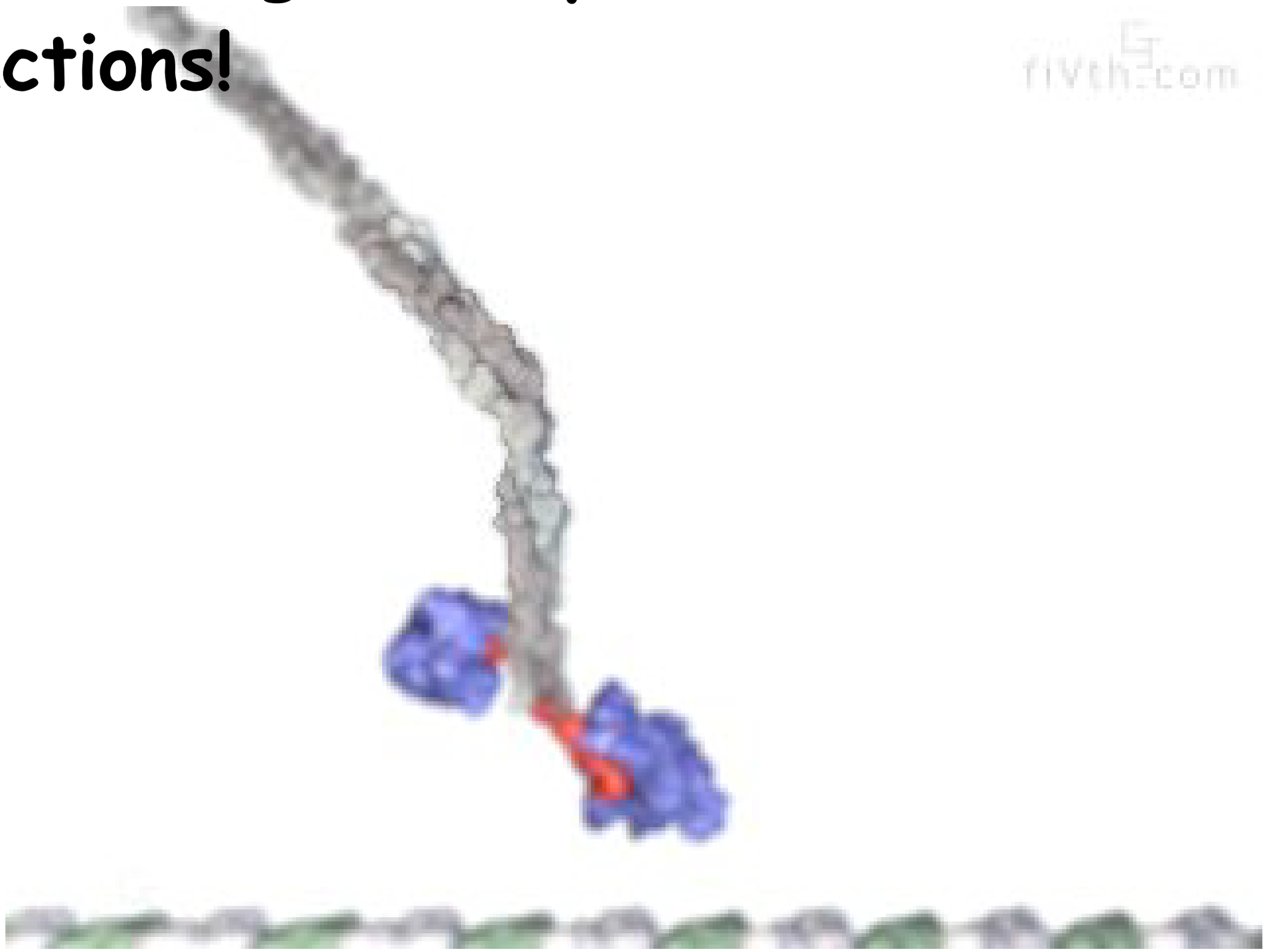
COHERENT, INCOHERENT and QUANTUM CONTROLLED VIBRATIONAL DYNAMICS IN PROTEINS: My FAILED Attempt to Change the Face of Protein Dynamics

Bob Austin

(Aihua Xie from OK State is an innocent victim)

This is magic. Enzymes COUPLE chemical reactions!



http://valelab.ucsf.edu/research/res_mec_overv.html

Collective (FIR, 100 ums) modes

This not magic, and it is dead.

Stan Ulam of Los Alamos/Pasta-Ulam-Fermi non-linear physics fame made two wonderful remarks:

1) "Ask not what physics can do for biology, ask what biology can do for physics"! Not a popular position anymore, risky.

2) "calling something "non-linear" is akin to calling most of the animals in the zoo "non-elephants."

Functional Protein Dynamics (as opposed to a physicist's protein dynamics) are highly non-linear, highly non-ergodic and occur over a high time range, from picoseconds to seconds and beyond. Can we ever model these dynamics in a meaningful way?

One possibility is to study energy self-trapping, the localization of "mechanical" U energy via nonlinear interactions, Jij

Self-trapping of energy is a non-linear process where energy localizes in a particular mode (in my case vibrational modes, but can be more general than this.).

Normal mode dynamics are NOT energy trapping processes, they are linear and ergodic. Pasta, Fermi and Ulam in 1953 first discovered non-linear trapping in coupled anharmonic system (computer!)

It is "easy" to build a mechanical toy that demonstrates energy trapping in a high Q (Q =30) linear coupled pair of anharmonic oscillators.

Anharmonic effects are the things that make the world interesting! The linear world is all cold crystals,

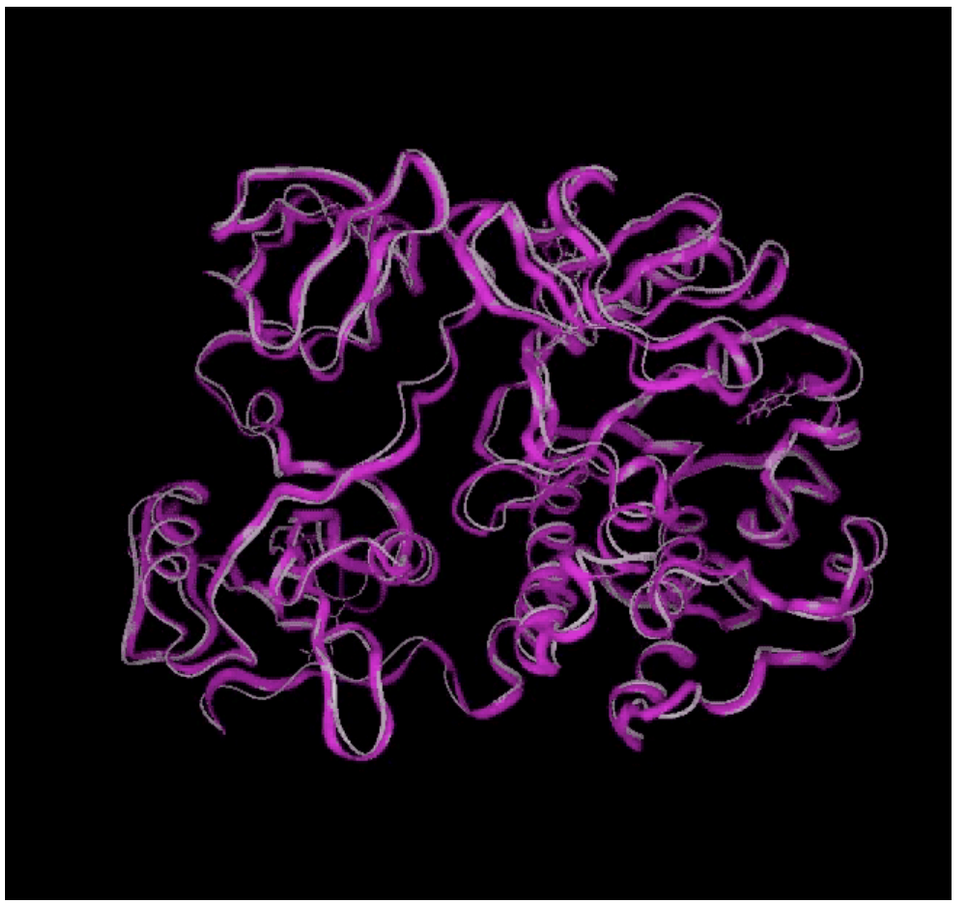
You all have seen this: weakly coupled pendula with normal mode beating:

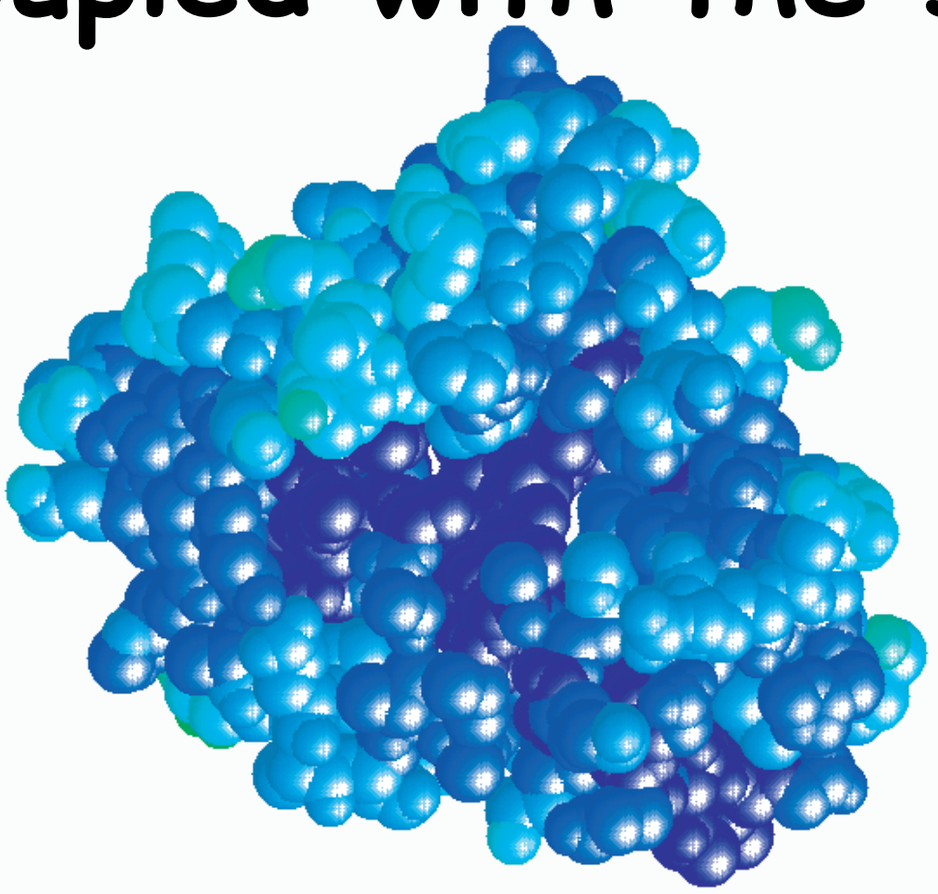
But have you seen this:

$$g(\theta) \sim g(0)[1 - \theta^2/3]$$

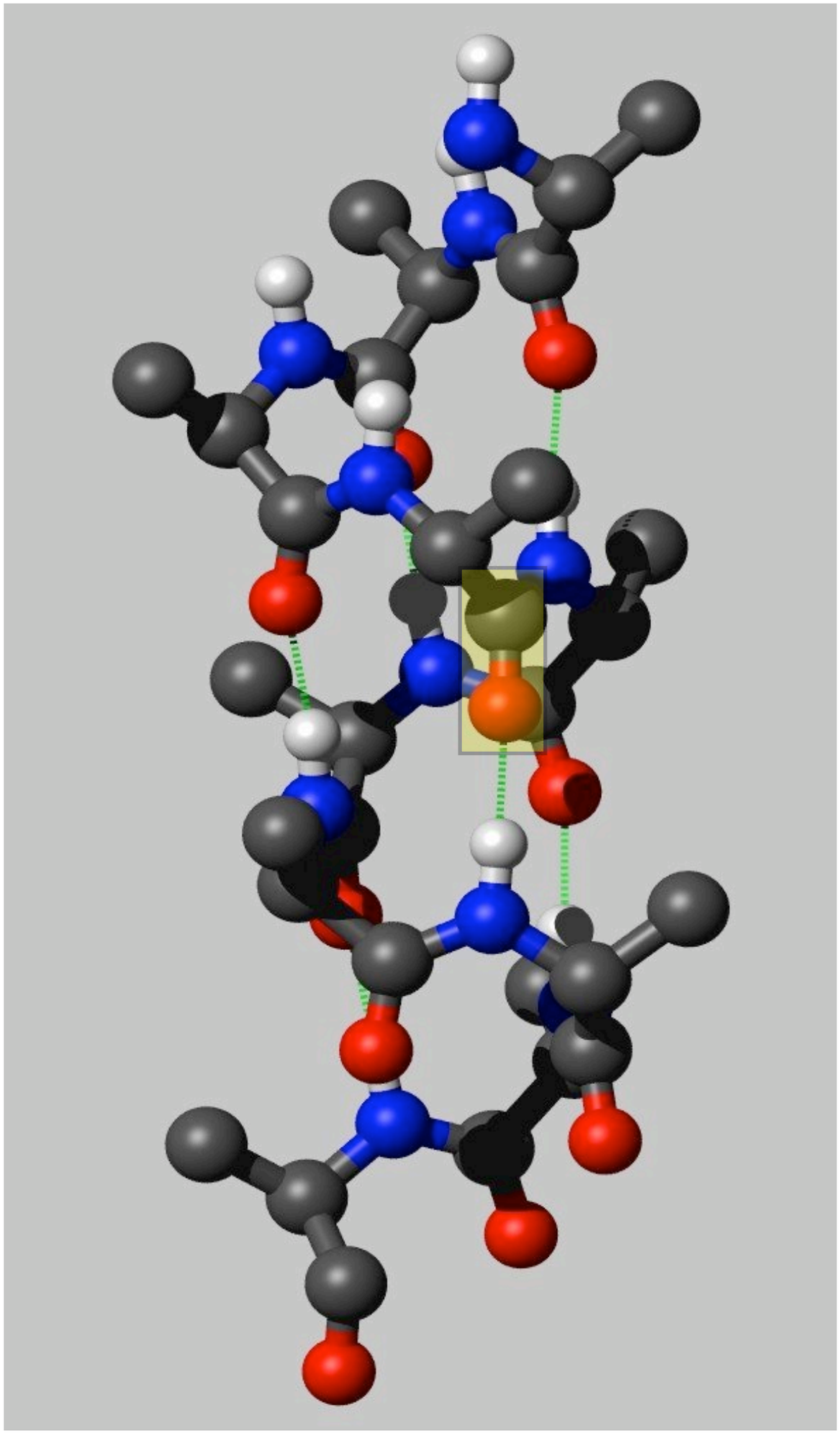
Note that energy trapping is both a nonlinear process and a phase coherent process.

