In all, nearly 1200 Doppler measurements were made (*14*). The spectrum from β Hydri contains a concentration of power quite similar to that of the sun. Indeed, the overall shape of the power spectrum is in striking agreement with what one would expect by appropriately scaling the solar spectrum (see the figure), and the value of the total power is more or less consistent too. The deviations from theoretical expectation will help us to improve our understanding of the interaction between convection and pulsation.

It is difficult to associate individual peaks in the power spectrum with specific modes because the inevitable daytime gaps in data obtained from only a single observing site add extra periodicities to the signal, introducing many more peaks (called the window function) into the spectrum. Nevertheless, a value of a mean of the so-called large frequency separation Δ between adjacent mode frequencies ν of like degree l ($\nu_{n,l}$ and $\nu_{n-1,l}$) could be derived. The measured value for Δ (which is a measure of τ) is very close to that expected for β Hydri. Furthermore, the measured offset $\varepsilon = \nu_{0,0}/\Delta$, which is determined by the outermost layers of the convection zone, is similar to that of the sun. The mean value of the small frequency separation $\delta = \nu_{n,l} - \nu_{n-1,l+2}$, which measures the stratification of the core, indicates a well-evolved star, as β Hydri is believed to be.

Bedding *et al.* (*2*) report that complementary, albeit poorer data were obtained essentially at the same time from the smaller Leonard Euler Swiss telescope at La Silla in Chile, some 140° east of the Anglo-Australian Telescope. If all the data can successfully be combined, a nearly continuous data set will be achieved; the window function and consequently the mode identification will thereby be improved. But already, these observations point the way toward a future when a coordinated network of observatories around the world, such as the Whole Earth Telescope (*15*), will enable continuous Doppler observations of sunlike oscillations of a variety of stars in different phases of their evolution. Then asteroseismology will truly be under way.

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8. Here I ignore degeneracy splitting. There are about 18 observable multiplet frequencies associated with each (low) value of l. They are labeled by the order n of the mode, which in the sun satisfies $10 \le k \le 27$, where $k = n + 0.5l$. (The modes "observed" in β Hydri satisfy $12 \le k \le 20$.) Modes with lower k are confined too deeply in the stellar interior for their surface manifestation to be detected against the stellar noise; modes with higher k approach and even penetrate the visible surface (photosphere) and are scattered so severely by the intense turbulence in the surface layers that their frequencies are too ill determined to be of immediate use for diagnosing the stellar interior.
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18. In the theoretical spectrum, the amplitude of the artificial signal has been reduced by a factor of 1.9, which represents a discrepancy between theory and observation. Most of that discrepancy was overlooked by Bedding *et al.* (*2*), who compared solar mean amplitudes (having frequencies near the peak of mean power) with the greatest of the amplitudes of the β Hydri modes.
19. Homology arguments suggest that the frequency dependence of the amplitude spectrum of acoustic modes of sunlike stars scales as the acoustic cutoff frequency $\nu_c \propto ML^{-1}T_e^{3.5}$ in the atmosphere of the star, where M is the mass, L is the luminosity, and T_e is the (effective) surface temperature of the star. Accordingly, artificial β Hydri data were constructed by first scaling the frequency of the Fourier transform of solar whole-disc Doppler data (*16*) to that expected of β Hydri and adjusting the amplitude according to the theory of Houdek *et al.* (*17*). The transform was then inverted to obtain a time series to which was added Gaussian-distributed random noise with variance, relative to the mean amplitude of the final signal, chosen (by iteration) to be equal to that estimated by Bedding *et al.* (*2*). The signal was then "observed" through the same temporal window as was β Hydri. The resulting power spectrum (*18*) is shown in yellow in the figure. The high power at very low frequencies in the β Hydri spectrum (blue) results from slow uncorrected instrumental drift, which was not incorporated into the scaled solar spectrum.

PERSPECTIVES: DEVELOPMENT

The Path to the Heart and the Road Not Taken

Eric N. Olson

Life is full of decisions. One of the earliest is that facing embryonic mesoderm, which must decide whether to become heart or blood. Three papers from the Lassar and Mercola groups published in a recent issue of *Genes & Development* show that this decision is influenced by opposing gradients of positive and negative signals that intersect to create a specific heart-forming zone in the embryo (*1–3*). The idea that overlapping gradients of signaling molecules can generate sharp boundaries of gene expression in the embryo is not new. What makes these papers interesting, however, is that they shed light on the signaling molecules responsible for the formation of heart and blood, the first specialized mesodermal tissues to develop in vertebrate embryos. They also suggest potential strategies for the eventual therapeutic manipulation of cardiac and blood cell fates.

