changes in the strength or structure of the oceanic thermohaline circulation. Although there may be other interpretations of Gagan and colleagues' primary findings, the implications of their findings are quite wide reaching.

But does the coral Sr/Ca thermometer really work? The long ocean residence times of Sr and Ca would suggest that its Sr/Ca ratio should be relatively constant on 100,000-year time scales. If so, this proxy thermometer should not suffer from the same defect as the oxygen-isotope thermometer, namely ocean water variability. Some work (8) suggests, however, that this variability may be larger than supposed. There is also the issue of differing calibrations for the Sr/Ca thermometer among the various researchers in this fledgling field (8): these differences lead to discrepancies of up to 3°C. Some researchers have suggested that these discrepancies are associated with differences in the calcification rate (or growth rate) of the corals used in the different calibration studies. Alternatively, the calibration differences may be artifacts of local temperature variations, resulting from temperature differences between the site at which the coral used for calibration grew and the site at which the temperature records were taken from for calibration. Gagan *et al.* attempt to address these issues by deriving calibrations for *Porites lutea* corals from three widely separated sites where the corals grew in suboptimal environmental conditions. These corals were exposed to wide seasonal extremes in SST, salinity, coastal upwelling, and water column turbidity, but all yielded essentially the same calibration. In one of these studies, corals from the same locality but with a factor of 2 difference in annual growth rate were compared. Virtually no difference was found between these two corals for either the Sr/Ca or the $^{18}O/^{16}O$ thermometer calibrations.

Studies of this type certainly help to reassure us that these proxy thermometers (and salinometers) are working, although more careful studies of this type are necessary before the calibration issues can truly be put to rest. If thoroughly validated, this double-tracer technique promises to elucidate many important new clues about the dynamics of the coupled ocean-atmosphere-climate system for climate modelers to digest.

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UPDATE: MUSCLE CONTRACTION

Heartthrobs

Dottie Hanck

Each beat of the heart is triggered by an electrical stimulus that launches a cascade of events involving tens of proteins and free ions and ending in contraction of the heart muscle. We've come to understand most of the elements of this elegant cascade. In the heart, depolarization of the sarcolemma (the muscle cell membrane) opens voltage-dependent calcium channels; calcium ions enter the cytoplasm through these channels and bind to sites on release channels located close by in the membrane of the sarcoplasmic reticulum, a complex intracellular network of membranes. The calcium stored in the sarcoplasmic reticulum exits through the activated release channels into the cytoplasm, where it interacts with the actin-myosin machinery and initiates contraction.

In skeletal muscle, the cascade is the same except that the release channels are physically connected to the voltage-gated calcium channels. In this case, the voltage-dependent movement of the sarcolemmal calcium voltage-gated channels themselves, rather than the ions that enter through them, open the release channels. Two different muscles: same theme, minor variation. Puzzle solved—well, almost.

Santana *et al.* discuss a puzzling result noticed by several laboratories. In heart, under conditions of stress or excitement when β-adrenergic inputs are highly active, calcium can be released from the sarcoplasmic reticulum even after all known pathways for calcium to get through the sarcolemma are blocked. Maybe Mother Nature didn't really vary the theme after all; perhaps sometimes in heart voltage-gated calcium channels can directly couple to sarcoplasmic reticulum channels to release calcium. On page 1027 of this issue Santana and colleagues dash our hopes that this reasonable explanation is correct.

These authors used one of the cleanest pharmacological tools known—tetrodotoxin, a puffer fish toxin that blocks sodium channels with high specificity. Surprisingly, in the presence of tetrodotoxin the residual calcium release disappears; this result is not what's expected if voltage-gated calcium channels are directly coupled to release channels. None of the pathways by which calcium may be crossing the sarcolemma seem suitable to explain these data. So which protein is acting uncharacteristically?

Santana and colleagues accuse the voltage-gated sodium channel, even though there are no previous data to indicate that appreciable calcium can permeate these channels. This is not the only provocative proposal they make; they also suggest a new connection between sodium channels and drugs such as ouabain and digoxin, which inhibit the sodium/potassium ATPase and so indirectly augment cardiac contractility. The authors suggest that these two drugs can also augment flux of calcium through the sodium channel. This action may help these drugs regulate contraction under pathophysiological conditions like heart failure.

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