

So far, we have assumed the makespan as our cost metric

In an ER center, we are likely more interested in the waiting time

■ This can be defined simply as the sum of the start times of the initial tasks

$$w = \sum_{i=1}^{n} s_i^{first}$$

lacksquare Where s_i^{first} is the start time of the first task of patient i

Patients are color-coded: it makes sense to track different waiting times

- Ideally, we should also accord priority to the more severe cases
- ...But let's do one step at a time

We can build waiting time variables, similar to what we did for the makespan

```
def add waittime variables (mdl, levels, codes by idx, tasks, eoh):
    codes = ['red', 'yellow', 'green', 'white']
    fbc = {c: [] for c in codes}
    for idx in levels.keys():
        fbc[codes by idx[idx]].append(tasks[idx, 0, 0])
    obj by code = {}
    for code in codes:
        obj by code[code] = mdl.NewIntVar(0, len(codes by idx) *eoh, f'wt {code}')
        if len(fbc[code]) > 0:
            mdl.Add(obj by code[code] == sum(t.start for t in fbc[code]))
    obj by code['all'] = mdl.NewIntVar(0, len(codes by idx) * eoh, 'wt global')
    mdl.Add(obj by code['all'] == sum(obj by code[c] for c in codes))
    return obj by code
```

First, we collect the first task for each patient, by code:

```
def add_waittime_variables(mdl, levels, codes_by_idx, tasks, eoh):
    ...
    fbc = {c: [] for c in codes}
    for idx in levels.keys():
        fbc[codes_by_idx[idx]].append(tasks[idx, 0, 0])
    ...
```

Then, we build and constrain the waiting time variables

```
def add_waittime_variables(mdl, levels, codes_by_idx, tasks, eoh):
    ...
    obj_by_code = {}
    for code in codes:
        obj_by_code[code] = mdl.NewIntVar(0, len(codes_by_idx)*eoh, f'wt_{code}')
        if len(fbc[code]) > 0:
            mdl.Add(obj_by_code[code] == sum(t.start for t in fbc[code]))
    obj_by_code['all'] = mdl.NewIntVar(0, len(codes_by_idx) * eoh, f'wt_globai')
```

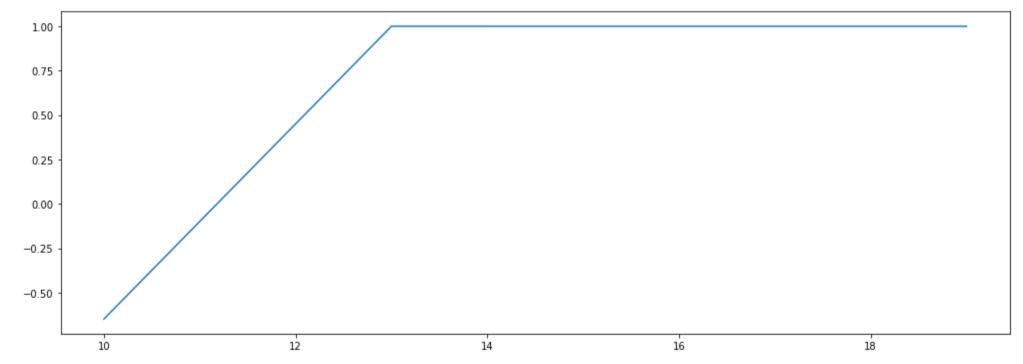
We can formulate an updated problem model:

```
In [2]: npatients = 5
        mdl = cp model.CpModel()
        levels, codes by idx = er.build levels(fdata.iloc[:npatients])
        eoh = er.get horizon(levels)
        rl, dl = {idx:0 for idx in levels}, {idx:eoh for idx in levels}
        tasks, last = er.add all vars(mdl, levels, rl, dl)
        er.add all precedences (mdl, levels, tasks)
        er.add cumulatives (mdl, tasks, capacities)
        er.add all no overlap(mdl, levels, tasks)
        obj by code = er.add waittime variables(mdl, levels, codes by idx, tasks, eoh)
        mdl.Minimize(obj by code['all'])
        slv = cp model.CpSolver()
        slv.parameters.max time in seconds = 10
        status = slv.Solve(mdl)
        er.print outcome(slv, levels, tasks, codes by idx, status)
        Solver status: optimal, time(CPU sec): 0.01, objective: 2.0
        0 \text{ (green)}: visit(0-1), RX(1-3), visit(3-4)
        1 (green) : visit(0-1), lab(1-5), visit(5-6)
        2 (white): visit(0-1), otolaryngological visit(1-5), visit(5-6)
        6 (green) : visit(1-2), ultrasound(2-4), RX(4-6), lab(6-10), CT scan(10-14), visit(14-15), CT sc
        an (15-19), visit (19-20)
        7 (green) : visit (1-2)
```