Although globular proteins are complex nanoscale objects, they can be roughly characterized as having an inner core which is not in contact with the solvent and an outer shell which is strongly coupled with the solvent.

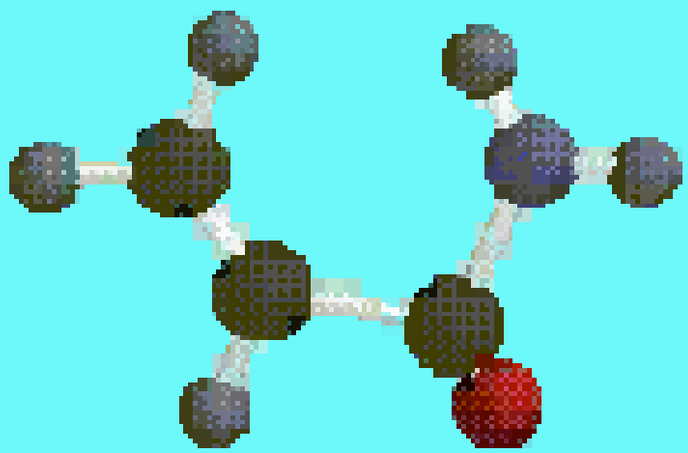




Mb, color coded by Debye-Waller factor S, <x^2> ~ S



The alpha-helix is an important structural element.



The amide-I mode is a C=O stretch coupled to N-H, 6 um (1650 cm-1)

The secret, forbidden, blasphemous question is:

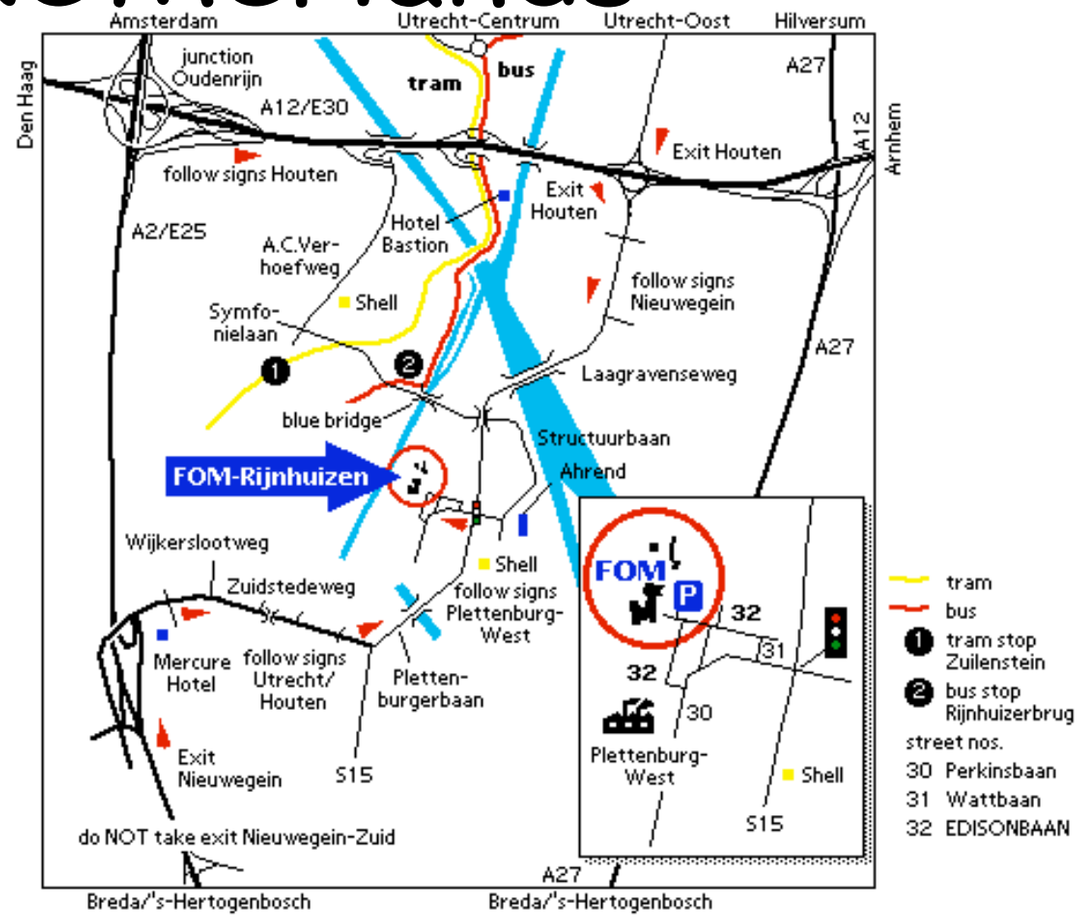
Is it possible for vibrational excitations in the amide I "band" to move along the alpha-helix and self-trap, STORING energy? You can use the language of solitons if you want to, but you will be driven from the Church.

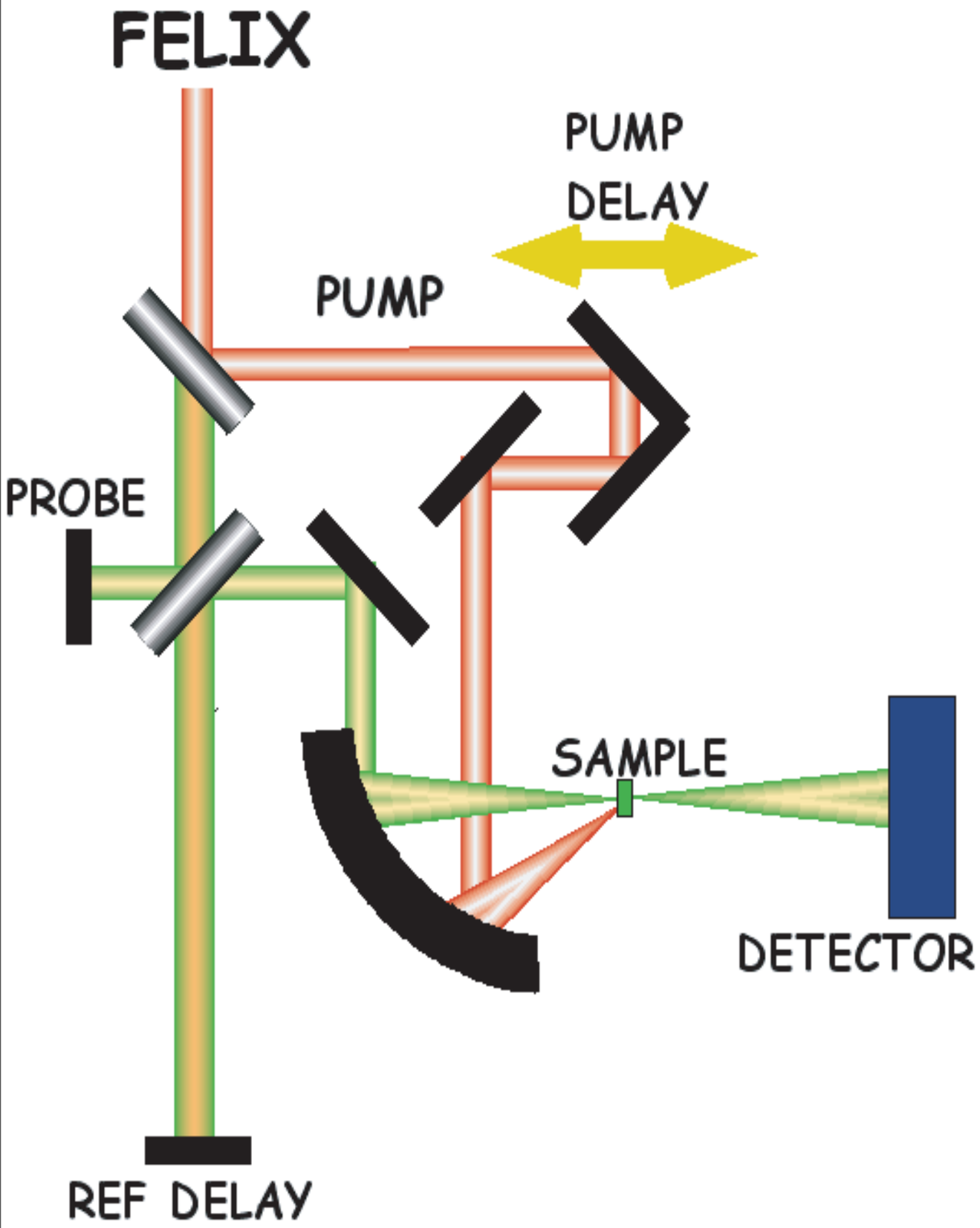
Another name: coherent energy flow.

A sub-text of this talk is a plea for the physics community to be involved with the development (of course) of new light sources but also the application of new light sources, particularly accelerator-based light sources which of course are our intellectual children.

China is involved in the new generation of Free Electron Lasers which is rapidly growing.

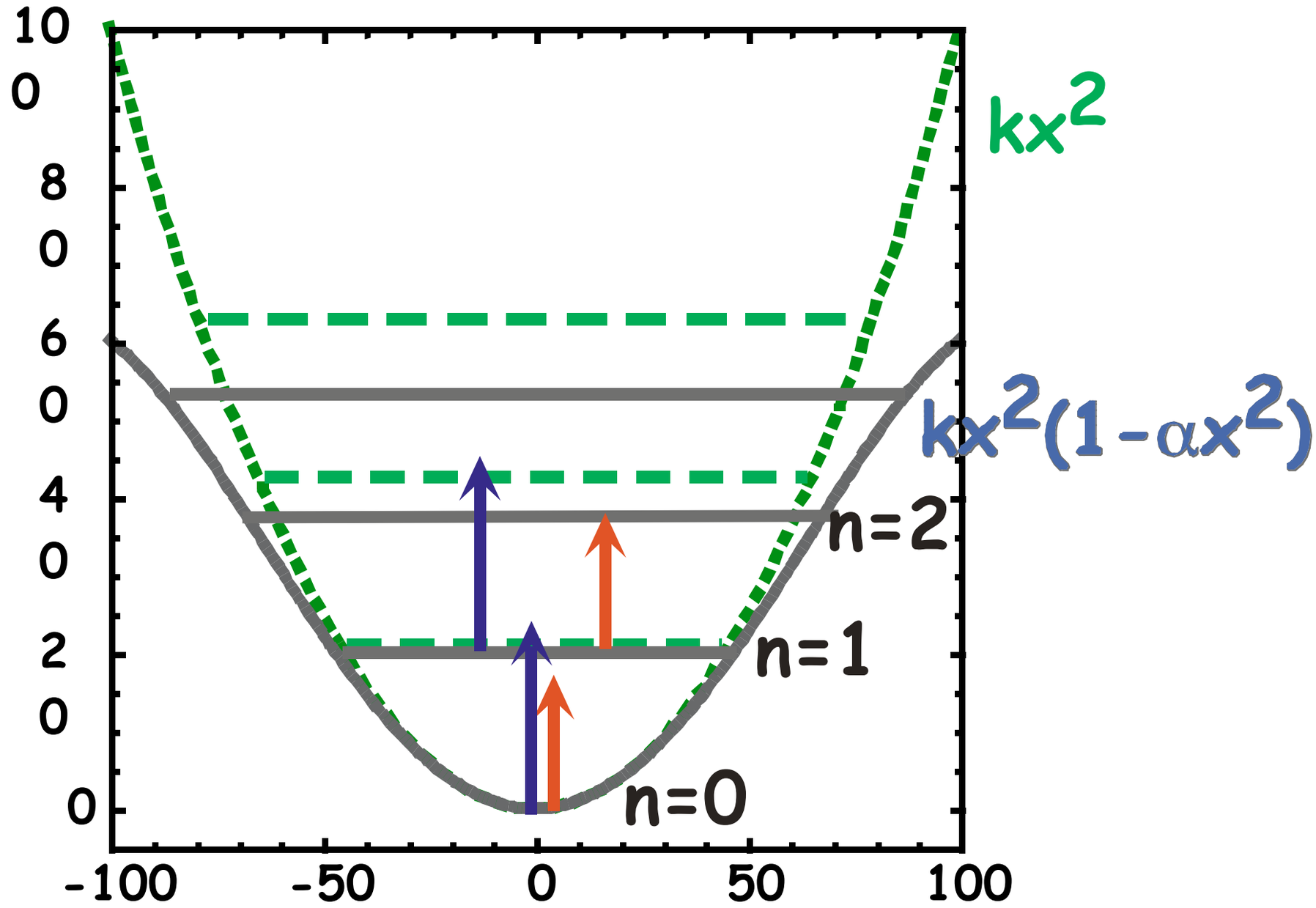
FELIX: the marvelous IR-FIR (3 microns to 100 microns!!!) Free Electron Laser near Utrecht, the Netherlands





Pump-probe experiments are direct probes of anharmonic effects: a harmonic system cannot be saturated. In the IR, you can selectively pump modes.