The heart forms soon after gastrulation in a specific region of the anterior mesoderm adjacent to the endoderm; blood cells arise from the posterior mesoderm (*4*). Experiments with surgically manipulated embryos suggest that antagonistic signals control the decision of early mesodermal cells to become heart or blood (*5–7*). The heart does not form if anterior endoderm is extirpated from embryos, pointing to an instructive role for anterior endoderm in this process. Furthermore, when combined with posterior mesoderm in vitro, anterior but not posterior endoderm induces heart formation at the expense of blood development (*5*, *6*).

Several peptide growth factors mimic the heart-inducing activity of anterior endoderm. The most potent of these are bone morphogenetic proteins (BMPs) 2 and 4. Beads soaked in these BMPs, or fibroblasts engineered to express them, induce anterior mesodermal cells that would otherwise give rise to the head to adopt a cardiac cell fate (*7*). BMPs are expressed in the lateral endoderm along the entire anterior-posterior axis of the embryo, whereas heart induction is restricted to the anterior mesodermal region. This implies that additional factors, either positive or negative, cooperate with BMPs to activate the cardiac program in vivo.

The neural tube and adjacent notochord are especially potent sources of signals that repress cardiogenesis in neighboring mesoderm. Surgical removal of the anterior neural tube leads to heart formation in head mesenchyme, and co-

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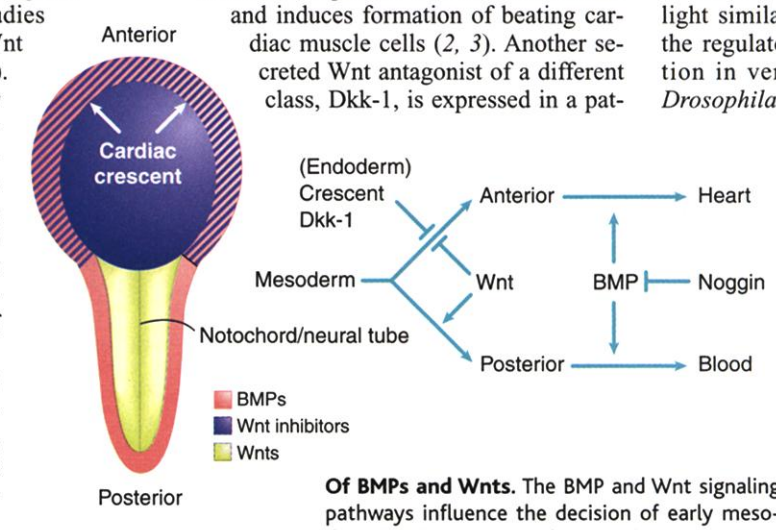
culture of neural tube and notochord with anterior mesodermal explants can override the heart-inducing activity of anterior endoderm (*1*).

What is the identity of the heart-inhibitory factors that emanate from the neural tube? And why are some cells more sensitive than others to cardiogenic signals? The three new studies implicate members of the Wnt family of morphogens (*1–3*). There are numerous *Wnt* genes in vertebrates, many of which are highly expressed in the neural tube [reviewed in (*8*)]. Among these, Wnt3a and Wnt8 blocked cardiogenesis when misexpressed in the anterior heart-forming regions of chick and frog embryos (*1, 3*). Under conditions where heart induction was prevented by these Wnts, primitive red blood cells were formed in the precardiac region (*3*).