We will now try to compare the complexity with that of the previous one

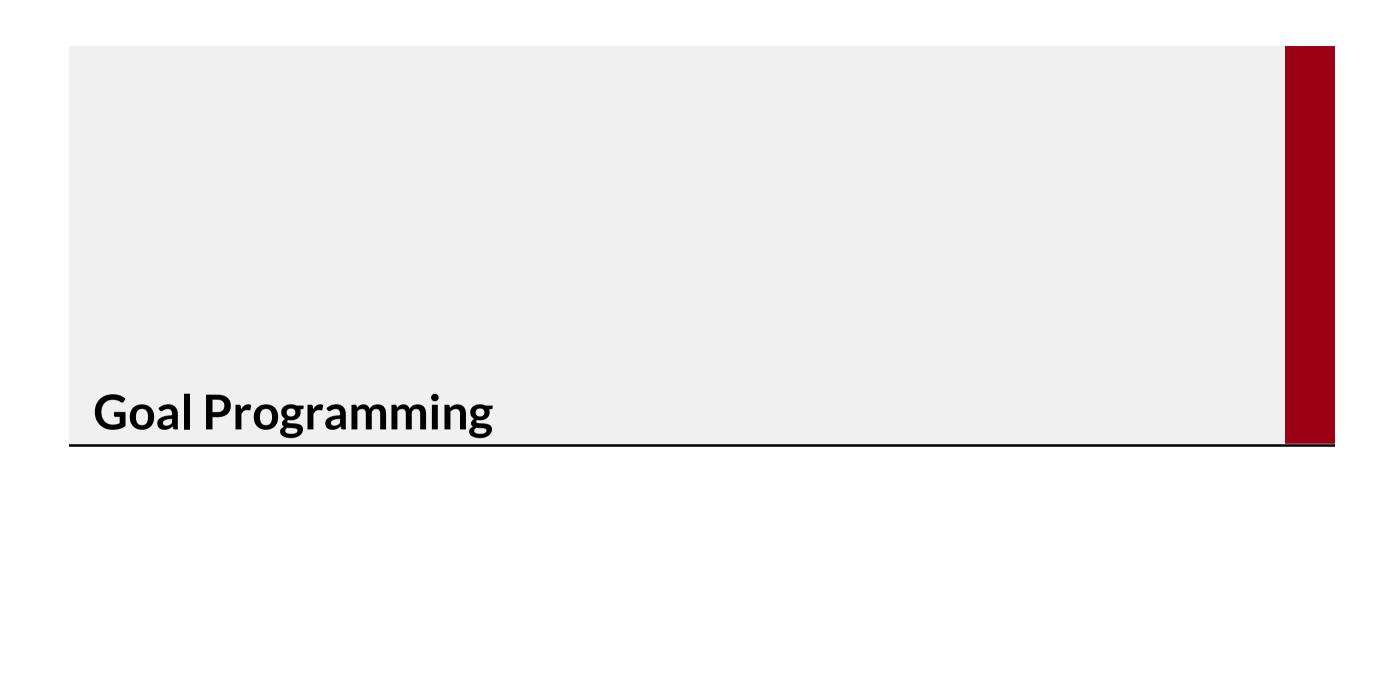
```
In [5]: def solve basic waittime problem (npatients, capacities):
            mdl = cp model.CpModel()
            levels, codes by idx = er.build levels(fdata.iloc[:npatients])
            eoh = er.get horizon(levels)
            rl, dl = {idx:0 for idx in levels}, {idx:eoh for idx in levels}
            tasks, last = er.add all vars(mdl, levels, rl, dl)
            er.add all precedences (mdl, levels, tasks)
            er.add cumulatives (mdl, tasks, capacities)
            er.add all no overlap(mdl, levels, tasks)
            obj by code = er.add waittime variables(mdl, levels, codes by idx, tasks, eoh)
            mdl.Minimize(obj by code['all'])
            slv = cp model.CpSolver()
            slv.parameters.max time in seconds = 10 # time limit
            status = slv.Solve(mdl)
            return status, slv.UserTime()
```

```
In [12]: tlist, plist = [], range(10, 20, 3)
    for npt in plist:
        s, t = solve_basic_waittime_problem(npt, capacities)
        tlist.append(t)
    er.plot_scalability_evalulation(plist, np.log10(tlist), figsize=figsize)
```



```
In [12]: tlist, plist = [], range(10, 20, 3)
          for npt in plist:
              s, t = solve basic waittime problem(npt, capacities)
              tlist.append(t)
          er.plot scalability evalulation(plist, np.log10(tlist), figsize=figsize)
            1.00
            0.75
            0.50
            0.25
            0.00
           -0.25
           -0.50
                                    12
                                                                        16
                  10
                                                      14
                                                                                          18
```

Sum-based objectives are much harder in CP and max-based objectives



Goal Programming

Any practical application of our method faces two big issues

First, we have limited scalability

- The problem is computationally challenging
- Note that we may still be getting good solutions quite early
- ...But we need to compare multiple solution approaches to know that
 Second, we need to handle patient priorities
- We need to make sure that (e.g.) red-coded patients are handled first
- ...Then yellow, green, and finally white patients

We can actually address both with a single technique!

