fat and starvation-resistant. Exciting times lie ahead for explorations of the metabolic and adaptive changes that occurred as different cavefish populations evolved, and such studies might uncover the underlying evolutionary forces responsible for this striking metabolic adaptation. ■

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CARDIOLOGY

The tornadoes of sudden cardiac arrest

A clever combination of techniques has enabled, for the first time, simultaneous visualization of the 3D waves of electrical and mechanical activity that are responsible for many cases of sudden cardiac death. SEE LETTER P.667

JOSÉ JALIFE

Sudden cardiac arrest is a common cause of death in people with coronary artery disease[1], and also kills many young people who have heritable heart diseases. In both cases, sudden death often occurs because of a heart-rhythm defect called ventricular fibrillation[2,3], in which the heart rate increases dramatically and cardiac-muscle contractions in the heart's ventricular chambers become uncoordinated, rendering the heart unable to pump blood. Blood pressure decreases, leading to unconsciousness, and death follows unless a defibrillating electrical shock is applied. The mechanism underlying this anomaly has been debated for more than a century. On page 667, Christoph *et al.*[4] show that the use of panoramic fluorescence imaging with a voltage-sensitive dye, combined with ultrasound imaging, could considerably advance our understanding of ventricular fibrillation. The study has potential implications for a broad range of researchers, from physicists to cardiologists.

Normal heart rhythm is maintained by cyclic changes in the electrical currents that drive and coordinate heart-muscle contraction. But during ventricular fibrillation, electrical impulses stop tracking their normal paths across the heart, and instead adopt a complex, vortex-like pattern similar to eddies in water or a tornado in the atmosphere. Fluorescence imaging of the voltage on the heart's surfaces has revealed[5] that these electrical vortices involve highly periodic, spiralling waves of activity organized around a central point called a rotor. The rotor, which is the organizing centre of fibrillation[6], spins rapidly and can meander across the heart's surface, generating turbulent, wave-like behaviour.

Until now, fluorescence imaging has allowed the visualization of rotors only on the surfaces of the heart's chambers, and so activity inside the ventricles has been inferred through computer simulations[7]. The 3D equivalent of 2D spiral waves (called scroll waves) and the filament-shaped rotors at their centres (vortex filaments) could only be reconstructed using simultaneous 2D video images of spiral waves on the outer and inner surfaces of the heart[8]. This is problematic, because it has not been possible to prove that the electromechanical changes that occur in the heart proper during ventricular fibrillation match predictions made by simulations. For example, cardiac defibrillation by an electrical shock is the only known treatment for ventricular fibrillation, but our understanding of how it works is currently based on numerical predictions.

Christoph *et al.* have overcome this hurdle, thanks to a clever combination of techniques. The authors kept isolated pig and rabbit hearts alive by perfusion with a warm solution through the coronary arteries. They induced ventricular fibrillation in the hearts, and used high-resolution 4D ultrasound imaging to document changing mechanical strain over time.

The group then combined these data with more-conventional 2D fluorescence imaging,

50 Years Ago

Throughout this week an unusual meeting has been taking place near Paris … experts from all over France — and some from other parts of the world — have been discussing what the world will be like in the year 2020. To keep the discussion within sensible limits, it has been set in a geographical context so that each day has been spent discussing the way in which different technological developments will affect the way land is used. It is clear that this meeting … is intended to be the first of a series which could, no doubt, last long enough for the results of this meeting to be compared with the reality of 2020.
From *Nature* 30 March 1968

100 Years Ago

Another Indian "miracle" has been explained by scientific investigation. The *Pioneer Mail* of January 11 reports a lecture by Sir J. C. Bose on "The Praying Palm Tree" of Faridpur. While the temple bells call the people to evening prayer, this tree has recently been seen to bow down in prostration, and to erect its head on the following morning. Large numbers of pilgrims have been attracted to the place, and offerings to the tree are said to have been the means of effecting marvellous cures. Sir J. C. Bose first procured photographs which proved the phenomenon to be real. The next step was to devise a special apparatus to record continuously the movement of the tree by day and night. The records showed that it fell with the rise of temperature and rose with the fall. The records obtained in the case of other trees brought out the fact that all the trees are moving, each movement being due to changes in their environment.
From *Nature* 28 March 1918