Short wavelength side (blue): bleach
long wavelength side (red): increasing absorbance



A word or 2 about protein IR spectroscopy.

$$\Delta\nu \sim \frac{1}{T_1} + \frac{2}{T_2}$$

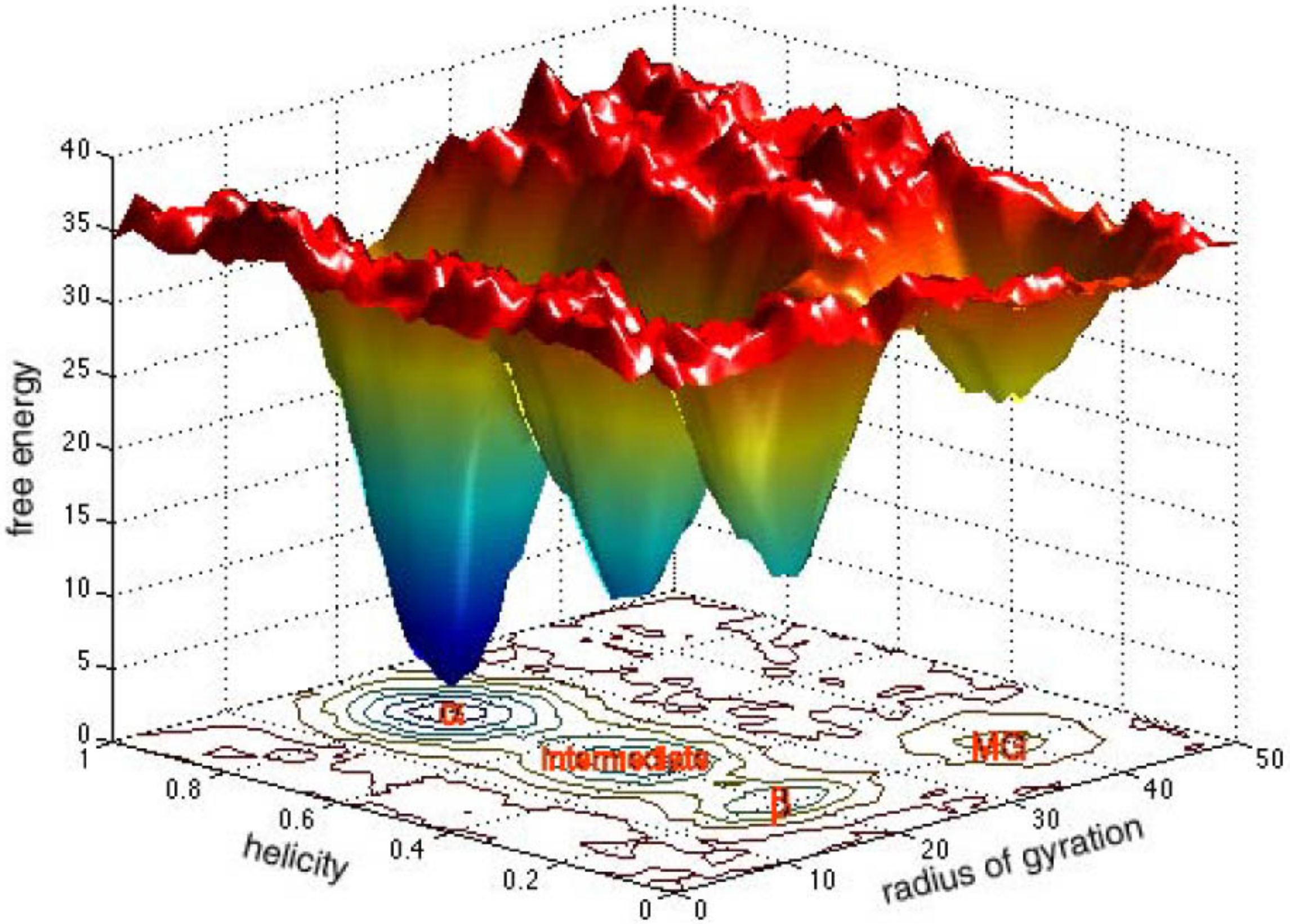
T1= longitudinal relaxation= vibrational lifetime

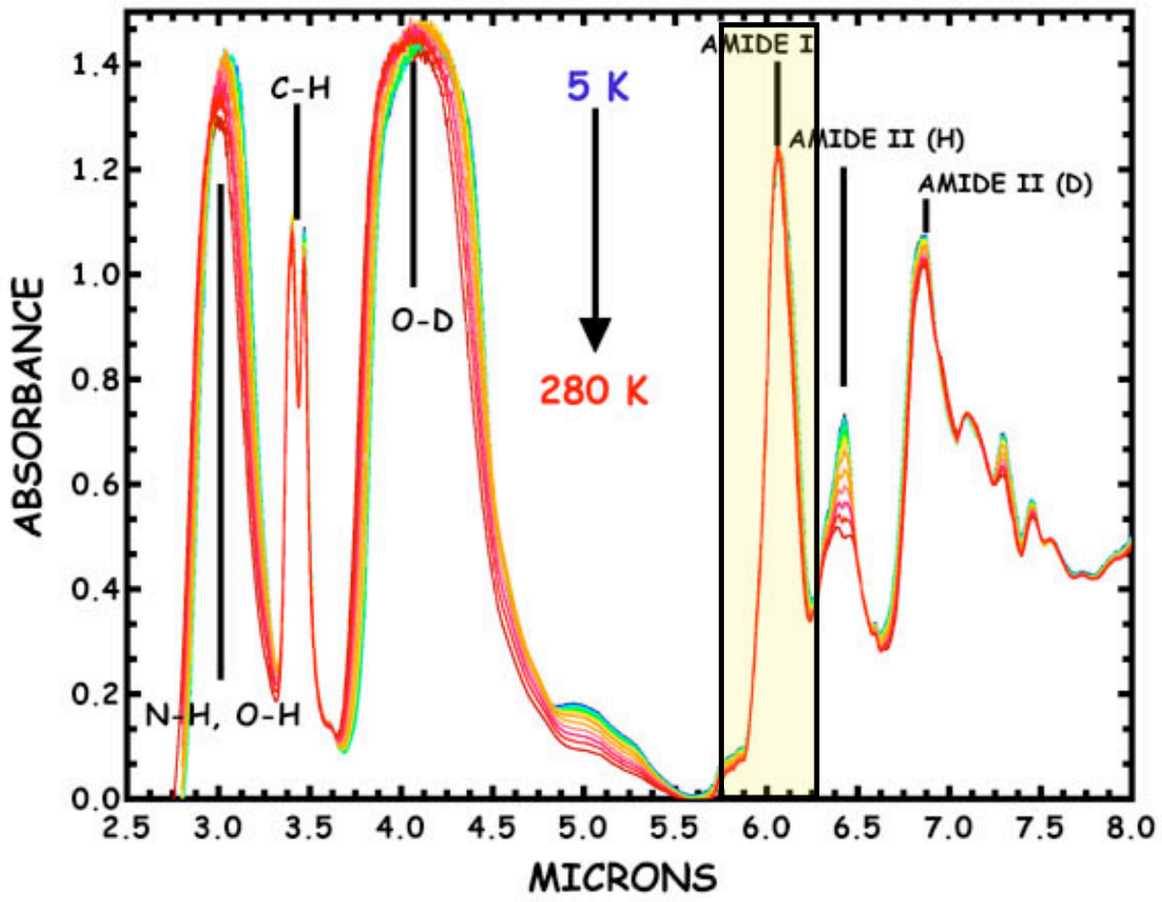
T2= transverse relaxation = dephase time

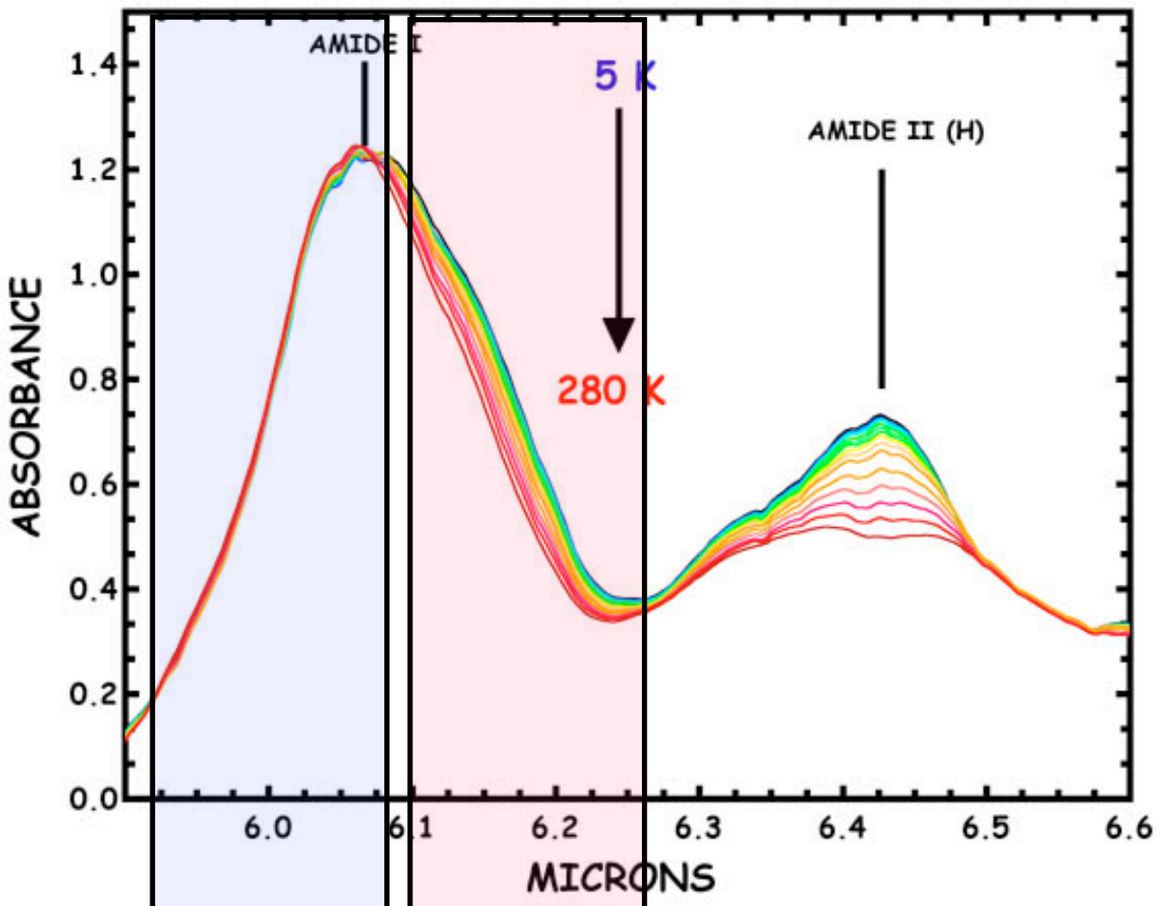
Proteins are complex biomolecules with many modes. You would expect not to find single amide-I line but rather a dense forest of lines, as in a semiconductor

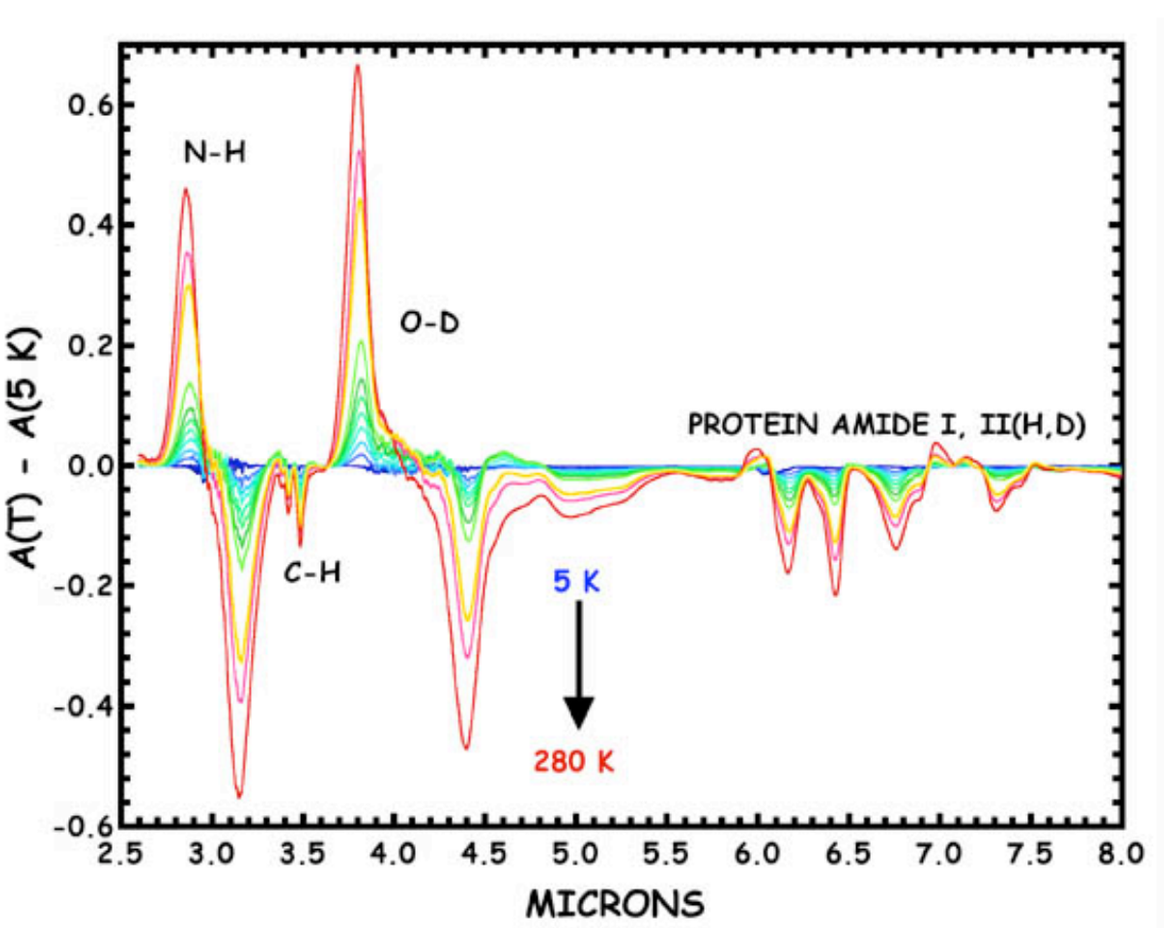
The temperature dependence of the IR bands is a measure of anharmonicity.

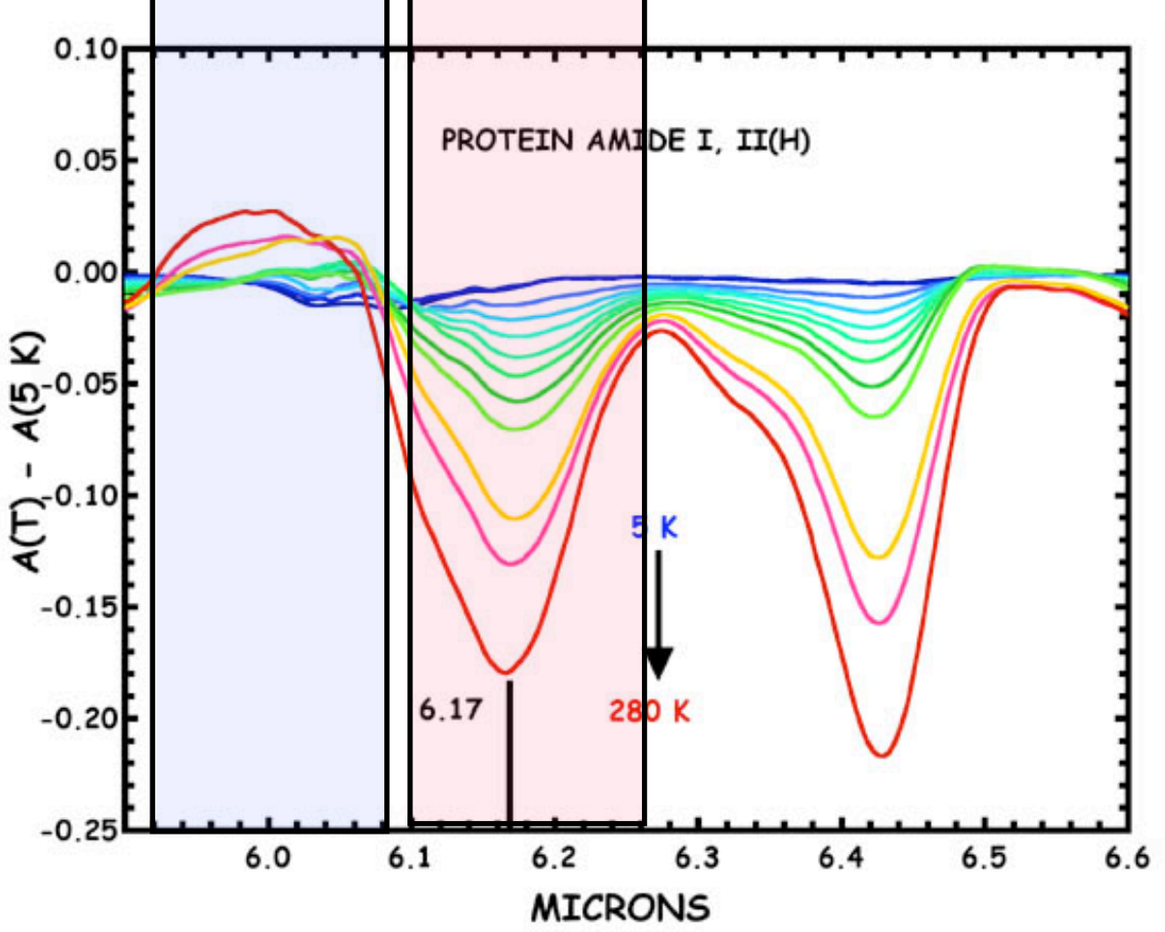
It can take TWO forms: a simple shift of the band as a function of temperature within one local well, giving rise to a derivative difference spectrum, and the appearance of NEW bands, indicating a jump to another local minimum.