(At least to some degree)

Goal Programming

Goal Programming is a strategy for handling lexicographic costs

- Let's consider a problem with multiple cost functions $f_0(x)$, $f_1(x)$, ...
- Let f_i be strictly more important than f_j iff i < j

Then Goal Programming refers to this simple algorithm:

- lacksquare Optimize $f_0(x)$ to obtain its optimal value z_0^*
- Post a new constraint in the model in the form $f_0(x) \leq z_0^*$
- Move to the next cost function and repeat

The approach is very simple, but it works well in practice

A typical example: the Capacitated Vehicle Routing Problem

- Thanks to GP, we get an upped bound on each cost at each step
- ...Which may provide a computational advantage

Implementing Goal Programming

As a first step, we need to handle upper bounds on the waiting times

```
def solve_bounded_waittime problem(levels, codes by idx, codes, capacities,
        ub by code={}, tlim=None):
    mdl = cp model.CpModel()
    eoh = get horizon(levels)
    rl, dl = {idx:0 for idx in levels}, {idx:eoh for idx in levels}
    tasks, last = add all vars(mdl, levels, rl, dl)
    add all precedences(mdl, levels, tasks)
    add cumulatives (mdl, tasks, {'visit': 3, 'ultrasound': 2, 'RX': 2})
    add all no overlap(mdl, levels, tasks)
    obj by code = add waittime variables (mdl, levels, codes by idx, tasks, eoh)
    for code in ub by code: # <-- Enforce upper bounds
        mdl.Add(obj by code[code] <= ub by code[code])
    mdl.Minimize(obj by code[codes[-1]]) # <-- Focus by default on the last code
    slv = cp model.CpSolver()
    if tlim is not None: slv.parameters.max time in seconds = tlim
```

Implementing Goal Programming

Then we need to code the approach in a function

```
def goal programming(levels, codes by idx, codes, capacities, tlim=None, verbose=1):
    wt by code, ttime = \{\}, 0
    for i, code in enumerate(codes):
        1 tlim = None if tlim is None else (tlim-ttime) / (len(codes)-i)
        status, slv, tasks = solve bounded waittime problem(levels, codes by idx,
                          codes[:i+1], capacities, ub by code=wt by code, tlim=l tlim)
        ttime += slv.UserTime()
        if verbose:
            print outcome(slv, levels, tasks, codes by idx, status, (i == len(codes)-1))
        if status in (cp model.OPTIMAL, cp model.FEASIBLE):
            wt by code[code] = int(slv.ObjectiveValue())
            starts = {tidx:slv.Value(tasks[tidx].start) for tidx in tasks}
        else:
            wt by code, starts = None, None
            break
    if wt by code is not None:
```

