schizophrenia

“ I seem to be thinking rationally again in the style that is characteristic of scientists. However, this is not entirely a matter of joy as if someone returned from physical disability to good physical health. “

— John Nash
activation of any particular assembly can be favored by ‘external’ as opposed to ‘local’ inputs

the strength of ‘local’ inputs may vary relative to ‘external’ inputs

if the strength of ‘local’ inputs is high, then the local connections will favor continued activation of the currently active assembly

if ‘local’ input strength is low, cell assemblies may be more likely to be activated by ‘external’ sources or, in the absence of strong ‘external’ inputs, there may be more spontaneous movement between assemblies
cell assemblies / attractors are, most simply put, combinations of neurons that are active together.

cell assembly activation may be triggered by ‘external’ inputs (including environmental stimuli)

any single neuron may participate in more than one pattern

the number of actual assemblies in a population of neurons is thought to be less than the total possible no. of combinations of active/inactive cells

any particular cell assembly may arise as a result of interconnectivity among its members

excitatory cells of the group of active cells may synapse upon each other, keeping each other depolarized / active

they may also keep inactive cells inactive indirectly by exciting inhibitory neurons

interconnections may keep particular assemblies active in the absence of the ‘external’ stimulus responsible for activating them (as in working memory)
according to Hebb, cell assemblies may also present as sequences of patterns that repeat.

In the figure above, each nexus point corresponds to a particular pattern of activity among a population of neurons.

Arrows denote movement between patterns and numbers indicate the ordering of movement between patterns (e.g., movement from the ‘west’ pattern to the center initiates the sequence and repeats on step 4).
schizophrenia –

a late onset disorder (manifesting during transition to adulthood and therefore coinciding with maturation of the prefrontal cortex)

symptoms include:
- disordered thought and/or speech
- flat affect
- catatonia
- paranoia
- hallucination

attention deficits include:
- sustained attention
- set-shifting
- working memory

clues to causes:
- increased numbers of D2 and D4 dopamine receptors
- antipsychotics are often dopamine receptor antagonists
- diminished numbers of ‘parvalbumin’ type GABA neurons
- alterations in beta/gamma-frequency LFP rhythms
- smoking/nicotine self-medication in schizophrenics
- ‘hypofrontality’ – decreased responsiveness of PFC
hallucinations, impairment in sustaining attention, poor working memory, poor intra-dimensional and extra-dimensional set-shifting
– might all these symptoms be related to instability in the activity patterns produced by prefrontal cortex?

above: schematic of an attractor network where each square corresponds to a specific activity pattern among a population of neurons – red dots denote ‘basins’ into which activity patterns are more likely to fall – moving out of such attractors demands a ‘push’ to get over the hills separating different attractors
1. Dopamine activation of D1 and D2 receptors produces opposite effects on the responses of PFC neurons to GABAergic inputs.

2. At any given time, D1 or D2 receptors may dominate the response to dopamine (factors include receptor affinity and amount of dopamine release). D1 domination will favor maintenance of current activity patterns while D2 domination favors instability.

3. In normals, the relative influence of D1/D2 receptors varies appropriately according to task demands.

   - Positive symptoms in schizophrenia result from heightened influence of D2 receptors which reduce the ‘energy’ barrier between attractor states.

   - Negative symptoms result from over-influence of D1 receptors yielding unchanging patterns.
1. Neurons that fire in synchrony with respect to gamma LFP rhythms (red-blue) form 'cell assemblies' or 'attractors'. Neurons whose activity patterns are not synchronized cannot interact with each other.

2. EEG recordings can assess the extent of gamma-synchronization in cortex resulting from presentation of 'Mooney' faces. Gamma power peaks ~200ms after presentation – the degree of the response peaks in adulthood.

3. Schizophrenic patients exhibit depressed responses to 'Mooney' faces. Moreover, the coherence of gamma-frequency activity among brain regions is weaker.

Decreased numbers of GABA neurons could potentially mediate these effects.

All figures from Uhlhaas and Singer, Nat. Rev. Neuro., 2010.