Wnts bind to the Frizzled family of transmembrane cell surface receptors, activating an intracellular signal transduction cascade that represses glycogen synthase kinase–3 (GSK3) (*8*). In the absence of Wnt signaling, GSK3 is active and phosphorylates the cytoplasmic protein β-catenin, resulting in its degradation by ubiquitin-mediated proteolysis. Activation of Wnt signaling inhibits GSK3, thereby preventing phosphorylation of β-catenin, which is then able to move to the nucleus. Here, β-catenin associates with members of the LEF-1/TCF family of transcription factors, which activate the transcription of Wnt target genes. Consistent with the notion that Wnt signaling blocks cardiogenesis, Schneider and Mercola found that overexpression of GSK3 in posterior mesoderm, which would be expected to antagonize Wnt signaling, activates heart formation in inappropriate sites (*2*). However, because GSK3 has many targets, it may also induce cardiogenesis through other pathways. It will therefore be interesting to determine whether blocking of intracellular Wnt signals by other means, for example, by expression of inhibitory mutants of LEF-1, also induces cardiac gene expression.

The Wnt signaling pathway is also blocked by a family of secreted proteins that share homology with the extracellular ligand-binding domain of the Wnt receptor (*8*). One such antagonist, crescent, is expressed in the region of anterior endoderm permissive for heart formation, which suggests that it might interfere with Wnt signaling in this territory and thereby promote cardiogenesis (see the figure). This model is supported by the finding that overexpression of crescent in posterior mesoderm represses blood cell formation and induces formation of beating cardiac muscle cells (*2, 3*). Another secreted Wnt antagonist of a different class, Dkk-1, is expressed in a pattern overlapping that of crescent and is also sufficient for induction of heart formation in posterior mesoderm (*2, 3*). BMP signaling can also be blocked by the BMP antagonists noggin and chordin, which are secreted from the notochord and cooperate with Wnts to prevent cardiogenesis (*2*).



Of BMPs and Wnts. The BMP and Wnt signaling pathways influence the decision of early mesodermal cells in the vertebrate embryo to become heart or blood. BMP signaling plays a permissive role in heart and blood formation, which are localized to the anterior and posterior mesoderm, respectively. Wnt signaling promotes development of blood and inhibits cardiogenesis. The Wnt antagonists, crescent and Dkk-1, are expressed in the anterior endoderm and promote cardiogenesis by interfering with the Wnt signaling pathway. **(Inset)** Depicted are the expression patterns of signaling molecules that influence heart formation in the early embryo. Cardiogenesis is restricted to the anterior of the embryo where expression of BMPs and the Wnt inhibitor crescent overlap.

Obviously, it takes more than BMP and Wnt signals to determine whether an uncommitted mesodermal precursor cell will choose to become heart or blood. How do BMPs, Wnts, and other extracellular signals evoke such unique developmental choices? Presumably, the signal transduction pathways controlled by BMPs and Wnts regulate the expression of specific developmental control genes required for the formation of the heart and blood lineages. Deciding between heart and blood cell fates must depend on both the identity and environment of the precursor cell, because Wnt signaling in other cell types dictates, for example, the decision to become an adipocyte rather than a skeletal muscle cell (*9*). Why heart and blood represent opposing developmental choices, and whether this reflects the involvement of a common "downstream" factor that activates one pathway while inhibiting the other, remains to be determined. In this regard, it is interesting to note that members of the GATA family of zinc-finger transcription factors are key players in both cardiac and hematopoietic development.

The results of these studies also highlight similarities and differences between the regulatory strategies for heart formation in vertebrates and in the fruit fly *Drosophila*. In *Drosophila*, the BMP-like protein Decapentaplegic (Dpp) is expressed in ectodermal cells immediately adjacent to the heart-forming region in the dorsal mesoderm, and expansion of the Dpp-expressing region in transgenic embryos results in a corresponding expansion of the heart (*10*). Thus, the cardiac-inducing activity of the BMP signaling pathway appears to be evolutionarily conserved. However, in contrast to the inhibitory activity of Wnts in vertebrate cardiogenesis, Wnts are required for heart formation in *Drosophila* (*11*). This apparent reversal of the role of Wnts in cardiogenesis is likely to reflect independent changes in cardiogenic regulatory mechanisms during the evolution of vertebrates and flies from a common ancestor, as well as the inherent differences in organization of the body plans of these organisms.

Finally, the inability of adult cardiac muscle cells to divide poses major challenges to cardiovascular medicine. The potential to modulate the decision of a cell to become heart or blood could have implications for regeneration or repair of the adult myocardium by respecifying noncardiac cells to a cardiac cell fate. Thus, understanding how these two roads diverge ... could make all the difference.

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