Implementing Goal Programming

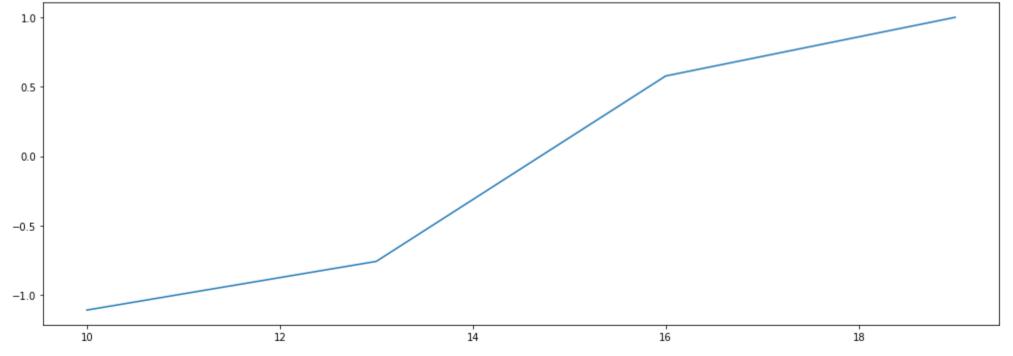
Finally, we can test the approach

We choose a priority for our codes, then we call the goal_programming function

```
In [8]: codes = ['red', 'yellow', 'green', 'white']
        npatients = 10
        levels, codes by idx = er.build levels(fdata.iloc[:npatients])
        _, _, _ = er.goal_programming(levels, codes_by_idx, codes, capacities, tlim=10)
        Solver status: optimal, time(CPU sec): 0.01, objective: 0.0
        Solver status: optimal, time(CPU sec): 0.01, objective: 0.0
        Solver status: optimal, time(CPU sec): 0.02, objective: 9.0
        Solver status: optimal, time(CPU sec): 0.04, objective: 3.0
        0 \text{ (green)}: visit(0-1), RX(1-3), visit(3-4)
        9(qreen): visit(0-1)
        12 (red): visit(0-1), RX(3-5), visit(5-6)
        6 \text{ (green)}: visit(1-2), ultrasound(2-4), RX(4-6), lab(6-10), CT scan(10-14), visit(14-15), CT sc
        an (15-19), visit (19-20)
        7 \text{ (green)}: \text{ visit } (1-2)
        8 \text{ (green)}: \text{visit}(1-2), \text{RX}(2-4), \text{prescription}(4-8), \text{visit}(8-9)
        1(green): visit(2-3), lab(3-7), visit(7-8)
        10 (green): visit(2-3), lab(3-7), CT scan(7-11), visit(11-12)
        11 (green): visit(2-3), visit(13-14)
        2 (white): visit(3-4), otolaryngological visit(4-8), visit(8-9)
```

We can now evaluate the scalability of the approach

```
In [13]: tlist, olist, plist = [], [], range(10, 20, 3)
    for npt in plist:
        levels, codes_by_idx = er.build_levels(fdata.iloc[:npt])
        t, o, _ = er.goal_programming(levels, codes_by_idx, codes, capacities, tlim=10, verbose=0)
        tlist.append(t)
        olist.append(o['all'])
        er.plot_scalability_evalulation(plist, np.log10(tlist), figsize=figsize)
```



Warm Starting

A drawback of GP is that search restarts from scratch at each iteration

- This can be mitigated by warm starting the solver
- In Google ortools, this is done via so-called "hints"

```
def goal programming (levels, codes by idx, codes, capacities,
        tlim=None, verbose=1, hints=None):
        status, slv, tasks = solve bounded waittime problem(levels, codes by idx,
                codes[:i+1], capacities, ub by code=wt by code,
                tlim=1 tlim, hints=hints) # <-- here we pass hints
        . . .
        if status in (cp model.OPTIMAL, cp model.FEASIBLE):
            . . .
            starts = {tidx:slv.Value(tasks[tidx].start) for tidx in tasks}
            hints = starts # <-- hints are the start in the last solution
        • • •
```

Warm Starting

And finally we need to take into account the hints in the model:

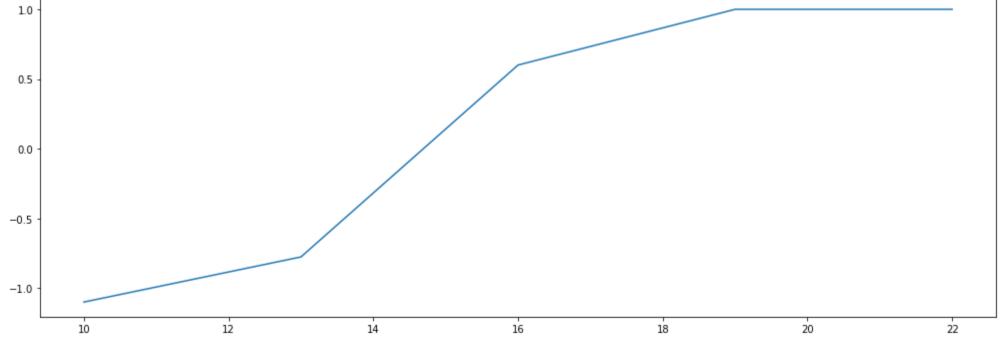
- The solver will try to assign to each value the corresponding hint
- In case this proves impossible, it will search as usual
- If properly done, this guarantees that we start from a known feasible solution

