

So I now have an animation to give you a flavor for not only the emergence from the pupal case but actually the locomotor activities, which are also affected. So here's a fruit fly in a tube, and that fruit fly is jumping around and on the actogram here, very similar to the actograms that Joe showed, there's a morning peak of activity when the lights go on, and there's a much larger evening peak of activity when the lights go off. This constitutes the daily rhythms of the fruit fly in a light/dark cycle. Now if one assays the flies under constant conditions, constant darkness, very similar to the records that Joe showed for mice, the flies only have a very modest morning activity peak, but in the evening during the time the lights would have gone off, the flies have a very robust activity. And you'll notice that every day the activity record drifts slightly, with respect to the day before, so these flies have an intrinsic rhythm of about 24.5 hours, every day about a half hour longer. A per short fly, this variant here, which has a 19-hour rhythm, also has about one bout of activity per day, but notice that every day that activity bout is about 5 hours earlier. So that these flies manifest a 19-hour rhythm and are very different from what you see for the wild type. Yet these animals can entrain to the light dark cycle so that if one assays these mutant flies in the light dark cycle, now they show the same morning and evening peaks, but notice that the evening peak is advanced by about 3 or 4 hours with respect to the wild type light dark cycle. SO these flies entrain, they show 24 hour rhythms so the external environment is dominant but the evening activity peak is advanced.