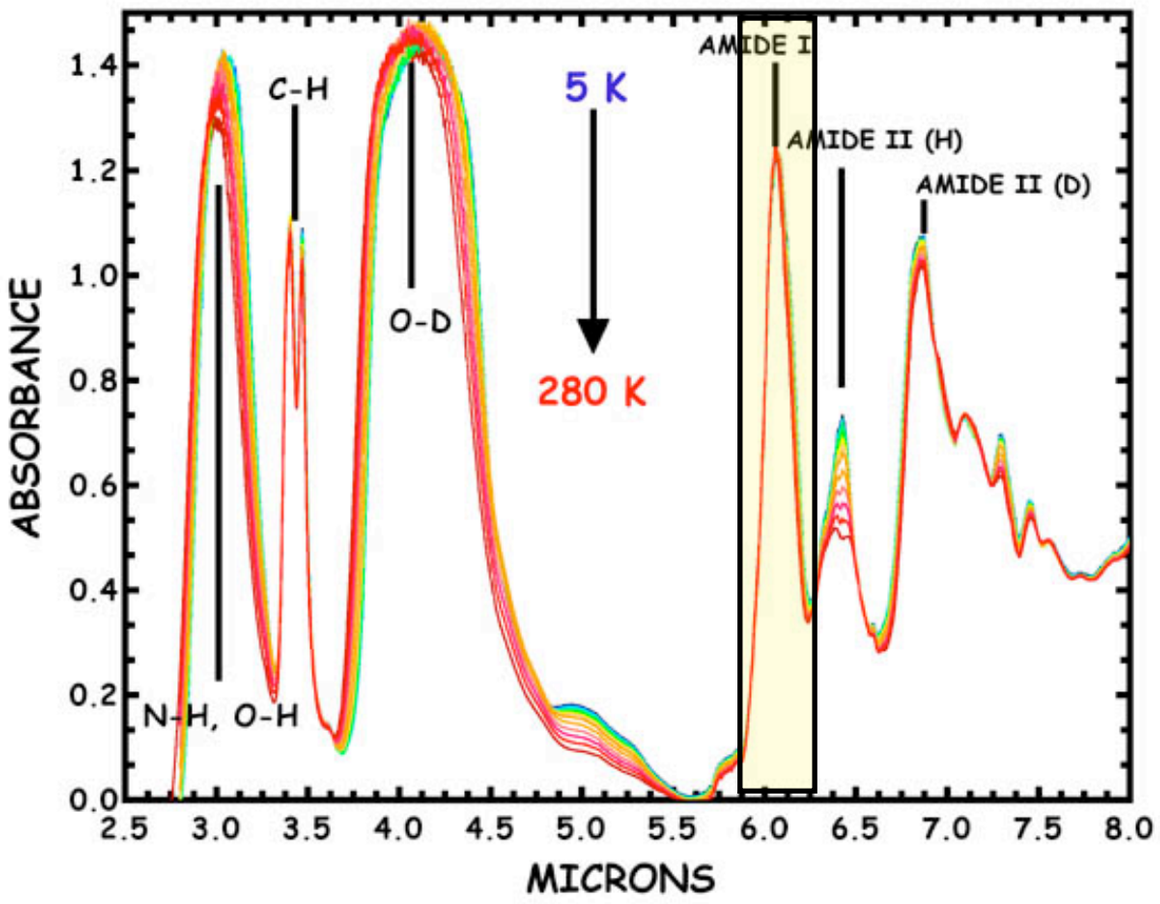

free energy
40
35
30
25
20
15
10
5
0
1
0.8
0.6
0.4
0.2
0
helicity
0
10
20
30
40
50
radius of gyration
α
Intermediate
β
MG

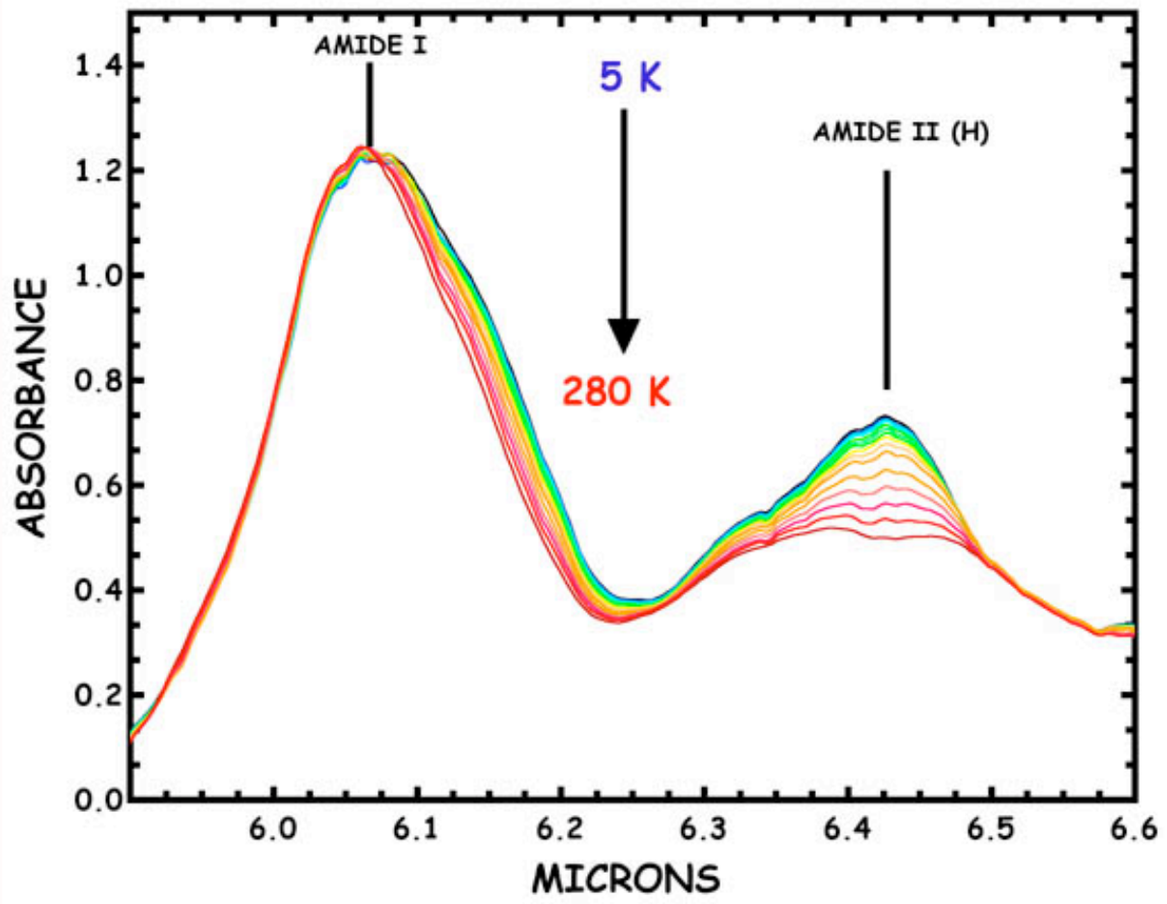

ABSORBANCE
MICRONS
C-H
O-D
N-H, O-H
AMIDE I
AMIDE II (H)
AMIDE II (D)
5 K
280 K


ABSORBANCE
MICRONS
AMIDE I
AMIDE II (H)
5 K
280 K


A(T) - A(5 K)
MICRONS
N-H
O-D
C-H
PROTEIN AMIDE I, II(H,D)
5 K
280 K


A(T) - A(5 K)
MICRONS
PROTEIN AMIDE I, II(H)
5 K
280 K
6.17

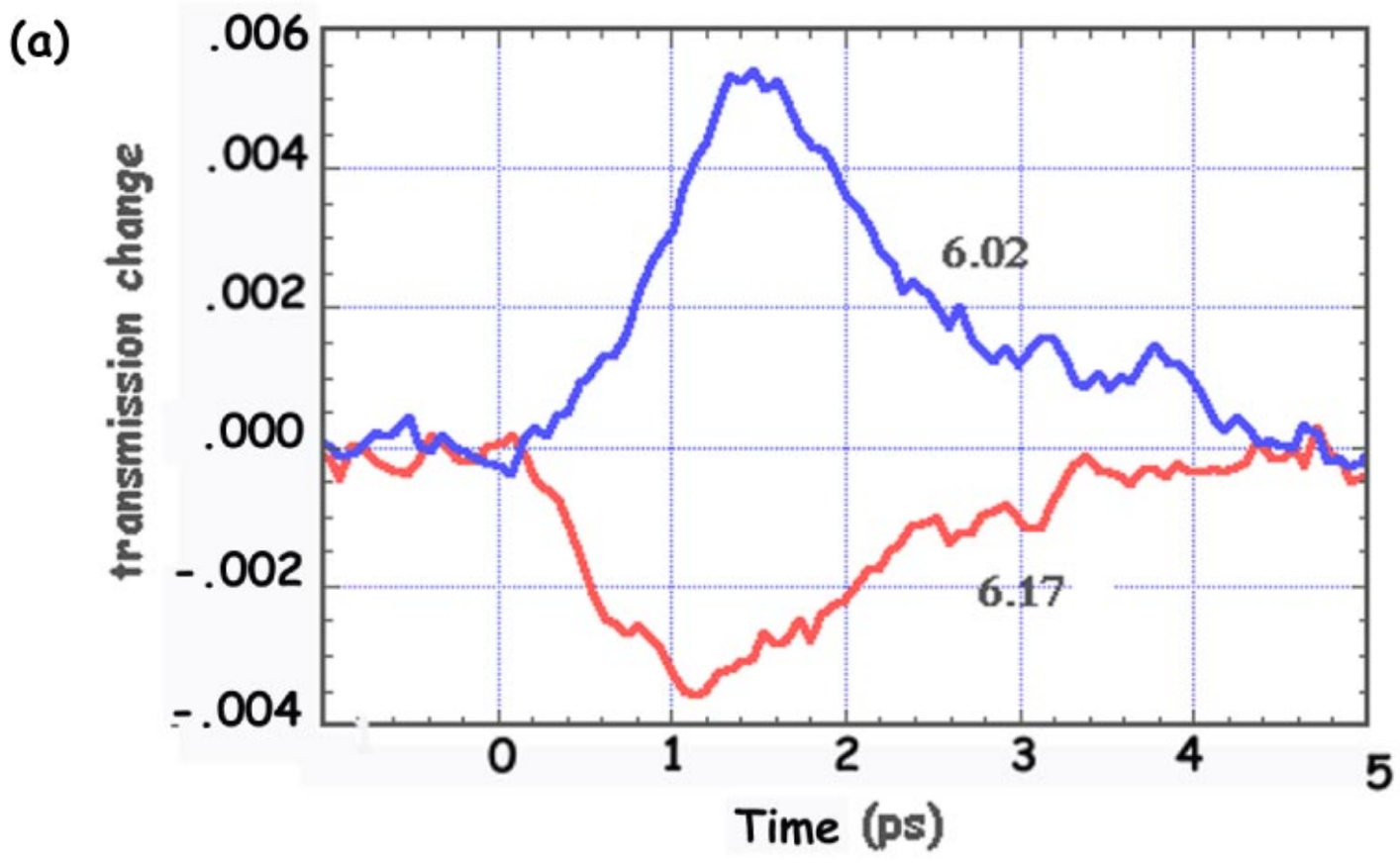


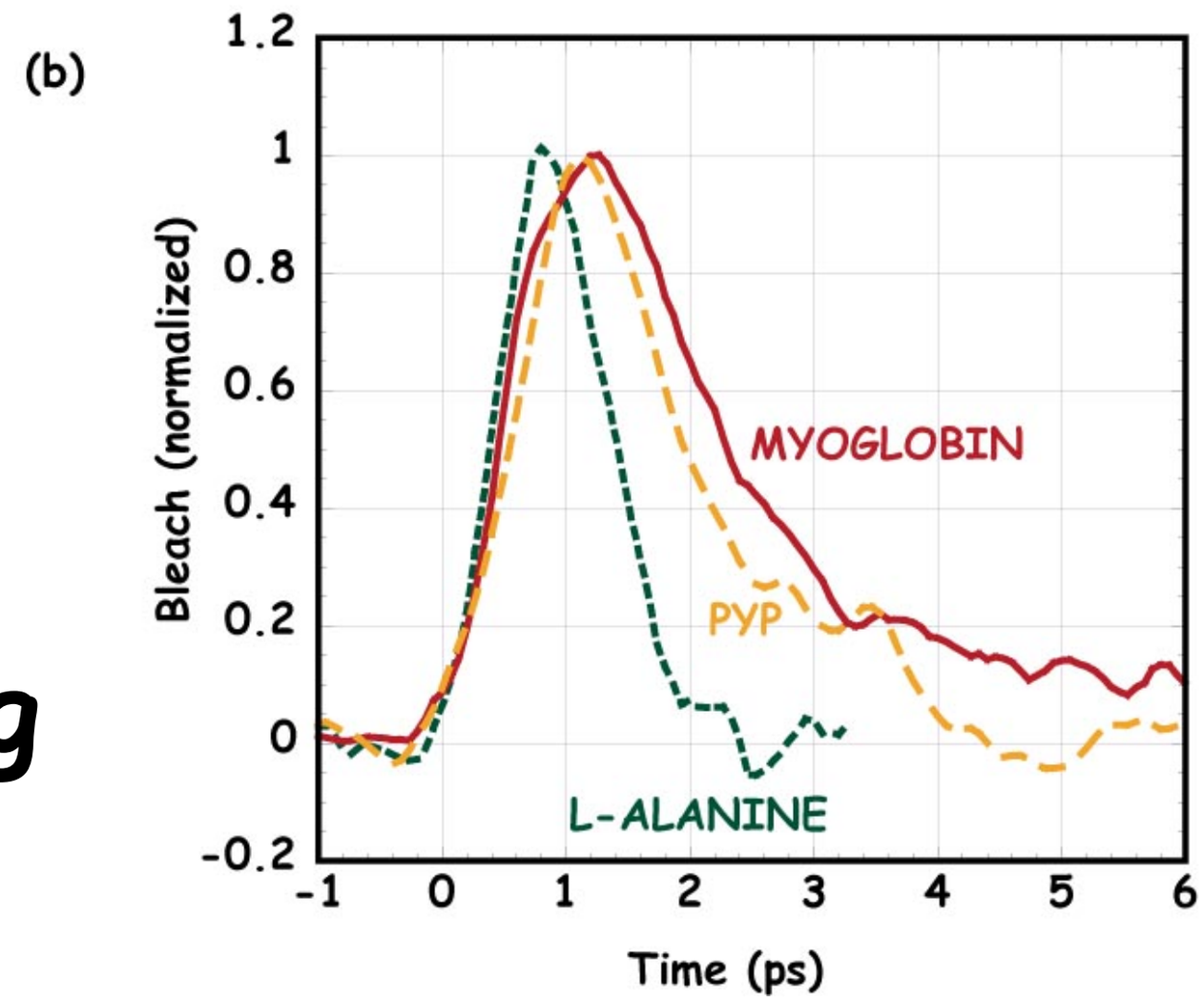


The Q of the amide I band is at least 30, and yet is heterogenously broadened. Hans Frauenfelder et al. did the experiments that showed conformational complexity in 1976, in fact (the energy landscape of proteins).