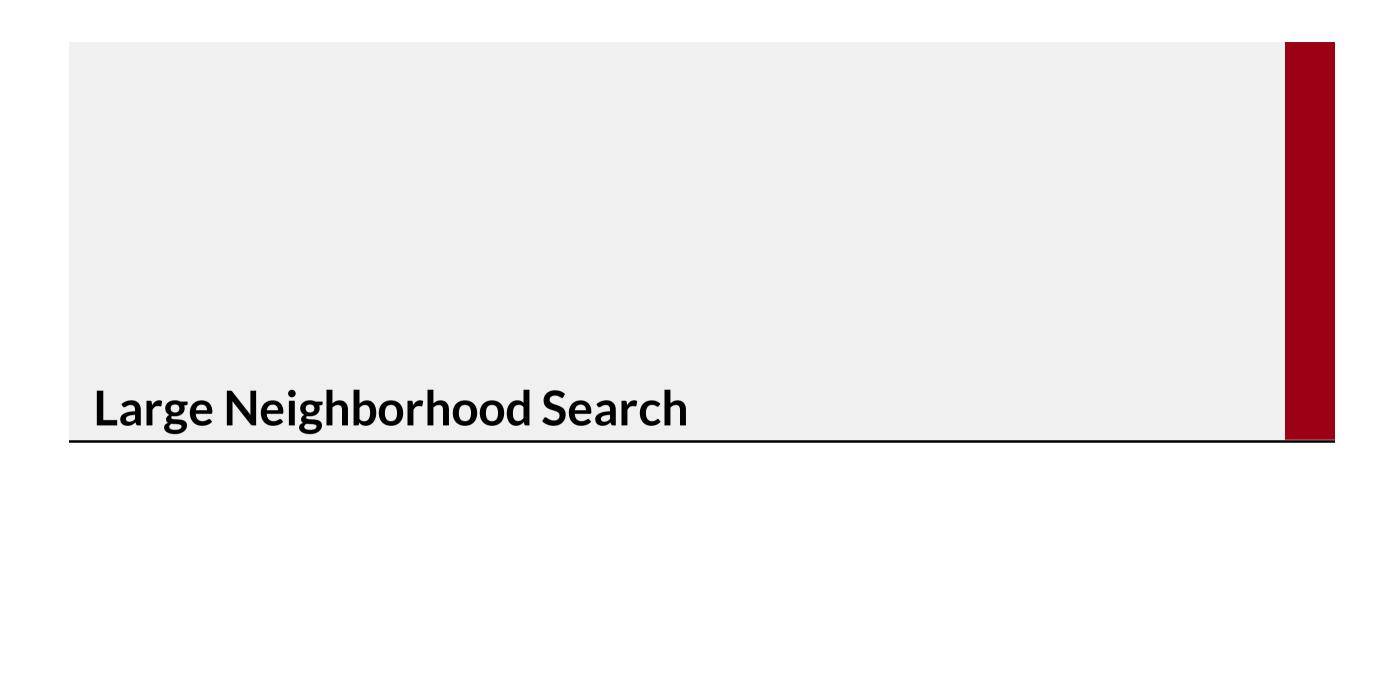
This is usually referred to as warm starting in the optimization field

Warm Starting

Let's test this updated implementation

```
In [14]: tlist2, plist2 = [], range(10, 23, 3)
    for npt in plist2:
        levels, codes_by_idx = er.build_levels(fdata.iloc[:npt])
        t, _, _ = er.goal_programming(levels, codes_by_idx, codes, capacities, tlim=10, verbose=0)
        tlist2.append(t)
    er.plot_scalability_evalulation(plist2, np.log10(tlist2), figsize=figsize)
```





Large Neighborhood Search

Exact optimization approaches (e.g. classical CP/SMT)...

- ...Enable convenient modeling and are very effective on small problems
- ...But have trouble dealing with large-scale optimization problems

Heuristic approaches (e.g. local search)...

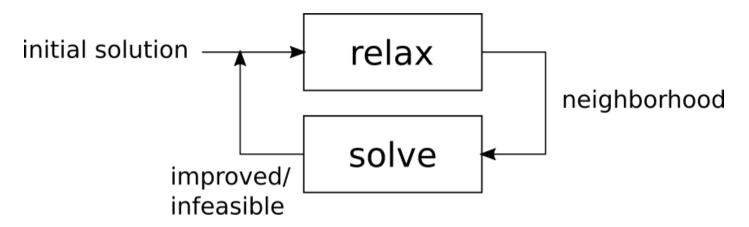
- ...Can deal with large scale problems
- ...But have trouble escaping local minima

The two approaches can be combined to obtain Large Neighborhood Search

- We operate by trying to improve an incumbent solution
- Improving solutions are searched in a large neighborhood
- Each neighborhood is explored via a complete search on a restricted problem
- ...Typically: we fix all variables, except a small subset (relaxed variables)

Large Neighborhood Search

Here's a visual scheme of how the approach works



LNS combines the strengths of its component approaches

- It can efficiently handle large-scale problems (like local search)
- It can escape local minima thanks to the use of large neighborhoods
- It retains the modeling flexibility of CP, SMT, MILP, etc.

Choosing which variables to relax at each iteration...

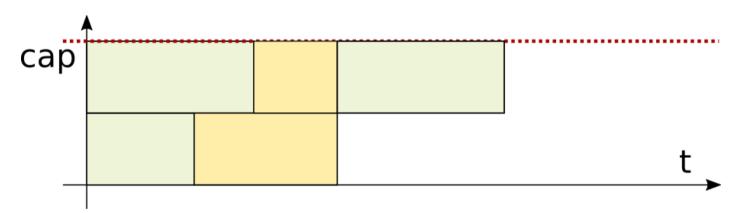
- ...Can be a major design decision, and can be done using domain knowledge
- ...But actually even a simple random selection often works very well

Variable Fixing in Scheduling

LNS can be very effective on scheduling problems...

