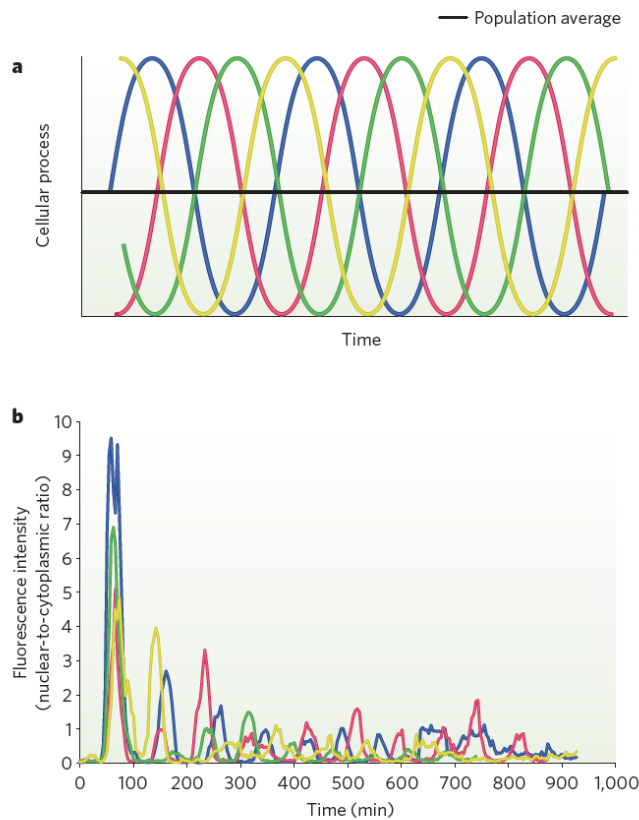


Box 2 | Oscillatory signal dynamics



Many cell-signalling and transcriptional processes show pulsatile, or even oscillatory, behaviour. If such processes occur out of phase in cells across a population, then techniques that measure biological parameters in the whole population of cells result in these dynamics being averaged out across the cell population and thus not being observable. This is illustrated in the schematic graph (a), which shows out-of-phase oscillations in a process occurring in single cells (each indicated by a different colour). Measuring this process in the cell population would result in a stable profile (black), the average across the cell population. Similar results are obtained from a real example (b). Translocation of NF- κ B from the cytoplasm to the nucleus, and back, was imaged in single neuroblastoma cells (of the SK-N-AS cell line) after stimulation with tumour-necrosis factor- α^3 (see also Fig. 2b and Supplementary Movie 2). Data for four cells are shown. After the first peak of fluorescence in the nucleus, the cells show out-of-phase oscillations. In recent years, numerous key signalling and cellular processes have been found to show such pulsatile or oscillatory dynamics. Examples of such systems are listed in the table.

Cellular signal	Period length	Reference example
Calcium	Seconds to minutes	15
ERK2	~15 min	101
Transcription cycles	Tens of minutes	9
NF- κ B	~100 min	5
Crz1 (similar to NFAT)	Random, pulses occur over minutes	25
Segmentation (Notch, WNTs, FGFs)	~90 min	116
STAT signalling	~2 h	102
p53	5–6 h	27
Cell cycle	~18 h	100, 119
Circadian rhythms	24 h	117, 118

ERK, extracellular signal-regulated kinase; FGF, fibroblast growth factor; NFAT, nuclear factor of activated T cells; STAT, signal transducer and activator of transcription.