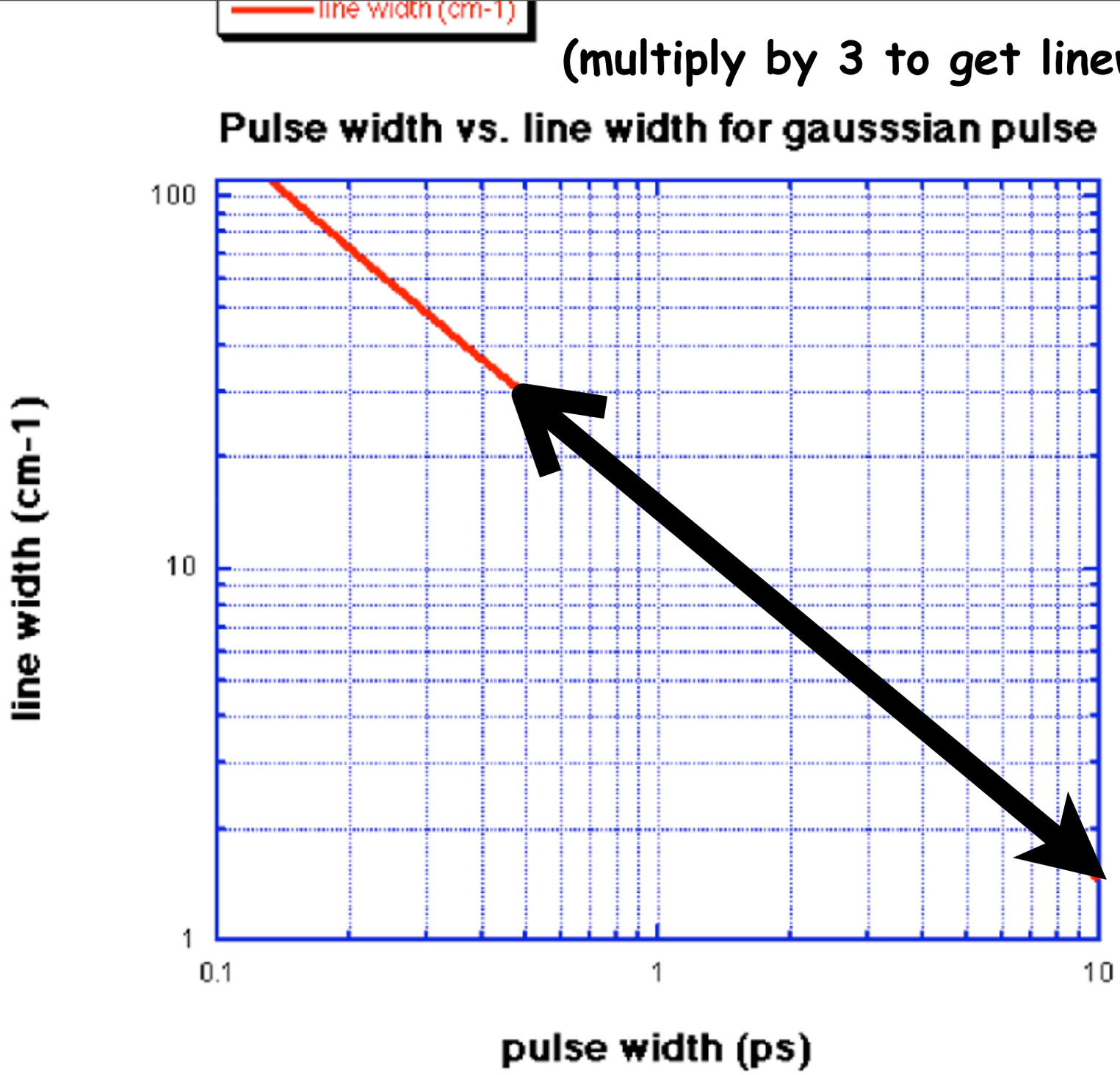
Trying to impress my parents with short pulses: pump-probe decays in the amide I band.

Small, fast, boring. Nothing magic.



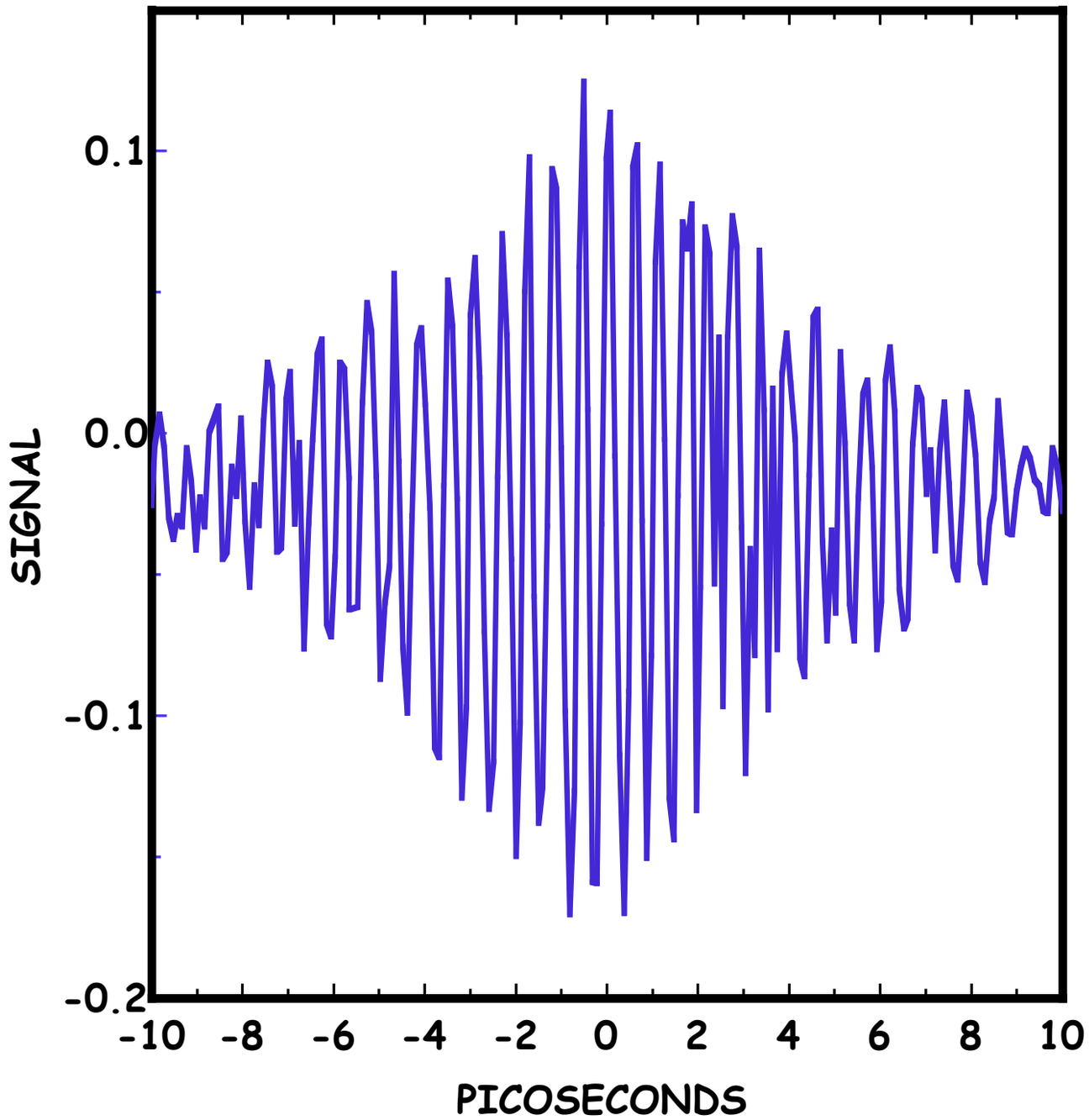


(multiply by 3 to get linewidth in nm

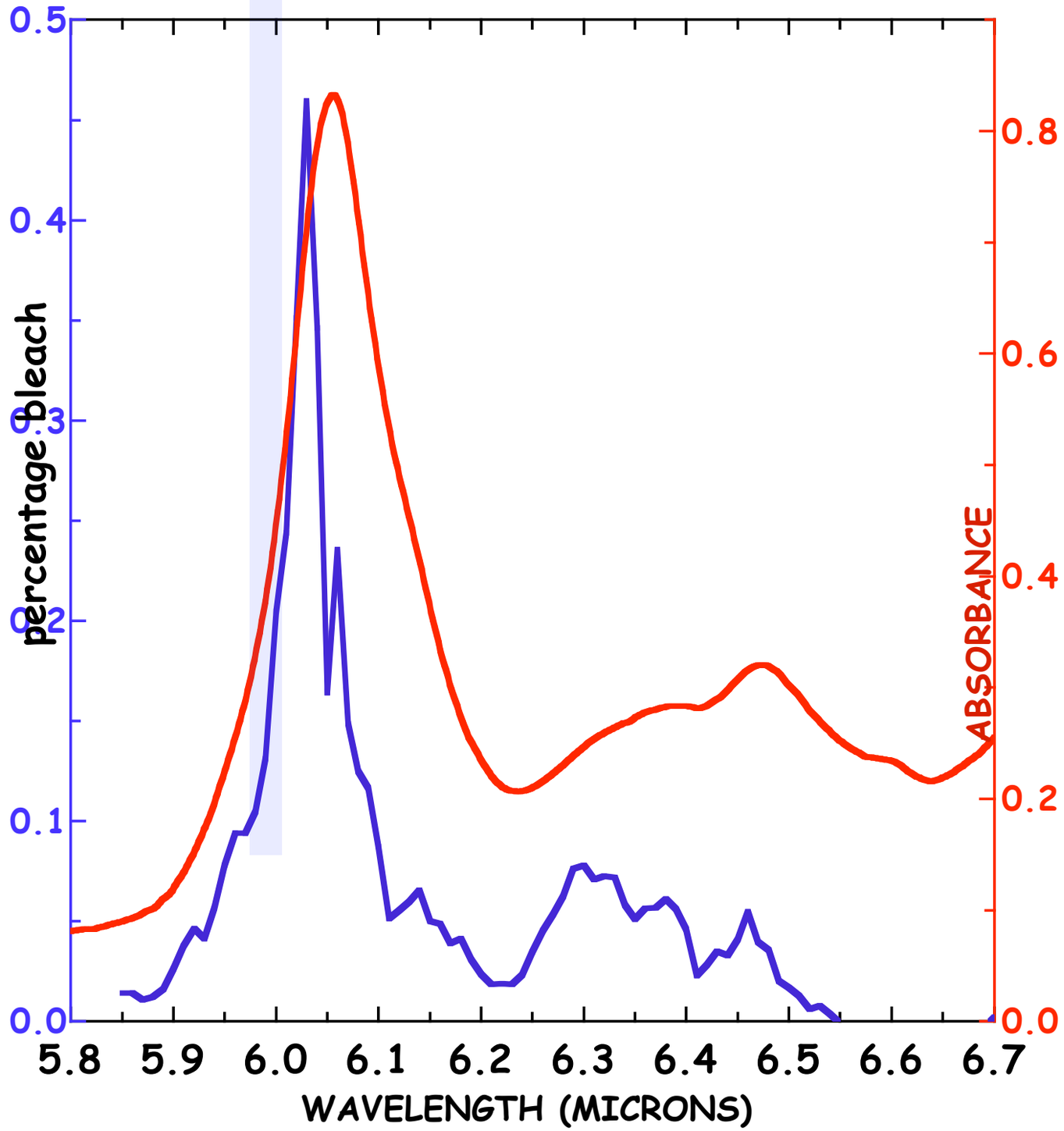


HOWEVER, FELIX is highly unusual in that it lets the USERS muck around with the FEL parameters! Something to do with Dutch liberalism, which isn't what you think it is.

Your parents are not impressed with the words "ultra-fast" in your paper titles, in fact it can be a stupid thing to do.