- ...But it is not straightforward to implement
- ...Since the classical "variable" fixing approach provides too little flexibility

Consider the following schedule for a resouce with capacity 2:



- Say the we choose to relax the green tasks, and keep the yellow ones fixed
- ...Then we still cannot make any improvement!

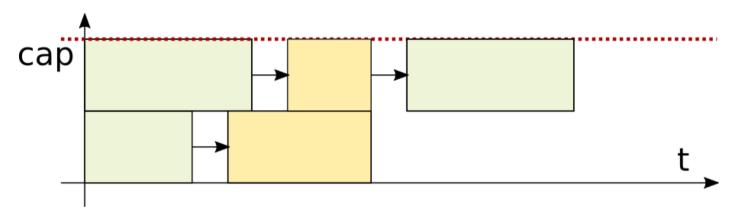
We need to retain some ability to shift tasks in time

- But we still need to keep them somewhat "fixed"
- ...Or there is no point in defining a neighborhood

Partial Order Schedule

The solution is converting a fixed-start schedule into a Partial Order Schedule

A Partial Order Schedule is an augmented task graph



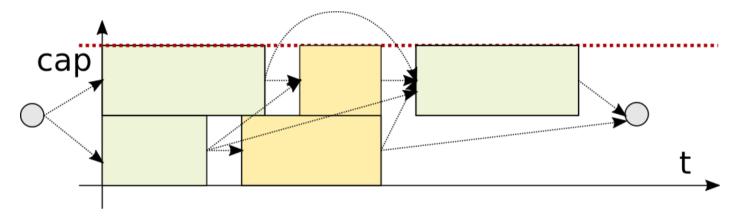
- The graph contains all the original precedence relations (in this case none)
- ...Plus additional precedences, introduced to prevent resource conflicts

In the figure:

- As long as the black arcs (precedences) are respected
- ...Tasks can be moved without any resource conflict

Partial Order Scheduling

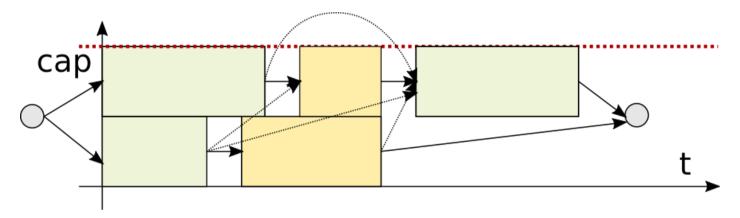
A POS can be obtained by solving a minimum flow problem



- First, we introduce a fake "source" and "sink" task
- lacksquare Then, we build an arc for each pair of tasks such that $e_i \leq s_j$
 - The source can be connected only to the first tasks
 - ...And the sink has an incoming arc for each last task
- Then we say each task "requires" flow equal to its resource demand
 - In this example, all requirements are 1

Partial Order Scheduling

A POS can be obtained by solving a minimum flow problem



- Finally, we route the minimum amount of flow that satisfies the requirements
 - ...For example using some variant of the Ford-Fulkerson's method
 - We will not look into details into this
- The arcs with non-zero flow become part of the POS
 - In the figure, these are the arcs in black
 - You can check that the flow is actually minimum

Since we have only unary demands, our implementation can be simpler

First, let's prepare a function to collect and sort the tasks for each resource:

```
def sol to pos(levels, starts, capacities):
    aplus, aminus = \{\}, \{\}
    stasks = {r:[] for r in capacities}
    for idx, k, i in starts:
        ttype = levels[idx][k][i]
        if ttype in capacities:
            stasks[ttype].append((idx, k, i))
            aplus[idx, k, i], aminus[idx, k, i] = [], []
    for res in capacities:
        stasks[res] = sorted(stasks[res], key=lambda t: starts[t]) # <-- sort by start
    for res, cap in capacities.items():
        for in range(cap):
            stasks[res] = unit flow(levels, stasks[res], starts, aplus, aminus)
    return aplus, aminus
```

We store the POS as a collection of outgoing and ingoing arcs

This is called a forward and backward star representation:

```
def sol_to_pos(levels, starts, capacities):
    aplus, aminus = {}, {}
    ...
    for idx, k, i in starts:
        ...
        if ttype in capacities:
            ...
            aplus[idx, k, i], aminus[idx, k, i] = [], []
    ...
    return aplus, aminus
```

- The chosen representation allows for efficient graph traversal
- It also makes it easy to detect arcs implied via the transitive property

Then, we collect the tasks for each resource:

■ We sort each collection by increasing start time

Finally, we route single units of flows

```
def sol_to_pos(levels, starts, capacities):
    ...
    for res, cap in capacities.items():
        for _ in range(cap):
            stasks[res] = unit_flow(levels, stasks[res], starts, aplus, aminus)
    return aplus, aminus
```

- Each unit corresponds to one unit of resource capacity
- The flow represents how the resource is "passed" form one task to the next
- We do not build explicitly the possible arcs: they are implied by the start times

Here is the algorithm for routing each flow unit

```
def unit flow(levels, stasks, starts, aplus, aminus):
    nonprocessed = []
    src, dur = None, 0
    for dst in stasks:
        if src is not None and starts[src] + dur <= starts[dst]:</pre>
            aplus[src].append(dst) # Build an arc (forward star)
            aminus[dst].append(src) # Build an arc (backward star)
            src = None # Reset the source
        if src is None:
            src = dst # Set a new source
            dur = get dur(levels[src[0]][src[1]][src[2]])
        else:
            nonprocessed.append(dst) # Store as non-processed
    return nonprocessed
```

Let's test the function

```
In [15]: codes = ['red', 'yellow', 'green', 'white']
         npatients = 3
         levels, codes by idx = er.build levels(fdata.iloc[:npatients])
         _, _, starts = er.goal_programming(levels, codes_by_idx, codes, capacities, tlim=10)
         aplus, aminus = er.sol to pos(levels, starts, capacities)
         aplus
         Solver status: optimal, time(CPU sec): 0.00, objective: 0.0
         Solver status: optimal, time(CPU sec): 0.00, objective: 0.0
         Solver status: optimal, time(CPU sec): 0.00, objective: 0.0
         Solver status: optimal, time(CPU sec): 0.01, objective: 0.0
         0 \text{ (green)}: visit(0-1), RX(1-3), visit(3-4)
         1 (green) : visit(0-1), lab(1-5), visit(5-6)
         2 (white): visit(0-1), otolaryngological visit(1-5), visit(5-6)
Out[15]: {(0, 0, 0): [(0, 2, 0)],
          (0, 1, 0): [],
          (0, 2, 0): [(1, 2, 0)],
          (1, 0, 0): [(2, 2, 0)],
          (1, 2, 0): [],
          (2, 0, 0): [],
          (2, 2, 0): []}
```

POS Relaxation

A POS corresponds to a set of feasible schedules

- Tasks can be freely shifted, and no resource constraints is be violated
- There are no longer ordering decisions to be made
- Typically, choosing one of the possible schedules becomes a poly-time problem However, this means that we cannot really make significant changes

For using a POS in LNS, we need to relax it

Typically:

- We choose a set of tasks to relax
- ...And we disconnect them from the precedence network
 - First, we connect all task predecessors to the task successors
 - Then, we remove all the additional POS arcs linked to the relaxed tasks

POS Relaxation - Implementation

Here's an implemented algorithm for removing/relaxing POS tasks

```
def remove task from pos(aplus, aminus, task key):
    # Transfer transitive arcs
    for src in aminus[task key]:
        for dst in aplus[task key]:
            aminus[dst].append(src)
            aplus[src].append(dst)
    # Remove ingoing arcs
    for src in aminus[task key]:
        aplus[src].remove(task key)
    # Remove outgoing arcs
    for dst in aplus[task key]:
        aminus[dst].remove(task key)
    # Remove the node from the arc
    del aplus[task key]
    del aminus[task key]
```

POS Relaxation - Implementation

In our LNS approach we will relax all tasks related to selected patients

```
def remove_patient_from_pos(aplus, aminus, target_idx):
    aplus_res = copy.deepcopy(aplus)
    aminus_res = copy.deepcopy(aminus)
    for idx, k, i in aplus:
        if idx == target_idx:
            remove_task_from_pos(aplus_res, aminus_res, (idx, k, i))
    return aplus_res, aminus_res
```

Restricted Problem

We now need to take int account the additional precedences in the model

Even if we still need to assing all the start times...

- Precedence constraints are efficient to propagate
- They are effective at narrowing the variable domains
- ...And in this case they prevent many resource conflicts

If many POS constraints are added, the problem is much easier to solve

LNS - Initial Solution

We are ready to define our LNS approach

First, we need an initial solution:

```
In [17]: init_time = 5 # Time limit for the initial solution
    codes = ['red', 'yellow', 'green', 'white']
    npatients = 100

levels, codes_by_idx = er.build_levels(fdata.iloc[:npatients])

ttime, wt_by_code, starts = er.goal_programming(levels, codes_by_idx, codes, capacities=capacities=init_time, verbose=0)
    print(f'Initial solution in {ttime:.2f} sec, {wt_by_code}')

Initial solution in 5.01 sec, {'red': 5, 'yellow': 577, 'green': 1209, 'white': 10, 'all': 180
1}
```