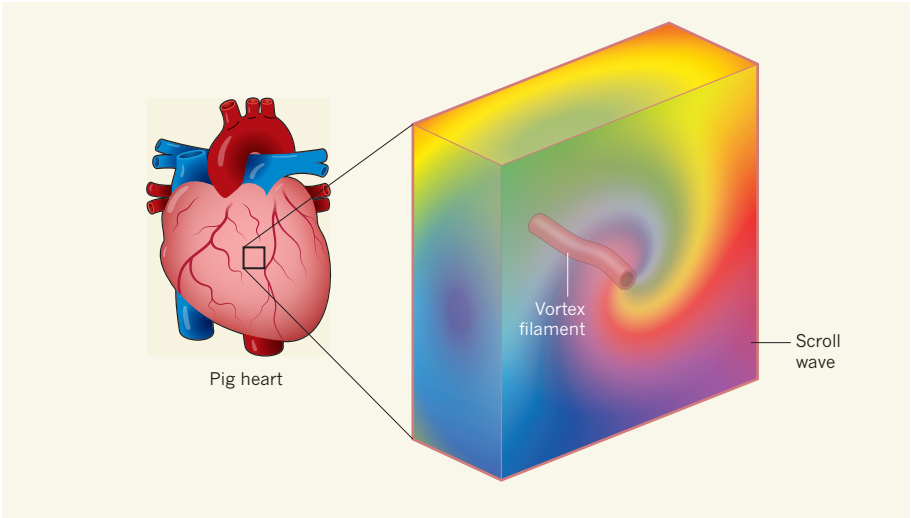

Figure 1 | Electromechanical vortices in a pig heart. In a deadly heart-rhythm defect called ventricular fibrillation, the electrical impulses that normally coordinate heartbeats become erratic. Christoph *et al.*[4] visualized these erratic electrical impulses, and the corresponding changes in mechanical strain, in 3D in isolated rabbit (not shown) and pig hearts. In line with previous predictions based on 2D data, the authors observed coexisting electrical and mechanical vortex filaments — areas of constant activity around which 3D 'scroll waves' of electromechanical activity swirl in rapid, highly periodic cycles (differences in activity indicated in different colours). The scroll wave shown here is a simplified schematic based on Figure 2 of the paper[4].

in which they took simultaneous measurements of three factors during each heartbeat: changes in electrical potential across cell membranes; changes in intracellular calcium-ion (Ca^{2+}) levels; and muscle contraction. The first two factors provide information about the molecular coupling between electrical and mechanical activity. Because this type of imaging can easily be distorted by spurious mechanical movements, Christoph *et al.* also took the crucial step of using computational motion-tracking techniques to correct any errors made during imaging. Together, these data enabled them to generate 3D maps of how mechanical and electrical waves propagate through the heart during ventricular fibrillation (Fig. 1).

Next, the authors generated computer simulations of electromechanical wave dynamics in virtual hearts that had realistic heart geometry based on computerized-tomography scans and information about muscle-fibre orientation, electrical impulses, electromechanical coupling and muscle contraction. From these simulations, they resolved more details of the dynamics of 3D scroll waves inside the contracting muscle. They found that coexisting electrical and mechanical vortex filaments occurred from the innermost to the outermost linings of the heart, and displayed complex patterns of intrinsically coupled electrical and mechanical waves that swirled at a high frequency through both ventricles.

Christoph and colleagues' findings are noteworthy because they confirm long-held predictions about the electromechanical behaviour of the heart during ventricular fibrillation. This first experimental observation of electrical and mechanical vortex filaments and their coupled dynamics also provides proof of a concept that began to emerge more than 60 years ago[9–14] — that 3D, vortex-like phenomena that occur in certain chemical reactions *in vitro* also cause fibrillation *in vivo*.

When this concept first began to emerge, it opened up a completely new field of cardiac electrophysiology[12–14], which is rapidly expanding today. Christoph and colleagues' study has the potential to contribute to this rapid advance. The tools that the authors used to identify mechanical vortex filaments are readily available in most cardiology units. They could theoretically be used to advance our understanding of cardiac defibrillation and possibly aid the development of pharmacological therapies for ventricular fibrillation. Before long, the authors' method might be used to monitor fibrillating human hearts from the body's surface, enabling investigation of the mechanisms underlying ventricular arrhythmias in patients who have structurally normal hearts — such as young people who have heritable heart diseases. However, more animal studies and further technical developments are likely to be needed to translate this strategy to people whose hearts have been scarred by a heart attack[1].

More work will also be required before the imaging technology can be applied to fibrillation in the heart's atrial chambers. Atrial fibrillation, like ventricular fibrillation, is maintained by high-frequency rotors, and it is the most common cardiac arrhythmia in humans. Unfortunately, currently available ultrasound probes lack sufficient temporal and spatial resolution to study atrial arrhythmias. Christoph and colleagues' study should stimulate further advancement of technologies that open the path towards the study and diagnosis of atrial fibrillation in patients.

Another caveat to clinical translation, acknowledged by Christoph and co-workers, is that the generation of mechanical waves requires transient release of Ca^{2+} from intracellular stores into the cell cytoplasm each time the cell receives electrical excitation. The amplitude of the Ca^{2+} transient, and of the mechanical contraction generated by it, depends on the rate of cell excitation. Ca^{2+} transients are readily observed at relatively low frequencies of excitation. But sometimes in ventricular fibrillation, the frequency is too high for Ca^{2+} release. In these cases, Ca^{2+} transients might disappear, or at least diminish substantially[15]. Consequently, mechanical waves might also diminish or disappear. This would result in dissociation between the electrical and mechanical waves, which, in turn, would impair the visualization of electromechanical wave dynamics inside the heart wall, because (except in very invasive experimental conditions) electrical waves can be visualized only from the surface.

Despite these limitations, imaging of electromechanical vortex filaments during cardiac fibrillation is an exciting technological accomplishment. Christoph *et al.* have observed, for the first time, complex interactions between electrical and mechanical rotors in 3D, and characterized their dynamics in detail. This important contribution is likely to lead to both scientific and therapeutic advances. ■

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