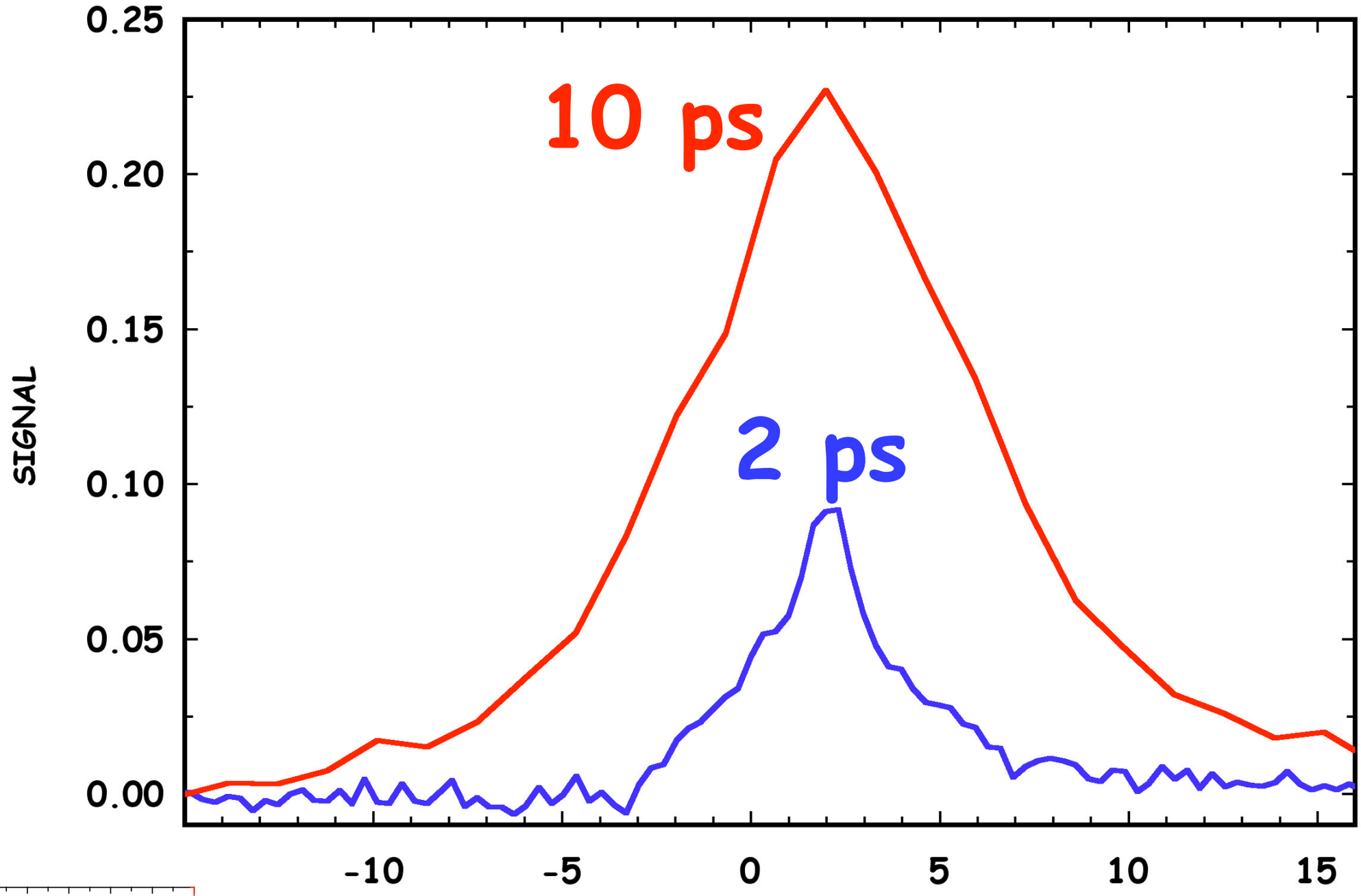


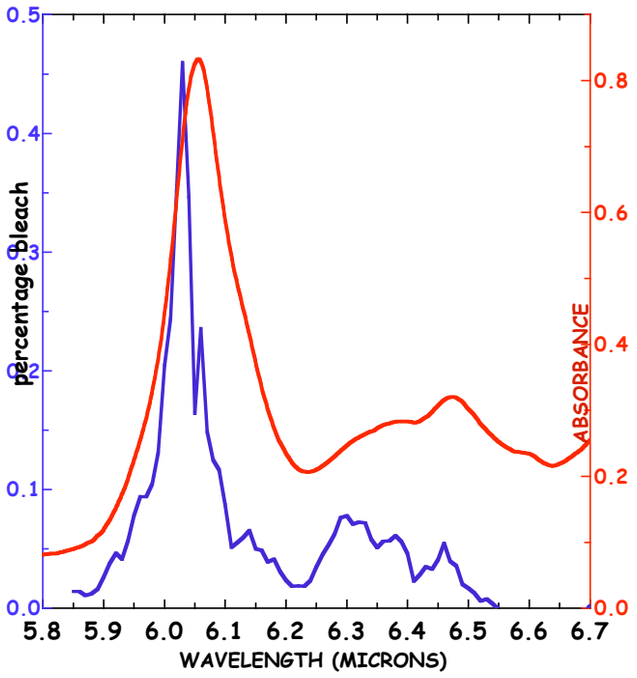
E vs.time of pulse



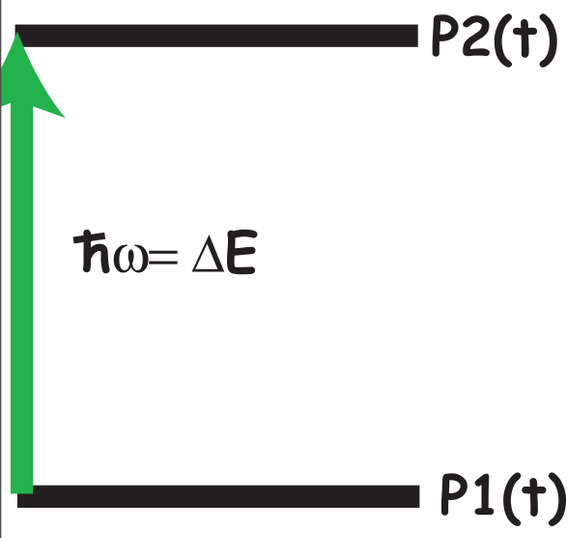
Width is .02 microns, 5 cm-1. Q= 300. This is really sinning in the sense that it implies long dephasing times!

Absolutely gigantic nonlinear signal, 50% transmission changes if narrow pulse is used! If you haven't fought for years with 0.5% transmission changes, you can't know what this feels like to see a huge, narrow signal come roaring out.

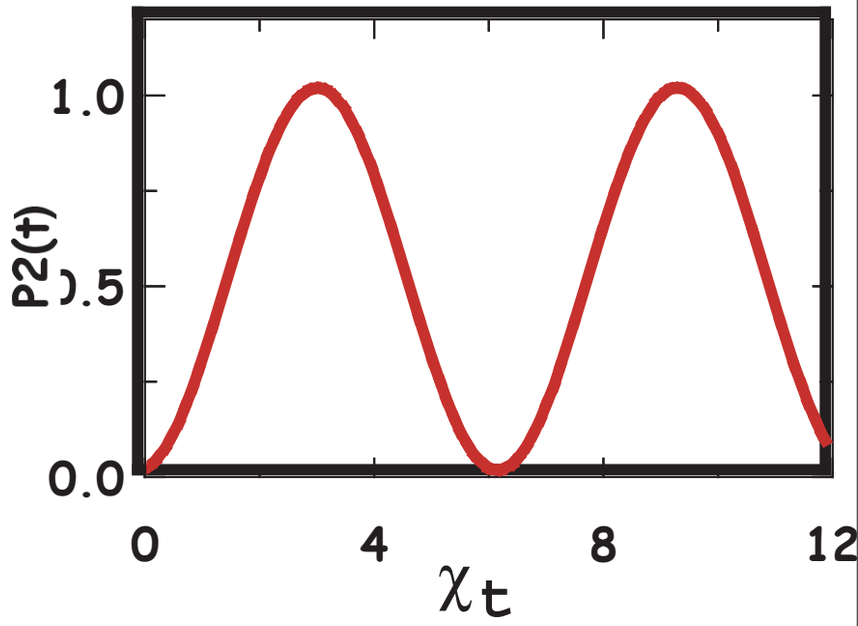




6.05 microns (blue side)



The rate at which the population P2(t) "flops" is given by the Rabi frequency $\chi = \mu E/h$, where μ is the electric dipole moment of the transition, E is the applied electric field, and h is Planck's constant.



2-level system (nothing more nonlinear than a 2-level system!) can completely invert in population, if T2 is long enough.

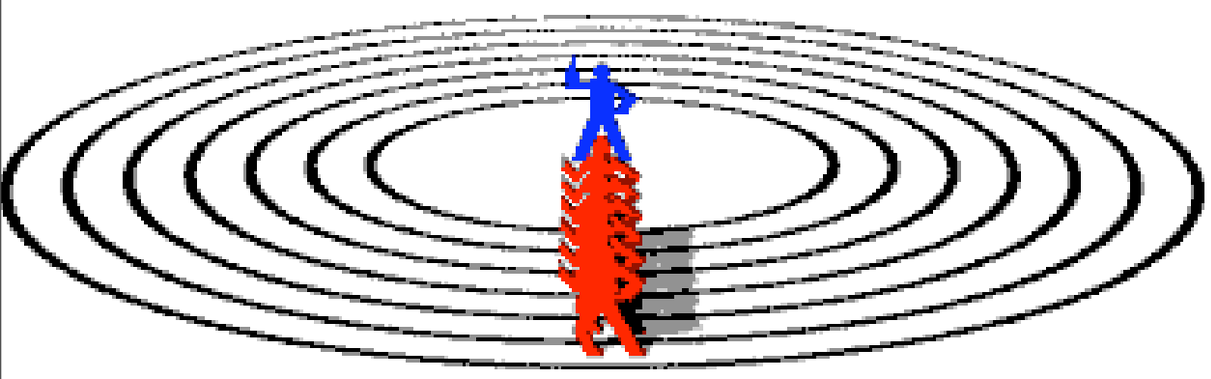
The FEL pump pulse: energy of 1 uJ, a pulse duration of 10 ps, and a focused diameter of 100 microns: optical electric field E of about 10^8 V/m, and a Rabi flopping frequency on the order of 0.1 psec-1, about what I see...

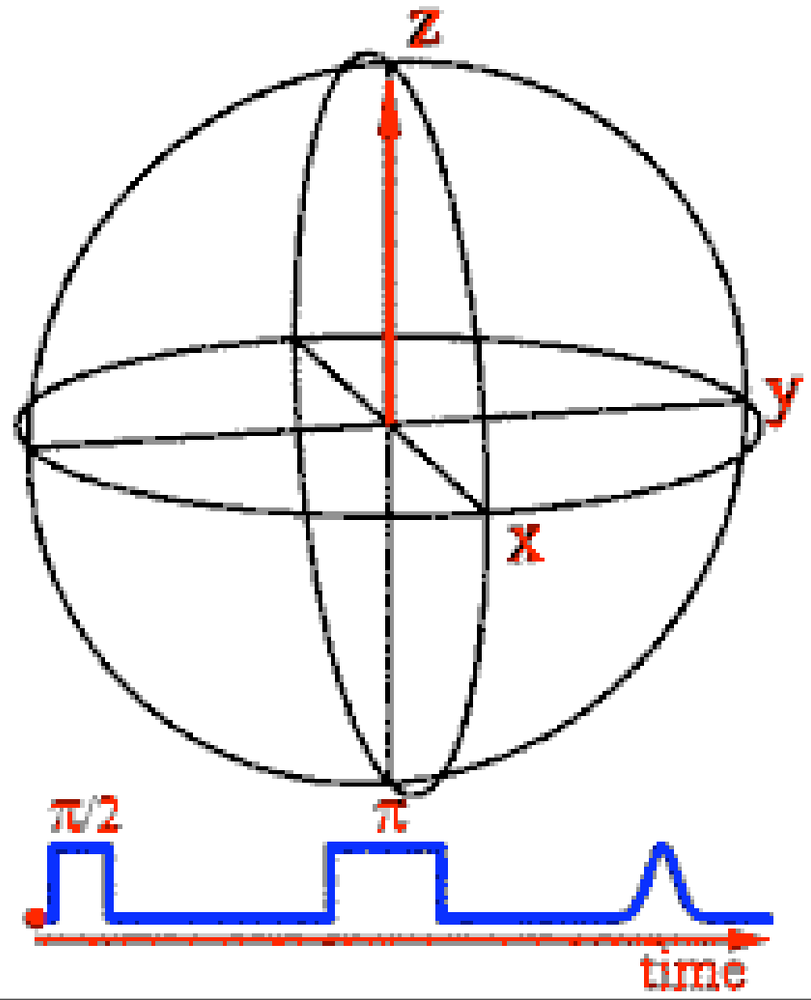
So.....can quantum mechanics and nonlinear dynamics really matter in biology?

There IS a way to probe not only the population inversion that can happen when you pump a resonant two level system (pump-probe), but also the phase coherence necessary for this to happen: photon echo.

Photon echo is a form of pump-probe where you look where there is no light..

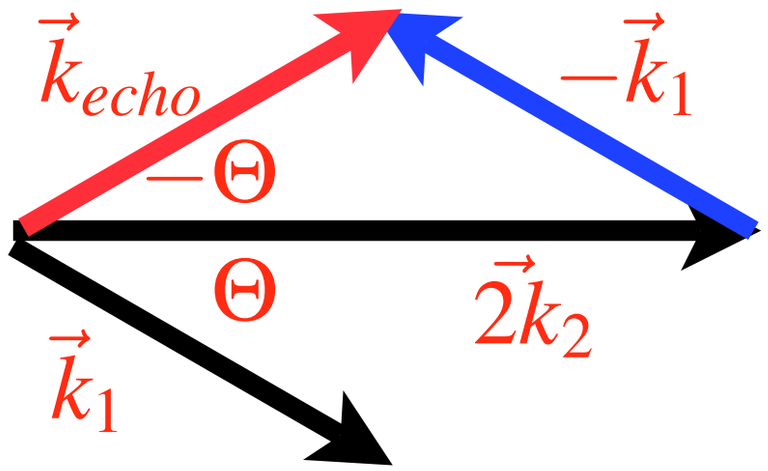
Spin echo was discovered BY ACCIDENT by Hahn. First feed pi/2 pulse, at time T feed in a pi pulse. IF the spins maintain their phase coherence, at time 2T the spins re-align and out pops the echo, from nothing. Requires long T2*.