- We can obtain this one as usual
- It's better if it's of decent quality
- ...But we don't want to spend more than a few seconds on this

LNS - Baseline

As a baseline, let's see the solution quality we can obtain in 30 seconds

```
In [22]: init_time = 30 # Time limit for the initial solution
    codes = ['red', 'yellow', 'green', 'white']
    npatients = 100

levels, codes_by_idx = er.build_levels(fdata.iloc[:npatients])

ttime, wt_by_code, starts = er.goal_programming(levels, codes_by_idx, codes, capacities=capacities=init_time, verbose=0)
    print(f'Initial solution in {ttime:.2f} sec, {wt_by_code}')

Initial solution in 30.02 sec, {'red': 5, 'yellow': 307, 'green': 1343, 'white': 22, 'all': 16
77}
```

LNS - Upper bounds

In LNS we will repeatedly be seeking for an improving solution

...So we need to modify our G.P. loop to take upper bounds into account:

- The bounds are then passed to the function that builds and solves the model
- ...Which was already designed to deal with the bounds from Goal Programming

LNS - Main Loop

Here is the main structure of our LNS implementation:

```
def scheduling lns (levels, codes by idx, codes, capacities,
        tlim, init time, it time, nb size, verbose=1):
    ... # Build initial solution
    while tlim - ttime > 0:
        aplus, aminus = sol to pos(levels, starts, capacities) # Obtain a POS
        relaxed = np.random.choice(patients, nb size, replace=False) # Relax patients
        for idx in relaxed: aplus, aminus = remove patient from pos(aplus, aminus, idx)
        ub by code = copy.deepcopy(wt by code) # Require an improvement
        ub by code['all'] -= 1
        ... # Re-solve
        ttime += max(itime, 0.1) # Update the time limit
        ... # Update the best solution
```

The full implementation can be found in our support module

Time to test! Waiting times are sorted by code, the last is the total

```
In [23]: # Configuration
         tlim = 30
         init time, it time, nb size = 3, 1, 4
         codes = ['red', 'yellow', 'green', 'white']
         npatients = 100
         levels, codes by idx = er.build levels(fdata.iloc[:npatients])
         er.scheduling lns(levels, codes by idx, codes, capacities, tlim, init time, it time, nb size);
         Initial solution in 2.90 sec, {'red': 5, 'yellow': 649, 'green': 1386, 'white': 10, 'all': 205
         0 }
         Total time: 3.67, neighborhood explored in 0.77 sec, waiting times 5,630,1364,10,2009
         Total time: 4.45, neighborhood explored in 0.78 sec, waiting times 5,625,1364,10,2004
         Total time: 5.20, neighborhood explored in 0.75 sec, waiting times 5,622,1364,10,2001
         Total time: 5.98, neighborhood explored in 0.78 sec, waiting times 5,613,1361,10,1989
         Total time: 6.63, neighborhood explored in 0.65 sec, waiting times 5,605,1359,10,1979
         Total time: 7.28, neighborhood explored in 0.66 sec, waiting times 5,590,1338,10,1943
         Total time: 8.04, neighborhood explored in 0.76 sec, waiting times 5,583,1333,10,1931
         Total time: 8.82, neighborhood explored in 0.77 sec, waiting times 5,567,1330,10,1912
         Total time: 9.60, neighborhood explored in 0.78 sec, waiting times 5,557,1330,10,1902
         Total time: 10.25, neighborhood explored in 0.65 sec, waiting times 5,549,1328,10,1892
         Total time: 11.03, neighborhood explored in 0.78 sec, waiting times 5,529,1324,10,1868
         Total time: 11.66, neighborhood explored in 0.62 sec, waiting times 5,508,1322,10,1845
         Total time: 12.14, neighborhood explored in 0.48 sec, waiting times 5,497,1315,10,1827
         Total time: 12.92, neighborhood explored in 0.78 sec, waiting times 5,487,1305,10,1807
         Total time: 13.68, neighborhood explored in 0.76 sec, waiting times 5,482,1305,10,1802
```

Considerations

LNS is the industrial optimizer's secret weapon

- It's flexible, robust, scalable, and not too difficult to implement
 - Except for scheduling problems, but you've now seen how to do it ;-)
- It's usually possible to do better than LNS, but it's also considerably harder

Goal programming is not only about lexicographic costs

- It's about simplifying a problem via constraints
- E.g. constraints may actually help in CP
- Sometimes special optimization are possible:
 - Include only some of the variables (e.g. red-codes only)
 - Simplified problem formulation (e.g. fixed number of vehicles)

Do not underestimate warm starts

- Without our little trick at the beginning
- ...The search for an initial solution with 100 patients would fail!