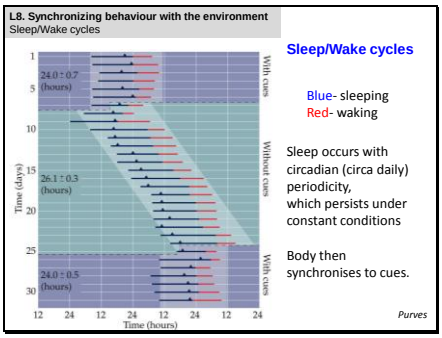
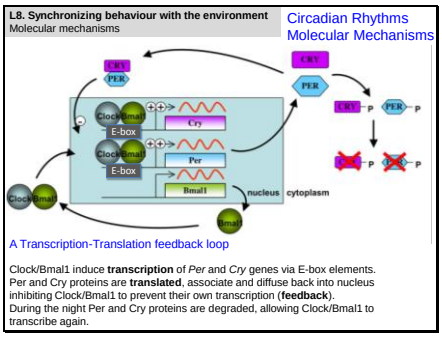
Slide 8



Person put in ww2 bunker with no external cues (light) but given other cues such as person interaction/radio/tv
With cues- eg radio etc
Without cues- remove external cues, takes time to adjust each day, wakes a little later but still has **free running rhythm** without cues- test for something controlled by endogenous mechanism

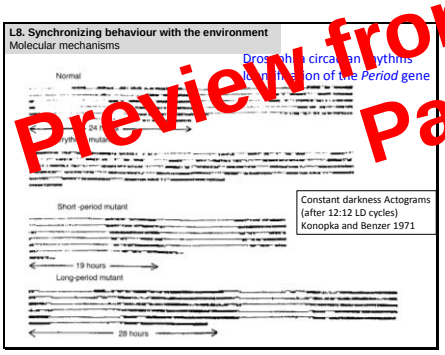
Slide 9



Each cell of tissues described/SCN has a rhythm. Trans feedback causes rhythm. Identified proteins involved by mutagenesis. Screen mutants and isolate those who didn't have rhythm and sequence them to find out which genes are responsible.

2 TF act as heterodimer (clock and Bmal1) interact with promoter regions of 2 proteins (Cry and Per) and induce their transcription- gives rise to proteins which associate with eachother, as dimers transport back to nucleus, bind to clock and bmal1 inhibiting them . Feedback inhibition of cry is relieved when per/cry is phosphorylated. This phosphorylation targets them for ubiquitination and degredation. This allows the cycle to start again, whole thing takes 24h.

Slide 10



First gene of the clock to be identified by Seymour Benzer in 1971. A defect in the human homologue of the period gene was identified as a cause of the sleep disorder FASPS (Familial advanced sleep phase syndrome)

When degraded can begin cycle of transcription/translation again.

How do we know? Mutagenesis screen. The mechanism is highly conserved
Took plant, opens/closes leaves in response to light. Put in complete permanent darkness and see still opening and closing and therefore circadian rhythm

activity levels = y axis, time=x axis Activity fly gives to infared beam (movement breaks beam and therefore recorded as activity).
Mutagenesis screen, look for mutant flys. Found one where had a rhythm but the period was only 19 hours