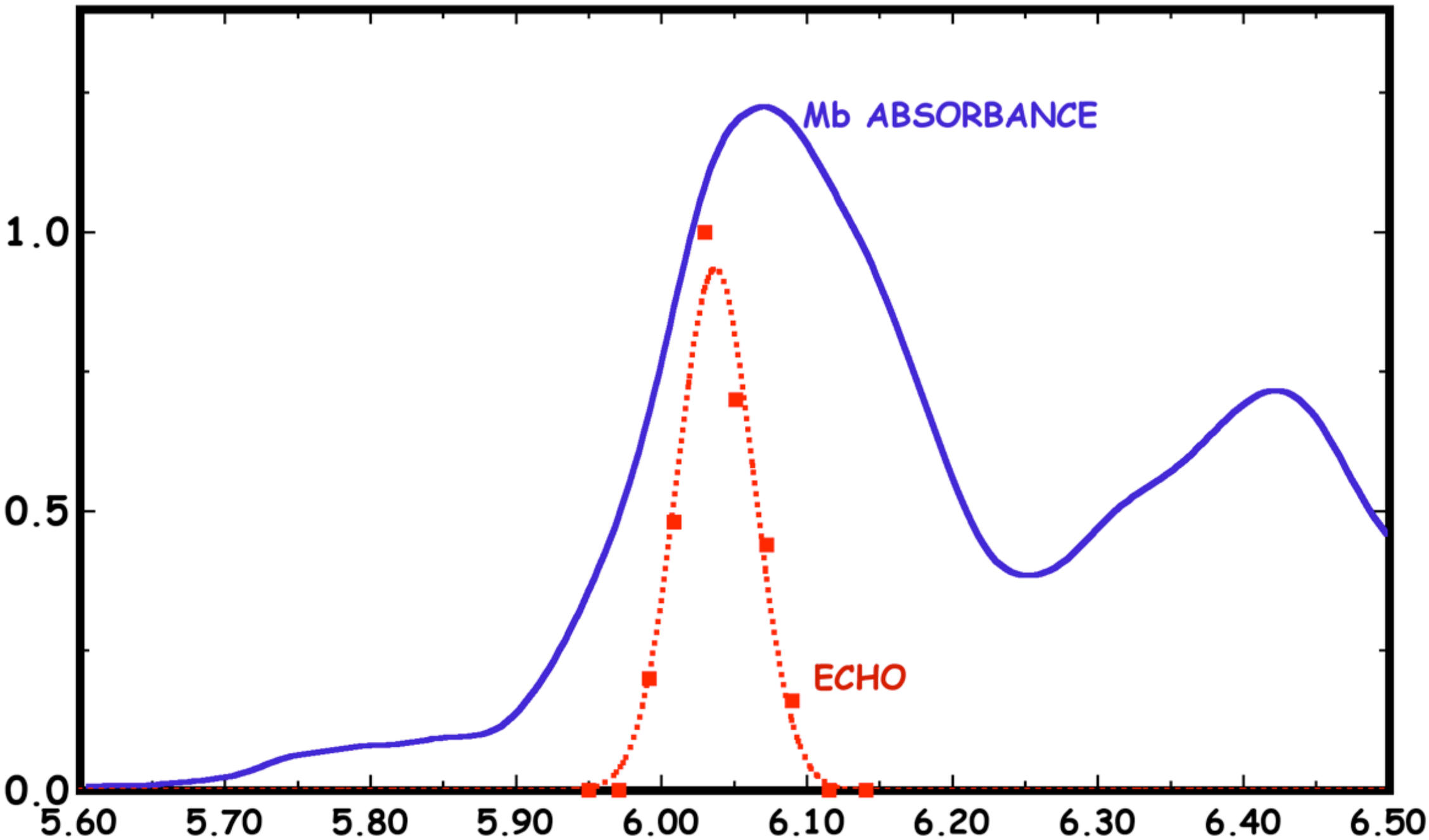


Photon echo is the exact analogy mapped over to electric dipole moments, and one sees a burst of light from nothing if the dipoles retain phase coherence. Since we use photons from a laser beam carrying linear momentum:

$$\vec{k}_{echo} = 2\vec{k}_2 - \vec{k}_1$$



In fact, there is SOMETHING that looks like a narrow photon echo exactly where the narrow pump-probe state was!

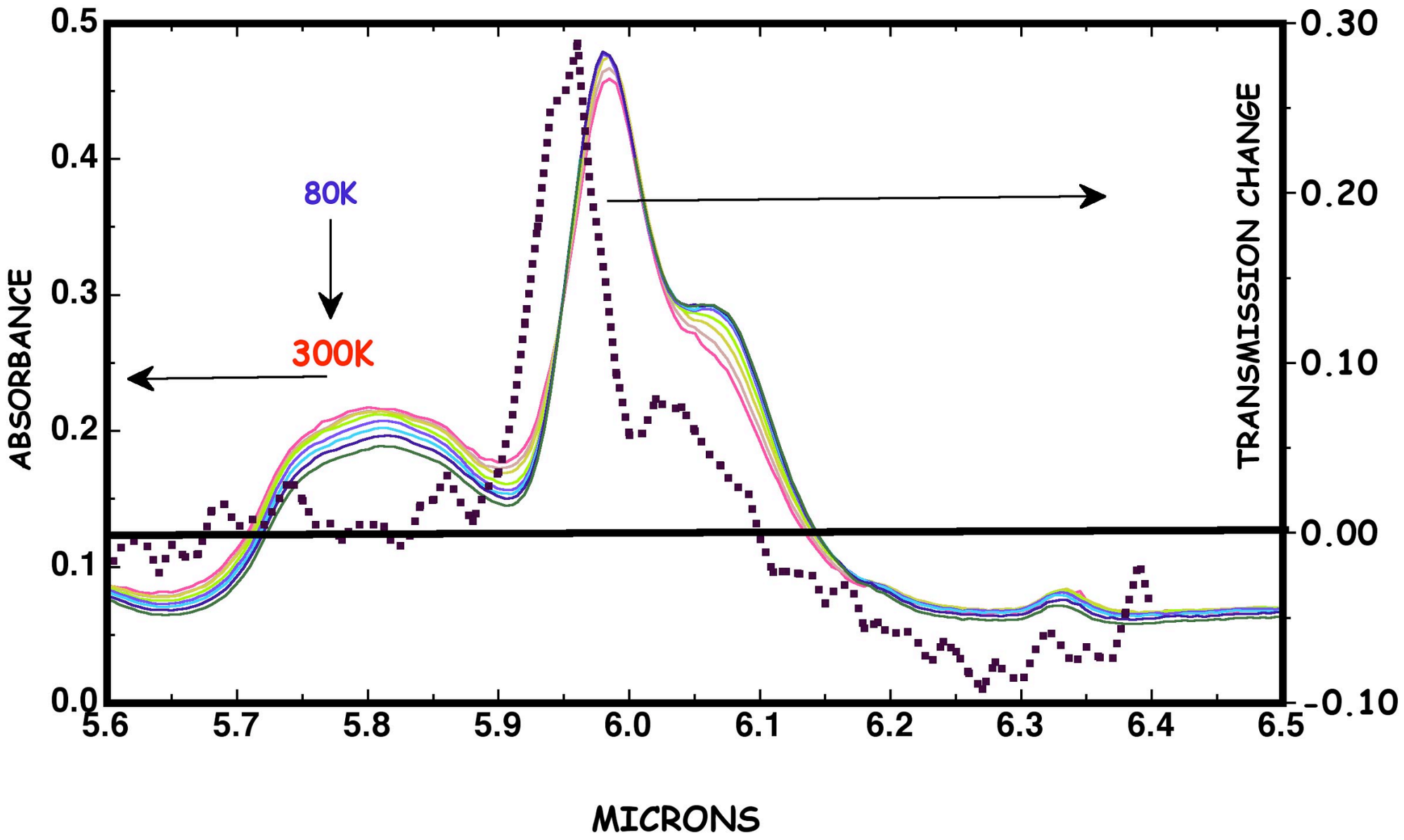


There are problems with interpretation of this pump-probe signal as due to a long-lived self-trapped state:

1) The signal is basically symmetrical in time around the maximum: more indicative of a coherent grating scatter than a long-lived state.

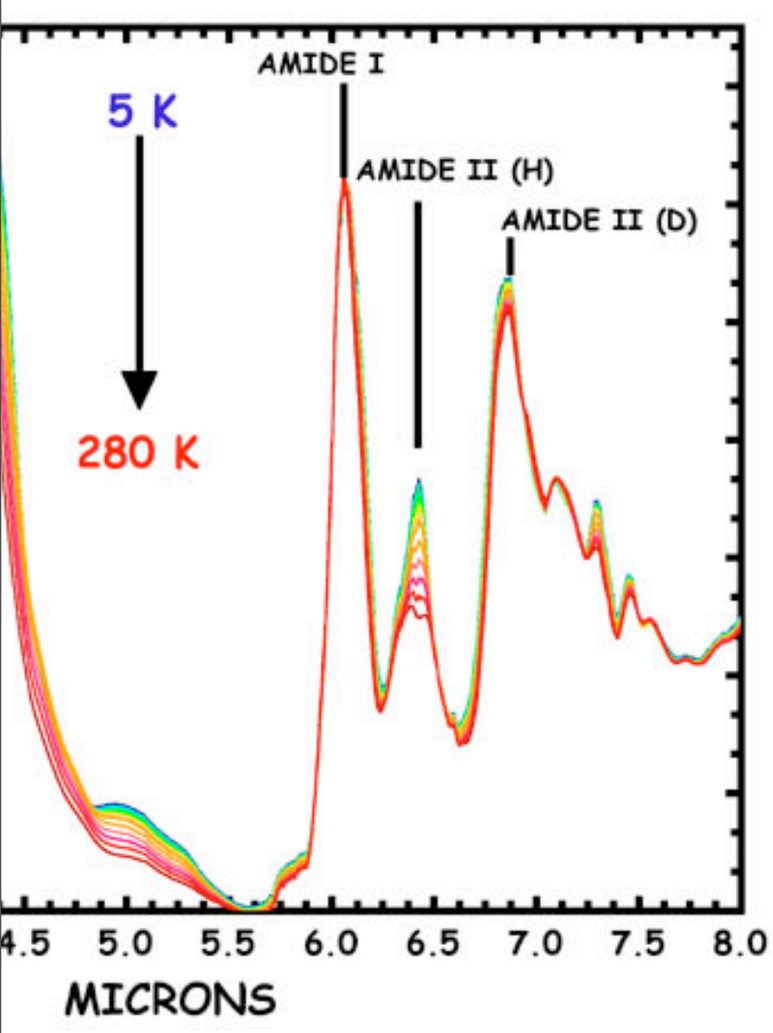
Origin of my big fight with my Dutch friends. I was called an asshole, Dutch will do this only when really provoked.

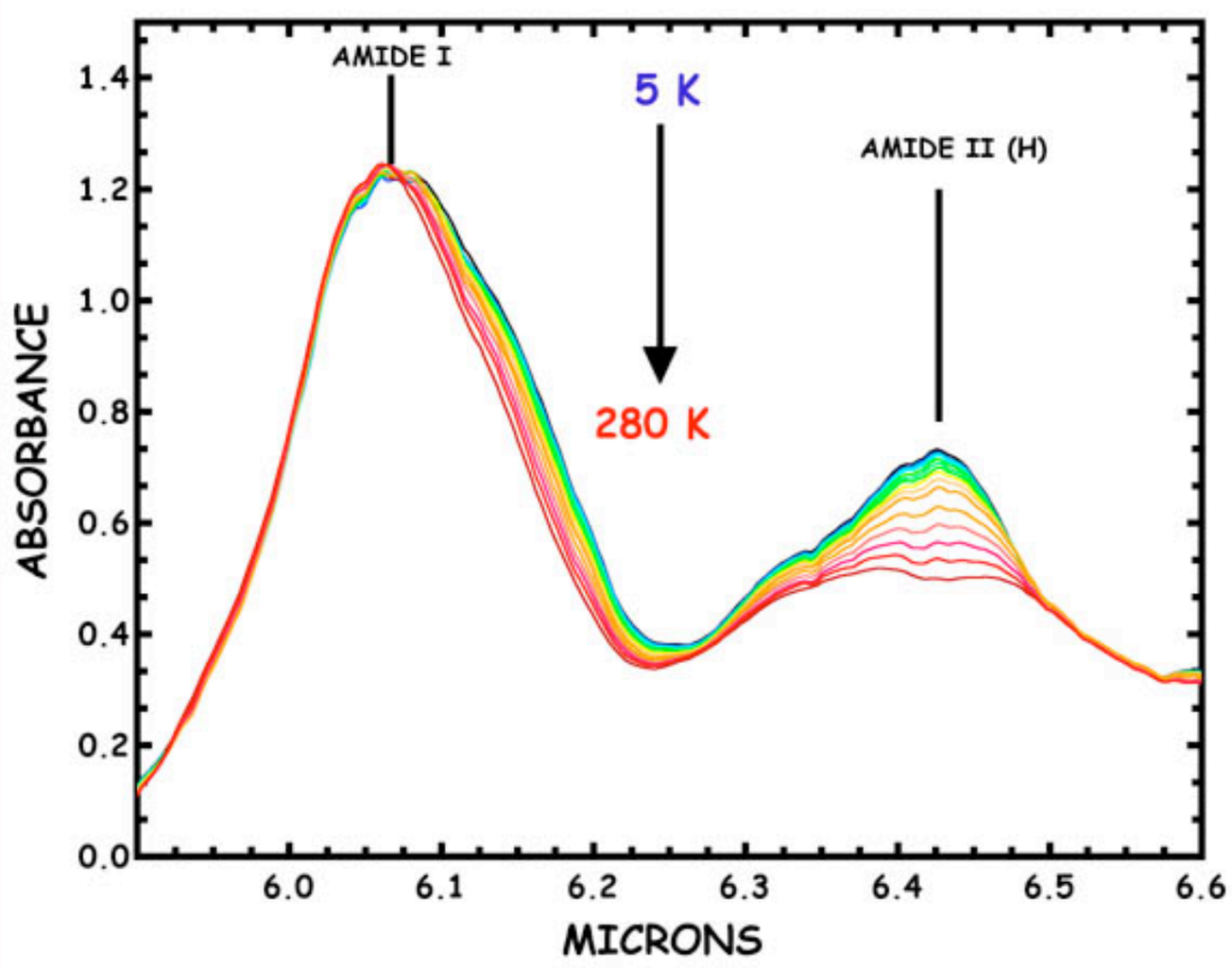
2) Even simple amino acids have similar signals, not a consequence of collective states in the protein.



I still am not 100% sure where I went wrong, but I think I did not appreciate the consequences of the Kramer's-Kroenig transform:

$$\epsilon_1(\omega) = 1 + \frac{2}{\pi} P \int_0^{\infty} \frac{\omega' \epsilon_2(\omega')}{(\omega')^2 - \omega^2} d\omega',$$

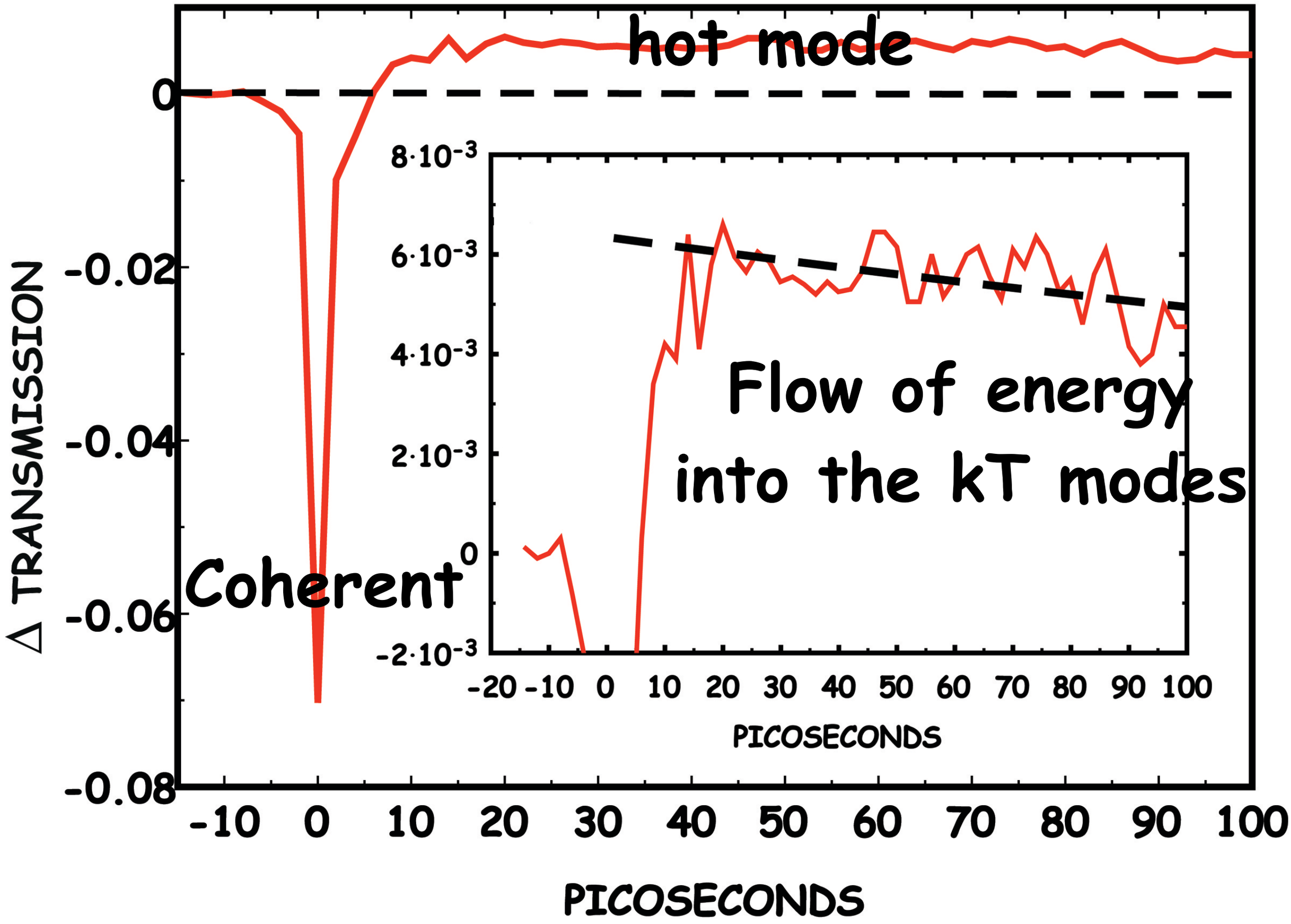




But, it is not even wrong...

At a deeper level, most protein dynamics are thermally activated, and the mid-IR vibrational levels I am pumping are never reached in normal biological reactions, and so even if there are long lived, narrow amide-I states they may be well irrelevant in biology. Taken me a long time to realize this, drugged by the intoxication of theory models..

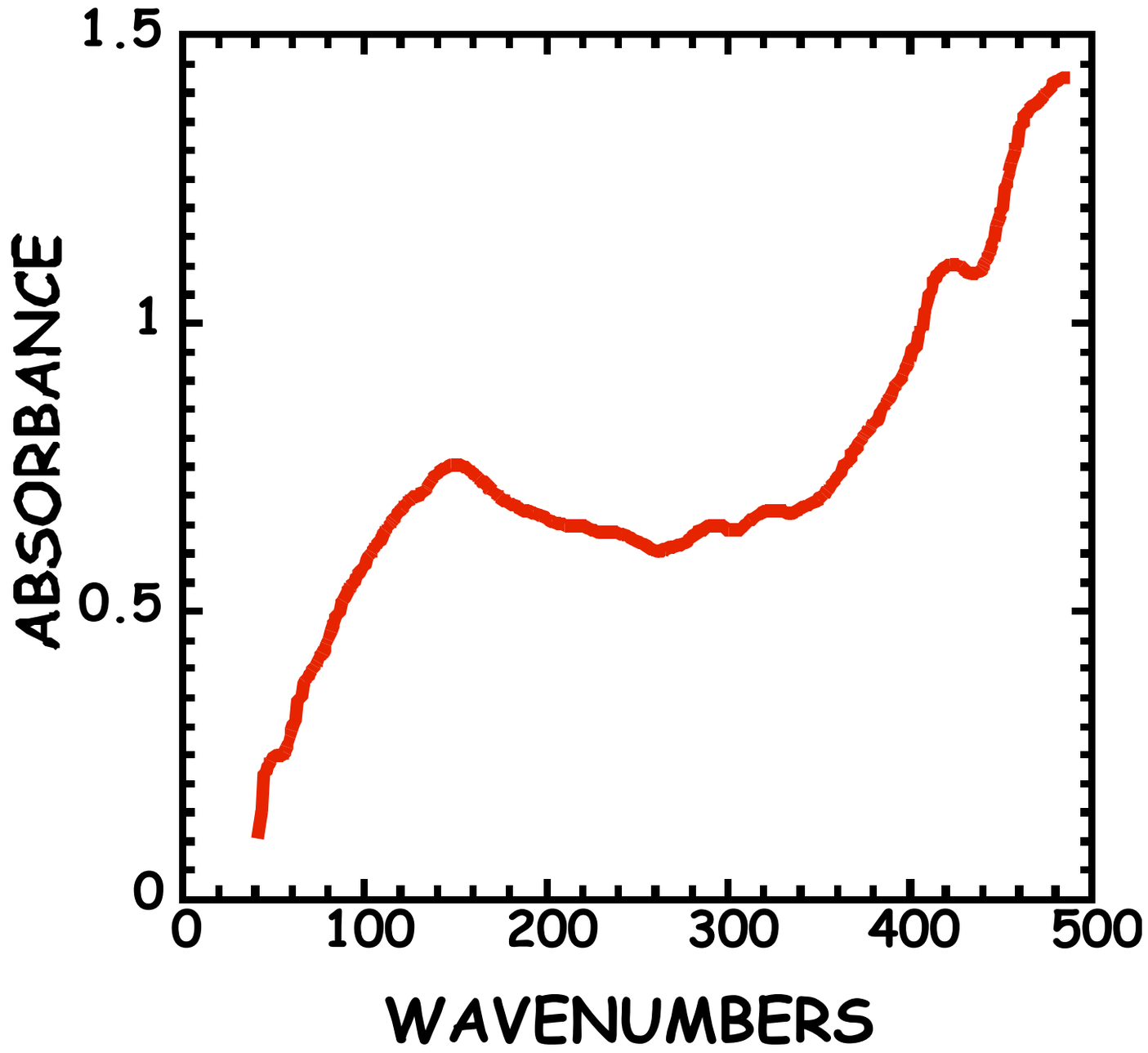
but.....


hot mode
Coherent
Flow of energy
into the kT modes
Δ TRANSMISSION
0
-0.02
-0.04
-0.06
-0.08
-10 0 10 20 30 40 50 60 70 80 90 100
PICOSECONDS
8·10⁻³
6·10⁻³
4·10⁻³
2·10⁻³
0
-2·10⁻³
-20 -10 0 10 20 30 40 50 60 70 80 90 100
PICOSECONDS

Now, if this is right then the "cooling time" of a protein into the normal mode continuum should be about 500 ps or

so, a long time...weakly coupled

As you might expect, the FIR spectrum of a protein is a broad "continuum".



BORING!

A BLOB!

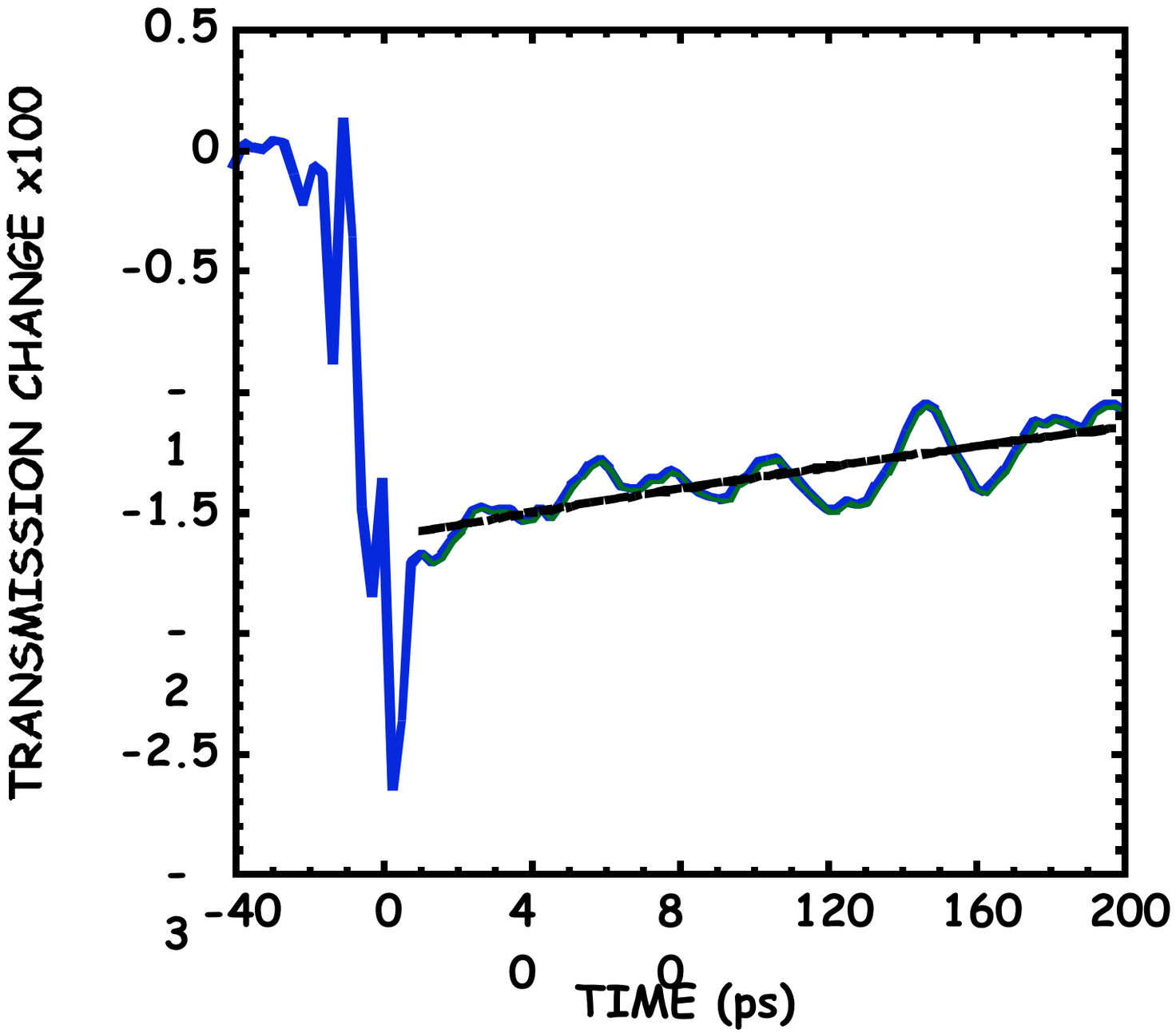
If the band of modes at 150 cm-1 was transform limited, lifetime would be about 100 fs.

Take NOTE!!!

These bands are broad, should have sub-picosecond T1 lifetimes! BUT, the normal mode density is VERY high and the conformational density complex, so linewidths here are NOT necessarily a measure of true T1 times. We don't know T2, we don't know T1, we don't know the anharmonicity coupling.

One of the great beauties of FELIX is the ability to seamlessly reach FAR-infrared wavelengths with picosecond high energy pulses. The collective modes are the pathways between conformational states in proteins, and are the "reaction coordinates" along which these nanomachines must move as they work.

Here is the experimental result for FIR pump/probe on bacteriorhopsin at 87 microns (115 cm^{-1}). Do you believe it? It is a very strange result. Lifetime of 500 ps= Q of about 300. You should be worried.



However, if indeed collective mode relaxation, through anharmonic coupling, is the pathway of protein conformational dynamics then this result says that the characteristic fundamental time in protein relaxation is about 1 nanosecond.

This becomes the "speed-limit" of movement along the protein energy landscape caldera floor.

So.....are the FIR modes of proteins a lot more decoupled from the solvent than one would guess? Are the T2* times really long? Is a protein more of a quantum mechanical machine then one would have thought?

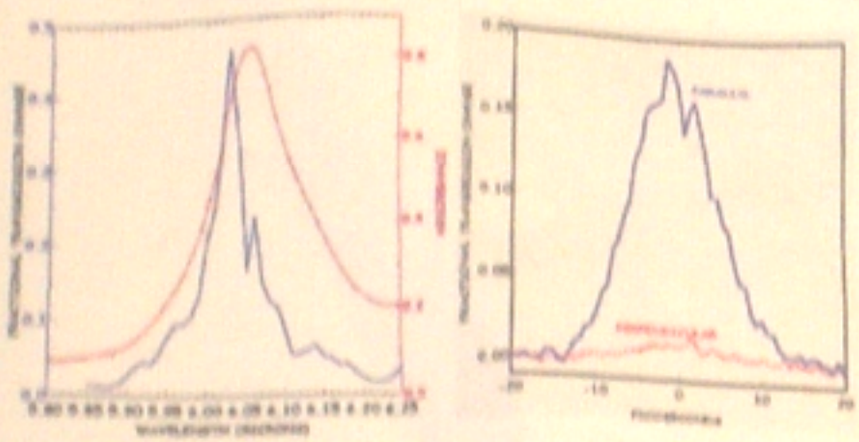
I don't know.

A fundamental experiment in the FIR that has never been done in a protein:

Photon echo in the FIR at the ps time scale. What are the dephasing times of the collective modes? True line widths? Temperature dependence?

My Sinderklass day farewell shirt

Don Austin
(uncle Bob)



the Dutch Windmills

the fight

Paul Gustave Doré (January 6, 1832 – January 23, 1883), a French artist, engraver, and illustrator.

and the happy end !

lance

Well, I am trying to figure out how high my abuse level is (it is pretty high but not infinite).

There may be more to this story someday, maybe sombody here will pick up the lance.....

But, these questions would have never been asked and the experiments never done without that Dutch FEL. The new FEL-based light sources will be wonderful sources of coherent radiation from the X-ray to the FIR, so I hope one of you young kids picks us the lance!